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14 a 17 de Setembro de 2024
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Title	Nascemos hipertensos ou desenvolvemos hipertensão arterial?
Author	Adriana Castello Costa Girardi
Affiliations	Cardiopneumologia- Universidade de São Paulo
Contact	accgirardi@gmail.com
Abstract	A questão de se nascemos hipertensos ou desenvolvemos hipertensão ao longo da vida envolve a compreensão de fatores genéticos e ambientais, bem como da interação entre eles. Nesta palestra, com foco principal no papel dos rins no desenvolvimento e progressão da hipertensão arterial, discutirei os tipos de hipertensão monogênica, que envolvem mutações em transportadores de sódio expressos no túbulo renal, bem como em componentes neurohumorais que regulam o transporte de sódio ao longo do néfron. Adicionalmente, abordarei algumas variantes genéticas frequentes na população associadas ao aumento da pressão arterial e o conceito de herdabilidade perdida. Em relação aos fatores modificáveis, discutirei a importância do conteúdo de sódio e potássio na dieta. Para embasar a discussão, utilizarei artigos científicos da área básica e clínica, proporcionando uma visão abrangente e fundamentada sobre o tema.



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14 a 17 de Setembro de 2024
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Title	Morphological Features of Human Dendritic Spines
Author	Alberto Antonio Rasia Filho
Affiliations	Depto. Ciências Básicas da Saúde/Fisiologia- UFCSPA/UFRGS
Contact	rasiafilho@yahoo.com
Abstract	Dendritic spines are evolved cellular specializations that greatly increase the connectivity of neurons and modulate the “weight” of most postsynaptic excitatory potentials. Associated with astrocytes, which are larger and more complex in humans, spines provide neural networks with a high integrative and computational possibility and plasticity. These neural components enable the perception of sensory stimuli, emotional processing, abstract thinking, decision-making, memory and learning for behavioral displays. Human neurons vary from aspiny or “relatively aspiny” cells in the spinal cord to subcortical or neocortical neurons covered with a high density of intermingled spines. They are in a continuum of shapes and sizes visualized after three-dimensional reconstructions. The functional implications for these spines enlighten how cellular attributes determine neuron type-specific connectivity and brain wiring in normal and pathological conditions. Our basic morphological data can also be linked to various other current techniques. Perspectives in this research field involve morphology with transcriptome features, molecular classification of cellular diversity, and connectional and functional identification of coexisting subpopulations of cells in each human brain area.



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14 a 17 de Setembro de 2024
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Title	Respiratory changes associated with sleep in an experimental model of Parkinson`s disease
Author	Ana Carolina Takakura
Affiliations	Farmacologia- Universidade de São Paulo
Contact	takakura@icb.usp.br
Abstract	<p>Parkinson`s disease (PD) is a chronic neurodegenerative disorder affecting the motor system, leading to tremors, muscle stiffness, and movement difficulties. Alongside these symptoms, PD patients commonly experience respiratory and sleep disturbances that significantly impact their quality of life and disease progression. These alterations contribute to fatigue, irritability, and cognitive challenges, exacerbating classic motor symptoms and increasing the risk of psychiatric complications such as depression and anxiety. Studies link sleep alterations to the degeneration of specific brain areas crucial for respiratory and sleep-wake control. Managing respiratory and sleep issues in PD is intricate, as medications for motor symptoms may adversely affect sleep patterns, and there is no medication specifically for respiratory disturbances. Balancing symptoms with treatments that promote healthy breathing and sleep is crucial. Sleep alterations in PD are associated with changes in respiratory patterns, indicating a complex physiological dysfunction. In a toxin mouse model of PD, breathing frequency was reduced and the number of apneas increased during sleep stages. Cholinergic neurons in the laterodorsal tegmental nucleus (LDTg), vital for sleep-wake control and respiratory modulation, send projections to key respiratory nuclei in the brainstem. Stimulation of these neurons normalized respiratory parameters and sleep patterns, underscoring their fundamental role in modulating breathing. These findings highlight the association between PD-related neurodegeneration, respiratory changes, and sleep disturbances, offering insights into potential therapeutic targets for managing PD-related complications.</p>



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14 a 17 de Setembro de 2024
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Title	Estratégias educacionais inovadoras centradas no aluno.
Author	Ana Flávia Santos Almeida
Affiliations	Medicina- Faminas-BH
Contact	anaflaviafarma@yahoo.com.br
Abstract	Este curso oferece uma imersão nas mais recentes e eficazes estratégias educacionais que colocam o aluno no centro do processo de aprendizagem. Em um mundo em constante evolução, onde as demandas educacionais estão mudando rapidamente, é fundamental adotar abordagens inovadoras que atendam às necessidades dos alunos. Neste curso, exploramos métodos dinâmicos e adaptáveis que promovem a participação ativa dos alunos, incentivam a criatividade, desenvolvem habilidades de pensamento crítico e fomentam uma cultura de aprendizagem autônoma. Desde o uso de tecnologias emergentes até estratégias de aprendizagem colaborativa, os participantes serão capacitados a projetar experiências educacionais que inspirem, engajem e capacitem os alunos a alcançarem seu pleno potencial.



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14 a 17 de Setembro de 2024
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Title	Burden of liver disease in Brazil
Author	André Gustavo De Oliveira
Affiliations	Fisiologia e Biofísica- UFMG
Contact	ago@ufmg.br
Abstract	<p>Liver disease is a major cause of mortality and morbidity worldwide and its epidemiology depends on the genetic background, exposure to risk factors, access to healthcare and other sociodemographic characteristics. Brazil is a large country with diverse multicultural and ethnic heritages and important socioeconomic inequalities. The burden of liver disease in Brazil, its regions and population is unknown. We retrieved data from the Unified Health System regarding liver diseases and analyzed the mortality and morbidity from 1996 to 2022 by gender, race/ethnicity, age, region and overall. We calculated the age-specific risk of deaths by liver disease, age-standardization of the data, mean hospitalization and liver transplant-associated costs. Malignant neoplasm of the liver and intrahepatic bile ducts, alcohol-associated liver disease, fibrosis, and cirrhosis of the liver, other diseases of the liver, hepatic failure, chronic viral hepatitis were identified as the major causes of death and morbidity in Brazil in the period analyzed. The epidemiology of these diseases was diverse, with variations according to geographic regions, gender and race/ethnicity. The major economic burden of liver disease is related to liver transplants, a common outcome of the progression of these diseases. Liver disease in Brazil is a serious issue for the public health system due to the high number of deaths and increasing mortality rate. Our study contributes as a necessary prerequisite for the development of tailored public health policies aimed at mitigating the increasing burden of liver diseases in specific populations and regions.</p>



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14 a 17 de Setembro de 2024
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Title	A comunicação intestino-cérebro regula o ritmo biológico intestinal
Author	André Gustavo De Oliveira
Affiliations	Fisiologia e Biofísica- UFMG
Contact	ago@ufmg.br
Abstract	Os ritmos biológicos são flutuações fisiológicas em um determinado período de tempo, que permitem aos organismos predizerem as mudanças ambientais e otimizarem suas respostas biológicas. Alterações nesses ritmos estão associadas a desordens e doenças gastrointestinais e metabólicas como colite, síndrome do intestino irritável, obesidade e diabetes. Sabe-se que, além do ciclo claro/escuro, o horário da alimentação e a microbiota intestinal são determinantes para sincronizar ritmo circadiano do trato gastrointestinal. No entanto, os mecanismos que integram esses sinais provenientes do lúmen intestinal e geram os ritmos circadianos ainda são pouco conhecidos. Nos últimos anos, nosso laboratório tem investigado a participação do nervo vago na sincronização dos ritmos biológicos no trato gastrointestinal. Nossa hipótese vem do fato de que o nervo vago é composto por fibras aferentes e eferentes, isto é, forma uma conexão bidirecional entre órgãos periféricos e o sistema nervoso central, além de sua posição anatômica privilegiada capaz de detectar sinais provenientes do lúmen intestinal e integrar esta informação ao cérebro a partir de uma única sinapse com as células neuroendócrinas. Na palestra, apresentarei os resultados mais recentes do laboratório que sugerem que o eixo cérebro-intestino regula o ritmo biológico intestinal e hepático, bem como os efeitos da interrupção dessa comunicação sobre a fisiologia desses órgãos.



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Title	Gold nanoparticles as carriers of neuroprotective drugs for the Central Nervous System
Author	Andre Ricardo Massensini
Affiliations	Fisiologia e Biofísica- UFMG- UNIVERSIDADE FEDERAL DE MINAS GERAIS
Contact	massensini@gmail.com
Abstract	<p>Stroke is one of the leading causes of morbidity and mortality worldwide, resulting in irreversible damage to brain tissue and significantly impacting patients' quality of life. Despite significant advances in understanding the underlying mechanisms of stroke and the development of emergency treatments, current neuroprotective therapies are limited and fail to achieve the desired efficacy in preventing brain damage. Thus, there is a pressing need to explore new therapeutic approaches that can enhance brain tissue protection against ischemia and promote functional recovery after stroke. We propose to explore the use of gold nanoparticles (AuNPs) as carriers of neuroprotective drugs, aiming to overcome the limitations of conventional therapies and improve clinical outcomes for patients affected by this devastating condition. The hypothesis of this study is that AuNPs can play a crucial role in the effective and precise delivery of neuroprotective drugs to ischemic brain tissue, contributing to reducing infarct size and improving functional recovery after stroke. The ability of nanocarriers to cross the blood-brain barrier (BBB) allows drugs to be targeted directly to the site of injury, increasing the bioavailability and specificity of the therapy while potentially reducing the side effects associated with systemic drug administration. The use of AuNPs as carriers for neuroprotective drugs offers a unique opportunity to improve the efficacy of existing treatments. These nanocarriers have the ability to cross the BBB, enabling precise and efficient drug delivery to ischemic brain tissue. This can lead to a reduction in infarct size, thereby improving functional recovery after stroke. Additionally, the personalization of treatment, made possible by the ability of AuNPs to target drugs to specific areas of the brain, could lead to a more precise and effective approach to stroke management, tailored to the individual needs of each patient. Ultimately, the advancement of neuroprotective therapies in stroke treatment not only has the potential to save lives and improve the quality of life of survivors but also may reduce the costs associated with post-stroke treatment and rehabilitation, thereby alleviating the burden on healthcare systems and society as a whole.</p> <p>The AuNPs were synthesized by the citrate reduction method and subsequently functionalized with different neuroprotective drugs. The characterization of the nanoparticles was carried out using techniques such as UV-vis spectroscopy, transmission electron microscopy (TEM), and zeta potential. Neuroblastoma cell cultures were used to assess cytotoxicity, and brain tissue slices were used to evaluate the neuroprotective efficacy of the conjugated AuNPs. Cell viability assays (MTT and LDH) and apoptosis tests (caspase-3/8/9) were conducted to measure neuronal protection under induced oxidative stress conditions. In vitro BBB models were employed to investigate the ability of functionalized AuNPs to cross this barrier. The results indicate that AuNPs functionalized with neuroprotective drugs retain their physicochemical properties after conjugation, exhibiting an appropriate hydrodynamic diameter and stable zeta potential. The conjugated AuNPs demonstrated low cytotoxicity and high efficacy in protecting against neuronal apoptosis under oxidative stress conditions. Additionally, permeability studies showed that functionalized AuNPs have a significantly increased ability to cross the BBB compared to free drugs. The functionalization of AuNPs with neuroprotective agents proved to be particularly effective, suggesting a high therapeutic potential for the treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's. The antioxidant capacity of AuNPs, combined with the controlled release of neuroprotective drugs, suggests a synergistic mechanism of action that may offer significant therapeutic benefits. Gold nanoparticles functionalized with neuroprotective drugs represent an innovative and effective approach to treating central nervous system diseases. This study demonstrates that AuNPs can improve drug delivery to the brain, protect neurons from oxidative stress, and efficiently cross the blood-brain barrier. Future studies should focus on optimizing functionalization conditions and conducting evaluations in animal models to confirm the therapeutic potential observed in vitro. Acknowledgments: We thank FAPEMIG, CNPq, and CAPES for funding, and the technical support from the teams at CAPI, LCPNano, and CT-Nano UFMG.</p>





14 a 17 de Setembro de 2024
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Title	Mecanismos subjacentes ao efeito inibitório das gliflozinas sobre a atividade do NHE3 em túbulo proximal renal
Author	Andreia Boaro
Affiliations	Cardiopneumologia- FMUSP
Contact	andreiaboaro@iq.usp.br
Abstract	Os inibidores do cotransportador de Na ⁺ /glicose do tipo 2 (SGLT2), também conhecidos como gliflozinas, melhoram o controle glicêmico suprimindo a reabsorção de glicose no túbulo proximal renal. Inicialmente desenvolvidos como agentes antidiabéticos, as gliflozinas reduzem morte por causa cardiovascular e a taxa de hospitalização por insuficiência cardíaca (IC), independente da presença ou ausência de diabetes tipo 2. Recentemente, nosso grupo de pesquisa demonstrou que a empagliflozina restaura a euvolemia e previne a progressão da IC em ratos não diabéticos, ao menos em parte por meio da inibição da reabsorção de sódio mediada pela isoforma 3 do trocador Na ⁺ /H ⁺ (NHE3) em túbulo proximal renal. Contudo, os mecanismos moleculares pelos quais as gliflozinas inibem o NHE3 ainda não foram desvendados. Aqui abordaremos recentes descobertas acerca dos mecanismos subjacentes aos efeitos das gliflozinas sobre o NHE3 em túbulo proximal renal. Três hipóteses serão discutidas: (i) As gliflozinas inibem a atividade do NHE3 por meio da ligação direta ao sítio para sódio deste transportador. (ii) As gliflozinas inibem a atividade do NHE3 por meio da desestabilização do complexo multimérico NHE3-PDZK1-MAP17-SGLT2 em túbulo proximal renal. (iii) As gliflozinas inibem a atividade do NHE3 por meio de uma interação funcional entre NHE3 e SGLT2.



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Title	Impactos do exercício físico regular na hipertensão arterial pulmonar
Author	Antônio José Natali
Affiliations	Educação Física- Universidade Federal de Viçosa
Contact	anatali@ufv.br
Abstract	<p>A hipertensão arterial pulmonar (HAP), uma das classificações clínicas da hipertensão pulmonar, é uma doença rara, caracterizada como hipertensão pré-capilar diagnosticada com medidas hemodinâmicas de pressão média da artéria pulmonar > 20 mmHg, de pressão de oclusão da artéria pulmonar ≤ 15 mmHg e de resistência vascular pulmonar ≥ 3 unidades Wood, em estado de repouso. A HAP está associada ao remodelamento progressivo da artéria pulmonar por disfunção endotelial, inflamação, desbalanço redox, fibrose e lesões plexiformes, o que compromete a circulação pulmonar e gera um aumento da pós-carga do ventrículo direito, com conseqüente remodelamento ventricular e diminuição do volume sistólico, o que resulta em prejuízo da função cardiopulmonar, seguido de falha cardíaca e morte. Tal condição impacta negativamente a tolerância ao esforço físico e a qualidade de vida dos pacientes, os quais apresentam sintomas como dispneia, letargia e desconforto torácico. Apesar disso, a prática de exercício físico por pacientes com HAP estável tem se mostrado segura, benéfica e tem sido recomendada como terapia coadjuvante ao tratamento farmacológico. Pesquisas com o modelo de HAP induzida por monocrotalina têm sido realizadas para investigar os efeitos de diferentes tipos e protocolos de exercício físico, especialmente os mecanismos envolvidos, tanto na hipertensão severa (60 mg/kg de peso corporal) quanto na estável (40 mg/kg de peso corporal). Os resultados de estudos mostram que o treinamento aeróbico com corrida voluntária e corrida em esteira, bem como o treinamento resistido e o treinamento combinado (Aeróbico + Resistido), realizados durante o desenvolvimento da doença em ratos, aumenta a sobrevivência e a tolerância ao esforço físico. Além disso, o aumento da resistência da artéria pulmonar e a redução da função cardíaca são prevenidos pelos diferentes protocolos de treinamento físico. Tais benefícios são acompanhados da atenuação da progressão do remodelamento adverso nos tecidos pulmonar, cardíaco e muscular esquelético. Ademais, os prejuízos da doença na contratilidade e na movimentação de cálcio em miócitos ventriculares isolados são amenizados pelos distintos treinamentos físicos, em função de alterações nas proteínas reguladoras do ciclo de cálcio. Por fim, apesar dos benefícios observados, novos estudos são necessários para desvendar demais mecanismos que auxiliem na compreensão dos efeitos de diferentes protocolos de treinamento físico em indivíduos com HAP.</p>



14 a 17 de Setembro de 2024
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Title	Treinamento físico, expressão gênica e Sarcopenia.
Author	Daniel Barbosa Coelho
Affiliations	Departamento de educação física- UFOP- Universidade Federal de Ouro Preto
Contact	danielcoelhoc@gmail.com
Abstract	<p>A sarcopenia é um mal relacionado principalmente com a idade avançada. Considerando o aumento da expectativa de vida é de se esperar um agravamento destes casos dentro a população. Vários fatores para tratar e prevenir a sarcopenia vêm sendo discutidos. Vários genes relacionados ao desempenho esportivo têm sido associados à saúde na atualidade. Especificamente quanto a sarcopenia, que é definida como a perda de massa e função musculares com a idade, genes como o ACTN3 e da Enzima conversora de angiotensina (ECA) tem mostrado influência nesta situação. Desta forma, têm-se pesquisado como a manifestação dos diferentes genótipos mencionados influenciam na prevenção e tratamento da sarcopenia. Espera-se que como esses genes são influenciadores de aspectos musculares, tal como força, hipertrofia, recuperação e marcadores inflamatórios, que são comprometidos pela sarcopenia, que as características genotípicas possam contribuir positiva ou negativamente com o quadro de sarcopenia.</p>



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Title	Controle neuroendócrino da massa e função muscular esquelética em condições fisiopatológicas
Author	Danilo Lustrino
Affiliations	Fisiologia- Universidade Federal de Sergipe
Contact	lustrino@academico.ufs.br
Abstract	<p>O músculo esquelético é um tecido de alta plasticidade devido ao turnover de suas proteínas estruturais, desta forma alterações nas taxas de degradação ou síntese destas macromoléculas, as quais estão sob controle neuroendócrino, repercutem diretamente no tamanho da fibra muscular. Nesse sentido, utilizando um modelo experimental de dor crônica musculoesquelética que mimetiza a fibromialgia em humanos, demonstramos uma acentuada perda de força e massa muscular esquelética que foi associada a ativação da proteólise proteossomal e diminuição da síntese proteica em roedores. Embora a atrofia muscular observada em nosso estudo, não tenha sido mediada pela ação dos glicocorticoides, ela foi associada a atenuação da secreção de catecolaminas pela medula adrenal. Por outro, lado o tratamento com agonista seletivo dos receptores β2-adrenérgicos e ativação da via de sinalização intracelular do AMPc/PKA atenuou estes efeitos, indicando que a menor ativação do componente hormonal do Sistema Nervoso Simpático, além de contribuir para a manutenção da hiperalgesia também participa na diminuição da função e da massa muscular em modelo de dor musculoesquelética similar aquela observada em pacientes fibromiálgicos.</p>



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14 a 17 de Setembro de 2024
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Title	A hot topic in exercise physiology – Skeletal muscle adaptation and performance in long-term aerobic training in the heat
Author	DAWIT ALBIEIRO PINHEIRO GONCALVES
Affiliations	Educação Física- UFMG
Contact	dawit.eeffto@gmail.com
Abstract	<p>DAWIT ALBIEIRO PINHEIRO GONÇALVES, MSc, PhD- Exercise Physiology Laboratory (LAFISE) & Section of Sports Physiology (SFE) at Sports Training Center (CTE), School of Physical Education, Physiotherapy and Occupational Therapy (EEFFTO), Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil. Acute exposure to environmental heat stress (EHS) elevates core body temperature, which can induce thermal, cardiovascular, and metabolic stress. These alterations can be detrimental to exercise performance, especially in prolonged aerobic exercise. On the other hand, short- and medium-term (2-4 weeks) exposure to EHS during exercise allows for numerous specific physiological adaptations minimizing heat strain and increasing exercise performance. This process of training in the heat is referred to as heat acclimation (HA) when performed in artificial environments such as hot rooms and saunas or heat acclimatization when performed in naturally hot areas/environments. In addition to the beneficial effects of HA on exercise in the heat, some studies have reported that HA-induced physiological adaptations theoretically could improve aerobic exercise performance in cool-temperate conditions, but this hypothesis has been poorly investigated. At a mechanistic level, EHS can transiently activate or inhibit several signaling pathways that regulate cellular energy metabolism, contraction, and vascularization. However, the effects of long-term HA (> 4 weeks) on muscle fiber type, mitochondrial complexes, and exercise performance represent other important issues that have yet to be suitably addressed, and our research group has worked to unravel these mechanisms. Finally, in order to increase physiological strain without a subsequent increase in mechanical load by way of increased force or power output, we will discuss the possibility of using heat as a component of exercise prescription for managing external training load in athletes or even in patients with metabolic disease (e.g., obesity) or orthopedic injury (e.g., lesions in muscle, joint, and tendon) who were unable to perform moderate-high intensity exercise due to mechanical overload. Supported by FAPEMIG (APQ-01268-21 and APQ-02960-22), CAPES, PRPq/UFMG (27764*27) and CNPq/PROANTAR (442645/2018-0)</p>



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Title	Estresse térmico ambiental como um modulador da massa e função muscular esquelética
Author	DAWIT ALBIEIRO PINHEIRO GONCALVES
Affiliations	Educação Física- UFMG
Contact	dawit.eeffto@gmail.com
Abstract	<p>DAWIT ALBIEIRO PINHEIRO GONÇALVES, MSc, PhD- Exercise Physiology Laboratory (LAFISE) & Section of Sports Physiology (SFE) at Sports Training Center (CTE), School of Physical Education, Physiotherapy and Occupational Therapy (EEFFTO), Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil. Enquanto exposições agudas, dentro de certos limites, a baixas temperaturas ambientais podem favorecer o desempenho em exercícios aeróbicos prolongados, temperaturas elevadas podem ser prejudiciais ao desempenho aeróbico. Já o estresse térmico severo pelo frio pode causar distúrbios musculares esqueléticos (por exemplo, dor e atrofia), deteriorando a capacidade física. Os modelos animais disponíveis na literatura têm submetido roedores à exposição constante (24 horas por dia) ao frio (EF) por alguns dias, o que induz à atrofia muscular. No entanto, a exposição crônica contínua ao frio pode causar privação de sono e, como resultado, perda de massa muscular. Para evitar distúrbios do sono, o nosso grupo desenvolveu um modelo murino de exposição crônica intermitente ao frio (ECIF) exclusivamente durante a fase de vigília e os seus efeitos no desempenho físico aeróbico e na adaptação das mitocôndrias e tipos de fibra muscular e sua sinalização intracelular serão apresentados. Por outro lado, a exposição de curto e médio prazo (2-4 semanas) ao ambiente quente em “repouso” ou durante o exercício permite numerosas adaptações fisiológicas específicas que minimizam a perturbação térmica no organismo e podem aumentar o desempenho do exercício. Esse processo é referido como aclimação ao calor (AC) quando realizado em ambientes artificiais, como salas quentes, ou aclimação ao calor quando realizado em áreas / ambientes naturalmente quentes. No entanto, os efeitos da AC com treinamento aeróbico de longo prazo (> 4 semanas) no tipo de fibra muscular, complexos mitocondriais e desempenho do exercício representam questões importantes que ainda não foram adequadamente abordadas, e o nosso grupo de pesquisa tem trabalhado para desvendar esses mecanismos. Trabalhos têm demonstrado que somente a exposição ao ambiente quente pode estimular vias de sinalização intracelular que promovem biogênese mitocondrial, angiogênese e anabolismo proteico, sugerindo que essa intervenção poderia otimizar os efeitos do treinamento físico. Ainda, discutiremos a relevância do conhecimento das respostas termorregulatórias ao frio e quente no contexto dos pesquisadores brasileiros e militares que realizam pesquisas científicas na Antártica, o continente mais frio e mais seco do mundo, e da possibilidade de usar o aquecimento para estimular o crescimento muscular e como um componente da prescrição de exercícios para manipular a carga de treinamento externo em atletas ou mesmo em pacientes em reabilitação. Apoiado pela FAPEMIG (APQ-01268-21 e APQ-02960-22), CAPES, PRPq/UFMG (27764*27) e CNPq/PROANTAR (442645/2018-0)</p>





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Title	Vias de sinalização envolvidas nas respostas renais ocasionadas pelas variações de potássio na dieta
Author	Deise Carla Almeida Leite Dellova
Affiliations	Medicina Veterinária- Universidade de São Paulo
Contact	leite-dellova@usp.br
Abstract	<p>Respostas renais rápidas ao potássio ingerido são essenciais para prevenir a hipercalemia e também desempenham um papel central na regulação da pressão arterial. Embora a concentração extracelular local de K⁺ no tecido renal seja cada vez mais reconhecida como um importante regulador da secreção de K⁺, os mecanismos subjacentes que são relevantes in vivo permanecem controversos. Serão apresentadas as evidências de participação do eixo de sinalização mTORC2-SGK1-Nedd4-2-ENaC como um mediador chave das respostas rápidas das células tubulares ao aumento da [K⁺] plasmática in vivo. Nosso grupo de pesquisa tem demonstrado que o próprio K⁺ atua através da master kinase mTOR, dentro de seu complexo tipo 2 (mTORC2), para ativar a serum and glucocorticoid-regulated kinase 1 (SGK1), que por sua vez, estimula o canal de sódio epitelial (ENaC) para aumentar a excreção de K⁺ nas células principais do ducto coletor cortical (DCC); em parte, por um mecanismo que envolve a fosforilação da ubiquitin ligase (Nedd4-2). No DCC, a ação da aldosterona é particularmente importante para regular a transcrição do SGK1 e a atividade do ENaC. Nesta palestra, abordaremos o efeito da aldosterona em associação com o efeito K⁺ na regulação da atividade ENaC no néfron distal. Discutiremos também a relação entre as variações na concentração extracelular de K⁺ e a atividade das quinases With-No-Lysine (WNK). O papel da WNK na regulação do cotransportador de cloreto de sódio (NCC) no túbulo contorcido distal é bem conhecido, e mudanças na concentração extracelular de K⁺ alteram as atividades da WNK quinase neste segmento tubular. Por outro lado, a WNK1 é altamente expressa no néfron distal sensível à aldosterona, que inclui o DCC. No geral, nossos dados in vitro sugerem um papel para o WNK1 na regulação da atividade ENaC em células mpkCCD; particularmente, na via de sinalização que envolve a regulação do ENaC pelo aumento do K⁺ extracelular.</p>



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Author	Deise Carla Almeida Leite Dellova
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Abstract	<p>Respostas renais rápidas ao potássio ingerido são essenciais para prevenir a hipercalemia e também desempenham um papel central na regulação da pressão arterial. Embora a concentração extracelular local de K⁺ no tecido renal seja cada vez mais reconhecida como um importante regulador da secreção de K⁺, os mecanismos subjacentes que são relevantes in vivo permanecem controversos. Serão apresentadas as evidências de participação do eixo de sinalização mTORC2-SGK1-Nedd4-2-ENaC como um mediador chave das respostas rápidas das células tubulares ao aumento da [K⁺] plasmática in vivo. Nosso grupo de pesquisa tem demonstrado que o próprio K⁺ atua através da master kinase mTOR, dentro de seu complexo tipo 2 (mTORC2), para ativar a serum and glucocorticoid-regulated kinase 1 (SGK1), que por sua vez, estimula o canal de sódio epitelial (ENaC) para aumentar a excreção de K⁺ nas células principais do ducto coletor cortical (DCC); em parte, por um mecanismo que envolve a fosforilação da ubiquitin ligase (Nedd4-2). No DCC, a ação da aldosterona é particularmente importante para regular a transcrição do SGK1 e a atividade do ENaC. Nesta palestra, abordaremos o efeito da aldosterona em associação com o efeito K⁺ na regulação da atividade ENaC no néfron distal. Discutiremos também a relação entre as variações na concentração extracelular de K⁺ e a atividade das quinases With-No-Lysine (WNK). O papel da WNK na regulação do cotransportador de cloreto de sódio (NCC) no túbulo contorcido distal é bem conhecido, e mudanças na concentração extracelular de K⁺ alteram as atividades da WNK quinase neste segmento tubular. Por outro lado, a WNK1 é altamente expressa no néfron distal sensível à aldosterona, que inclui o DCC. No geral, nossos dados in vitro sugerem um papel para o WNK1 na regulação da atividade ENaC em células mpkCCD; particularmente, na via de sinalização que envolve a regulação do ENaC pelo aumento do K⁺ extracelular.</p>



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Title	Physiology, physical training, anabolic resistance, and prevention of sarcopenia
Author	Emerson Cruz De Oliveira
Affiliations	Departamento de Educação Física- Universidade Federal de Ouro Preto- UFOP
Contact	emersonpersonal@gmail.com
Abstract	<p>The maintenance of skeletal muscle relies on a delicate balance between increased protein synthesis and reduced protein degradation. Anabolic resistance occurs when anabolic stimuli, such as protein intake, hormonal signals, or muscle contraction, are less effective in stimulating muscle protein synthesis and reducing inflammation. This phenomenon occurs in contexts like aging, sedentary lifestyle, and critical illness. As we age, our skeletal muscle mass gradually declines due to anabolic resistance. The reduced responsiveness of muscle cells to protein and amino acids contributes to age-induced muscle loss, leading to sarcopenia. Sarcopenia is characterized by the gradual loss of muscle mass, strength, and performance as individuals age. It has wide-ranging effects on health, with serious implications for morbidity and mortality. The objective of this summary is to outline the topics that will be covered in the course 'Physiological Aspects and Therapeutic Options for the Treatment of Sarcopenia: Exercise as a Central Tool in Treatment.' The first part will address anabolic resistance mechanisms, the pathophysiology of sarcopenia, and its relationship with anabolic resistance. The second part of the course will cover physical training, inflammation, and sarcopenia. Finally, the last module will focus on gene expression and sarcopenia. By the end of this course, participants are expected to gain an understanding of the anabolic resistance process, its connection to sarcopenia, and how studies of inflammatory and genetic profiles can aid in comprehending the impact of physical training as a key tool in fighting sarcopenia.</p>



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Title	Alterações metabólicas e hepáticas na fase adulta induzidas pela obesidade infantil: balanço-redox e modulação pelos glicocorticoides
Author	Ernane Torres Uchôa
Affiliations	Ciências Fisiológicas- Universidade Estadual de Londrina
Contact	euchoa@uel.br
Abstract	Os primeiros anos de vida são críticos para o desenvolvimento, já que este é um período de plasticidade neuroendócrina, e o organismo está suscetível à programação metabólica. A supernutrição na lactação é um agente programador do metabolismo energético, e a redução do tamanho da ninhada nos primeiros dias de vida é um método de indução da supernutrição lactacional, levando à obesidade infantil, que resulta no desenvolvimento precoce da obesidade, que persiste até a idade adulta. Além disso, sabe-se que animais adultos com supernutrição lactacional apresentam disfunções hepáticas, estresse oxidativo, inflamação crônica de baixo grau e maiores concentrações de glicocorticoides circulantes. Nesse sentido, o aumento da concentração plasmática dos glicocorticoides tem sido apontado como possível mediador para o desenvolvimento da obesidade, uma vez que a adrenalectomia bilateral é capaz de reduzir a obesidade em diferentes modelos experimentais. Adicionalmente, há evidências de que a suplementação com compostos antioxidantes pode mitigar as comorbidades associadas ao estresse oxidativo e à inflamação crônica de baixo grau observados na obesidade. Desse modo, esta palestra pretende apresentar os achados recentes dos efeitos dos glicocorticoides nas alterações na lipogênese e via de sinalização da insulina hepática induzidas pela supernutrição na lactação de ratos adultos, bem como o perfil metabólico e o balanço redox hepático de ratos adultos com obesidade infantil, e os efeitos da vitamina C na vida adulta sobre esses parâmetros.



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Title	Nanoterapia em doenças respiratórias- onde estamos?
Author	Fernanda Ferreira Cruz
Affiliations	Laboratório de Investigação Pulmonar- Federal University of Rio de Janeiro
Contact	ffcruz@biof.ufrj.br
Abstract	A nanoterapia vem sendo explorada como método terapêutico para o tratamento de doenças respiratórias. Em estudos pré-clínicos, a nanotecnologia vem sendo utilizada em terapias farmacológicas e terapias avançadas. Para que o agente terapêutico alcance as unidades alveolares é importante que os compostos ativos consigam superar as barreiras físicas do trato respiratório para que possam ser administradas por via inalatória, visando a aumentar sua concentração no local da doença e diminuir seus efeitos adversos sistêmicos. Assim, serão apresentados estudos que demonstram a capacidade de nanoencapsulamento de fármacos, que utilizam vetores de terapia gênica em nanoescala, e que testam a utilização de nanopartículas associadas à terapia celular, particularmente, para o tratamento de doenças pulmonares.



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Title	Aprendizagem com jogos físicos e virtuais, no ensino superior (aula 2)
Author	Fernanda Klein Marcondes
Affiliations	de Biociências- Universidade Estadual de Campinas
Contact	ferklein@unicamp.br
Abstract	Nesta aula, será inicialmente abordada a aprendizagem por jogos, desenvolvimento e possibilidade de uso de jogos educacionais no ensino superior. Em seguida, por meio de atividade prática, em grupo, serão apresentados jogos educacionais, em versão impressa e digital, desenvolvidos para o ensino de Fisiologia Humana, abordando os temas: fisiologia cardíaca, integração sinapse- contração muscular- sistema nervoso autônomo, sistema gastrointestinal, tonicidade – osmolaridade- soluções endovenosas. Será apresentado como estes jogos têm sido combinados com estratégias para promover o engajamento discente e realizar avaliações formativas ao longo do processo ensino-aprendizagem. Após a atividade em grupo, será solicitado que os participantes compartilhem suas impressões sobre os jogos utilizados e discutam possibilidades de adaptação para suas disciplinas, cursos e instituições. Também será realizada breve apresentação de resultados de pesquisas sobre a percepção discente e os efeitos destes jogos sobre o aprendizado, nível de ansiedade e estresse de prova, em cursos de graduação em Odontologia, Medicina, Biologia, Farmácia, Enfermagem, Fisioterapia e Toxicologia Analítica.



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Title	Como a eletrofisiologia conversa com a endocrinologia
Author	Fernando Abdulkader
Affiliations	Departamento de Fisiologia e Biofísica- USP
Contact	fkader@icb.usp.br
Abstract	Nesta palestra discutirei como a técnica de patch-clamp, usualmente empregada para estudos nas neurociências, pode ser usada para estudar o acoplamento entre estímulo e secreção hormonal em células endócrinas, como as células beta pancreáticas secretoras de insulina.



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Title	Estratégias didáticas no Ensino de Fisiologia nos Ensinos Fundamental e Médio
Author	Gabriel Victoriano Dos Santos
Affiliations	Diretoria de Ensino de Jaú- Secretaria da Educação do Estado de São Paulo
Contact	gabrielvictoriano@professor.educacao.sp.gov.br
Abstract	<p>Diante da reorganização curricular proposta pela Base Nacional Comum Curricular (BNCC), muito tem se discutido a abordagem dos conteúdos dentro da educação básica. Nessas discussões, são questionados o alto desinteresse dos estudantes e o conseqüente baixa assiduidade e comprometimento no engajamento escolar. Parte desse desinteresse pode estar associado a adoção exclusiva de metodologias de ensino baseadas em metodologias tradicionais, isto é, aulas expositivas centradas no professor, preocupando-se pouco com a participação estudantil. Nesse sentido, a introdução das metodologias ativas de aprendizagem surge como uma estratégia didática relevante para resolver os desafios vivenciados pelos professores em sala de aula, tanto no ensino fundamental quanto médio. Uma dessas estratégias baseia-se no uso de Séries de TV nas aulas. Essa estratégia baseia-se no aumento do número de visualizações de séries nos últimos anos em relação aos filmes. Assim sendo, as séries possuem elementos que podem despertar o interesse dos estudantes. Portanto, o objetivo dessa apresentação oral é discutir o uso de séries de TV como estratégia didática no ensino de Biologia e Fisiologia na Educação Básica. Nessa metodologia de “Ensino baseado em Séries”, são utilizadas diferentes cenas de séries para estimular a discussão de alguns temas ou tópicos de biologia em sala de aula. A escolha da série baseia-se nos objetivos curriculares, objetos de conhecimento e o tempo disponível do professor para as suas aulas. É crucial realizar uma busca e curadoria criteriosa das séries a serem exibidas, sendo possível incluir sugestões dos próprios alunos. Após essa seleção, a série pode ser utilizada em discussões em sala de aula seguindo a sequência didática proposta por Victoriano et al. (2022), que detalha as etapas para a implementação. Nessa metodologia, é possível adaptar um estudo de caso a partir de um único episódio de série ou discutir temas da fisiologia a partir da seleção cenas de diferentes episódios e séries, ou com discussões durante e após a exibição dos vídeos com aplicação de questionários. Nessa apresentação oral, serão relatadas as experiências, no ensino fundamental e médio, do uso de séries como: Grey’s Anatomy, The Good Doctor, Dr. House, Chicago Med, The Big Bang Theory, The Last of Us, Uma Advogada Extraordinária, entre outras. Essa estratégia didática mostrou-se bastante positiva, aumentando o engajamento e participação estudantil, bem como despertou o protagonismo juvenil dos estudantes para buscar ativamente conteúdos de fisiologia em séries. Foi observado também aumentado das notas bimestrais e a busca por novos projetos de vida pelos estudantes.</p>



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Title	Aprendizagem Interativa na Saúde: Simulação Realística e Realidade Virtual
Author	GISELE EVA BRUCH
Affiliations	.- Faminas- BH
Contact	giseleweber@zebrafish.com.br
Abstract	<p>No ensino em saúde, a formação contínua e a atualização dos conhecimentos são fundamentais para garantir a segurança dos pacientes. Métodos tradicionais de ensino, como aulas expositivas e práticas supervisionadas, vêm sendo complementados por tecnologias inovadoras que oferecem experiências de aprendizagem mais dinâmicas e eficazes. Entre essas tecnologias, destacam-se a simulação realística e a realidade virtual (RV), que possibilitam a criação de cenários interativos e imersivos para a prática e o desenvolvimento de habilidades clínicas. A simulação realística envolve a reprodução de cenários clínicos com alto grau de fidelidade, utilizando manequins avançados, atores ou pacientes simulados, e equipamentos médicos reais. Esse método permite que os profissionais e estudantes de saúde pratiquem procedimentos, tomem decisões em tempo real e lidem com situações críticas em um ambiente controlado e seguro. A simulação realística promove a aprendizagem ativa, facilita o desenvolvimento de competências técnicas e não técnicas (como comunicação e trabalho em equipe), e permite a repetição de práticas sem risco para pacientes reais. A realidade virtual, por sua vez, utiliza tecnologias computacionais para criar ambientes tridimensionais imersivos, onde os usuários podem interagir com objetos e situações simuladas por meio de dispositivos como óculos de RV e sensores de movimento. A RV tem sido aplicada em diversas áreas, como treinamento cirúrgico, ensino de anatomia, simulação de emergências e reabilitação. Essa tecnologia oferece uma experiência de aprendizado altamente envolvente, permitindo que os usuários pratiquem habilidades complexas, explorem estruturas anatômicas detalhadas e experimentem cenários clínicos variados sem a limitação do espaço físico ou dos recursos materiais. A integração da simulação realística e da realidade virtual no ensino em saúde traz diversos benefícios. Entre eles, destacam-se a possibilidade de proporcionar experiências práticas intensivas e variadas, a redução do risco de erros em procedimentos reais e a capacidade de treinar grandes grupos de alunos simultaneamente. Além disso, essas tecnologias permitem uma avaliação objetiva do desempenho dos alunos, por meio de registros detalhados de suas ações e decisões durante os exercícios simulados. No entanto, a implementação dessas tecnologias também apresenta desafios. A criação e manutenção de laboratórios de simulação realística e ambientes de RV demandam investimentos significativos em infraestrutura e equipamentos, bem como a capacitação de instrutores e técnicos especializados. Outro desafio é a necessidade de desenvolver e atualizar constantemente os conteúdos e cenários simulados, de modo a refletir as evoluções científicas e tecnológicas na área da saúde. Embora enfrentem desafios de implementação, os benefícios proporcionados por essas tecnologias são inegáveis, refletindo-se em um atendimento mais seguro e eficiente aos pacientes.</p>



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Title	Adaptações cardiovasculares em resposta aos exercícios físicos em mulheres após a menopausa
Author	Guilherme Morais Puga
Affiliations	Faculdade de Educação Física e Fisioterapia- universidade Federal de Uberlândia
Contact	gmpuga@gmail.com
Abstract	Durante o climatério ocorre a falência da função ovariana em produzir hormônios esteroides e ovulação, acarretando em amenorreia permanente, denominada menopausa. Essa deficiência de produção de hormônios causa alterações como elevação do peso corporal, perfil lipídico e aparecimento de doenças metabólicas, e cardiovasculares. A reposição hormonal mostrou-se de baixa eficácia na prevenção dessas doenças, sendo assim, métodos alternativos de prevenção e tratamento são fundamentais para essa população. Dentre esses métodos, o treinamento com exercícios físicos é benéfico para essas mulheres, pois podem melhorar o perfil lipídico, regular a pressão arterial, ajudar no controle de peso e na redução da gordura em excesso, reduzindo o risco de desenvolverem doenças crônicas e também podem melhorar os sintomas climatéricos e a qualidade de vida dessas mulheres. Assim iremos abordar os principais achados e recomendações na literatura de efeitos de diferentes tipos de exercícios na saúde da mulher na pós-menopausa.



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Title	“Diferenças morfológicas e funcionais renais em função do sexo – influência da gonadectomia”.
Author	GUIOMAR NASCIMENTO GOMES
Affiliations	Fisiologia- Universidade Federal de São Paulo
Contact	guiomar.gomes@unifesp.br
Abstract	<p>A lesão renal pode ter desfechos diversos, os quais podem ser influenciados por características morfofuncionais renais que variam entre os sexos. Enquanto há relatos de diferenças ao longo dos segmentos tubulares, a existência de variações na morfologia glomerular relacionadas ao sexo ainda está em discussão. Apesar das disparidades no desenvolvimento da doença renal entre homens e mulheres, esta afeta ambos os sexos. Um exame detalhado dos parâmetros morfológicos e da função renal em ambos os sexos pode revelar diferenças fisiológicas e auxiliar na compreensão da progressão da doença. Objetivo: Avaliar detalhadamente a morfologia e função renal em ratos Wistar machos e fêmeas submetidos ou não à gonadectomia. Métodos: Ratos Wistar com dois meses de idade foram submetidos à gonadectomia ou cirurgia simulada (Sham), compondo quatro grupos experimentais: machos Sham (SM), fêmeas Sham (SF), machos gonadectomizados (GM) e fêmeas gonadectomizadas (GF). Todos os animais foram mantidos em gaiolas coletivas, em condições adequadas de temperatura e luminosidade. Aos seis meses de idade foram avaliados a pressão arterial (PA) e o peso corporal (PN), a seguir os animais foram colocados em gaiolas metabólicas para coleta de amostras de urina de 24 horas para avaliação da excreção de creatinina, proteínas e eletrólitos. Também foi coletado sangue da veia da cauda para avaliar as concentrações plasmáticas de sódio, potássio, uréia e creatinina. A área glomerular e a tubularização glomerular foram analisadas em lâminas coradas com HE. A expressão dos transportadores de sódio (trocaador NHE3, cotransportadores NKCC e NCC e canais ENaC) foi avaliada por imuno-histoquímica. CEUA/UNIFESP: 9009241022. Resultados apresentados como média \pm erro padrão; ANOVA a dois critérios seguida de teste de Tukey, $p < 0,05$. Resultados: Ratas fêmeas apresentaram menor peso corporal quando comparadas aos machos seguindo o padrão sexual para ratos (SM:462,8\pm9,2, GM:423,4\pm29,5, SF:284,9\pm6,7, GF:323,9\pm9,9, $g, p_{\text{sexo}} < 0,0001$). A gonadectomia em ratas interferiu negativamente na função renal (diminuiu o clearance de creatinina); entretanto, o mesmo não aconteceu no sexo masculino. (SM: 6,3\pm0,5, GM: 6,3\pm0,7, SF: 5,6\pm0,5, GF: 4,1\pm0,2, mL.min⁻¹.kg⁻¹, $p_{\text{sexo}} = 0,0045$). Em relação à pressão arterial sistólica, não foi observada diferença significativa entre os grupos (SM: 126\pm2,1, GM: 123\pm1,5, SF: 126\pm2,5, GF: 129\pm2,4mmHg); entretanto, o grupo GF apresentou valores de pressão arterial próximos ao limite superior da normalidade. O grupo de Sham-machos (SM) apresentou maior proteinúria (SM:12,8\pm0,9, GM:1,5\pm0,2, SF:2,9\pm0,2, GF:3,4\pm0,4, mg/24h, $p_{\text{sexo}} < 0,0001$, $p_{\text{gonadectomia}} < 0,0001$, $p_{\text{interaction}} < 0,0001$), que não persistiu após a gonadectomia, evidenciando a influência da testosterona na função glomerular. Não foram observadas diferenças entre os grupos nas concentrações plasmáticas de uréia ou íons. A média da área glomerular foi maior no sexo masculino em relação ao feminino, gonadectomizados ou não (SM:10.608\pm270, GM:10.123\pm462, SF:7.616\pm370, GF:7.945\pm374, μm^2, $p_{\text{sexo}} < 0,0001$). Além disso, a curva de distribuição da área glomerular de acordo com seu tamanho, seguiu o modelo de Gauss nas fêmeas, enquanto nos machos, a curva dos machos não seguiu este padrão. A porcentagem de tubularização glomerular foi maior nos machos do que nas fêmeas, e a gonadectomia reduziu a tubularização no grupo GM (SM:39,4\pm3,2; GM:17,7\pm26; SF:19,1\pm4,4; GF:18,1\pm0,9 %, $p_{\text{sexo}} < 0,0039$). Conclusões: Estes dados indicam que, na idade adulta, as diferenças no tamanho glomerular não são alteradas pela gonadectomia. No entanto, a falta de hormônios sexuais pode afetar aspectos funcionais específicos, cuja relevância varia conforme o sexo.</p>



14 a 17 de Setembro de 2024
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Title	Mesa redonda 2- Inovação em Fisiologia: Conhecimento e Impacto na Sociedade
Author	Jackson De Souza-Menezes
Affiliations	Não há- Universidade Federal do Rio de Janeiro- Campus Macaé
Contact	jacksonmenezes@gmail.com
Abstract	Discutir o processo de desenvolvimento tecnológico e de produtos a partir do conhecimento em fisiologia, abordando os passos necessários para sair do ambiente acadêmico e alcançar a entrega de soluções para a sociedade. Explorar também os aspectos legislativos e das agências de fomento que podem impulsionar o sistema, bem como oportunidades nas empresas, e como os fisiologistas podem se adaptar ao mundo da inovação, contribuindo não só com a importante pesquisa básica, mas também para a entrega de produtos e tecnologias aplicáveis, fomentando o empreendedorismo e a inserção de mestres e doutores nas empresas.



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Title	Curso Análises funcionais renais em condições fisiológicas e patológicas- Aula 3- Doença renal aguda e doença renal crônica
Author	Jackson De Souza-Menezes
Affiliations	Não há- Universidade Federal do Rio de Janeiro- Campus Macaé
Contact	jacksonmenezes@gmail.com
Abstract	A aula abordará a Doença Renal Aguda (DRA) e a Doença Renal Crônica (DRC), destacando suas diferenças, causas, fisiopatologia e tratamentos. Serão discutidos os mecanismos de lesão renal na DRA, incluindo hipóxia e inflamação, e a progressão da DRC, com ênfase na fibrose renal e perda de função. Além disso, serão apresentados dados recentes sobre biomarcadores e novas abordagens terapêuticas. A palestra visa integrar conhecimentos para melhorar o diagnóstico e manejo dessas condições.



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Title	Resumo da palestra 2 do simpósio Unraveling the mysteries of kidney disease
Author	Jackson De Souza-Menezes
Affiliations	Não há- Universidade Federal do Rio de Janeiro- Campus Macaé
Contact	jacksonmenezes@gmail.com
Abstract	Chronic Kidney Disease (CKD) is a major public health issue, with diabetes mellitus as the second leading cause according to the latest Brazilian Dialysis Census. CKD is strongly linked to obesity, hypertension, and family history. Microalbuminuria, though traditionally used to diagnose diabetic nephropathy (DN), has limitations such as delayed onset and lack of specificity for Diabetic Kidney Disease (DKD) and CKD progression. This highlights the need to explore alternative biomarkers.



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Title	Atualizando memórias: relembrando o passado e olhando para o futuro
Author	Janine Inez Rossato
Affiliations	-- UFRN
Contact	janine.rossato@ufrn.br
Abstract	<p>A consolidação estabiliza novas memórias, enquanto que a reconsolidação permite a retenção de um traço mnemônico desestabilizados durante sua recordação. Os estudos iniciais no campo da reconsolidação versaram principalmente sobre a amnésia decorrente do bloqueio deste processo, dando ênfase à perda da memória prévia já consolidada. Apesar de ser responsável por manter as memórias após sua evocação, o papel biológico do ciclo de desestabilização/reconsolidação ainda não é totalmente conhecido; neste sentido foi levantada a hipótese de que a reconsolidação liga novas informações às memórias reativadas já estabelecidas, permitindo que as mesmas possam ser atualizadas. A reconsolidação dá a impressão de ser um processo universal, no entanto, parece arriscado propor que todas as memórias ao serem lembradas retornem a um estado ativo, necessitando um novo processo para mantê-las. Em relação a isso, a memória de reconhecimento de objetos, que serve para julgar a familiaridade dos itens e é essencial para lembrar de eventos anteriores, somente se torna instável e suscetível à reconsolidação quando reativada em presença de novidade. Usando ferramentas farmacológicas mostramos experimentalmente que a reconsolidação efetivamente une e vincula informações novas ao acervo mnemônico previamente estabelecido, o que permite que estas informações possam indiretamente ser reativadas e se tornarem instáveis. Esses dados sugerem que os lembretes declarativos devem ser usados com cautela durante intervenções psicoterapêuticas baseadas na reconsolidação, já que essas terapias propõe o apagamento de memórias contraproducentes.</p>



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Title	Pressão arterial e seus determinantes em crianças e adolescentes: evolução dos valores pressóricos ao longo do crescimento
Author	Jose Geraldo Mill
Affiliations	Departamento de Ciências Fisiológicas- Universidade Federal do Espírito Santo
Contact	josegmill@gmail.com
Abstract	<p>A pressão arterial é uma variável de fundamental importância para manutenção da homeostasia e, em termos físicos, representa a força que a massa sanguínea exerce contra a parede arterial. A mediana dos valores pressóricos por ocasião do nascimento a termo situam-se entre 80 e 90 mmHg para a pressão sistólica e entre 40 e 50 mmHg para a pressão diastólica. O aumento ponderal exige crescimento da rede vascular e para manter níveis pressóricos estáveis e compatíveis com o funcionamento da microcirculação (filtração e reabsorção em equilíbrio) é necessário que a diferença pressórica entre a raiz da aorta e a árvore arterial terminal (arteríolas) também aumenta. Essa a razão pela qual a pressão arterial gradualmente aumenta ao longo da infância e adolescência buscando um patamar estável no início da idade adulta. Os fatores que interferem nesta elevação foram estudados em crianças e adolescentes (6-17 anos) de uma instituição do terceiro setor (Estação Conhecimento, Serra, ES) que fornece atividades de contraturno para escolares regularmente matriculados em escolas públicas do município. Foram incluídas no estudo 856 participantes que compareceram ao Hospital Universitário da Universidade Federal do Espírito Santo (Hucam-UFES/Ebserh) para realizarem em um único dia medidas de pressão arterial (métodos oscilométrico, Onrom 765-CP), antropometria, bioimpedância (InBody 270) e coleta de sangue em jejum para avaliação de parâmetros bioquímica. As características sócio demográficas (sexo, estágio de maturação sexual, escolaridade, doenças autorreferidas, uso de medicamentos, etc) foram obtidas por entrevista na qual um único observador (ao longo de todo o estudo) caracterizou os indivíduos em relação à raça/cor conforme fenótipos observados diretamente, incluindo cor da pele, textura do cabelo e formato do nariz e lábios. Dos 856 participantes do estudo, foram incluídos na análise 148 brancos, 236 pretos e 453 pardos. Na amostra global, havia 43,8% de meninos. A idade (média e dp) não diferiu entre os grupos, sendo de 11,2(2,9) anos nos brancos, 11,5(2,8) nos pretos e 11,4(2,8) nos pardos. As variáveis antropométricas foram similares entre os grupos, exceto para a massa magra que foi maior ($p < 0.5$) nos pretos (18,4) do que em brancos (16,7). A pressão arterial sistólica em pretos (104,1 mmHg) e em pardos (104,8 mmHg) foi maior ($P < 0.05$) do que em brancos (102,3 mmHg). O incremento pressórico com a idade (mmHg/ano) foi maior em pretos (1,37 mmHg/ano) do que em brancos (1,24 mmHg/ano). Essa diferença, ainda que pequena (1,4 mmHg/década de vida) e não significativa do ponto de vista estatístico ($p = 0,12$) é suficiente para explicar as diferenças pressóricas observadas entre negros e brancos. Diferenças também ocorrem, mas de maneira mais atenuada, em relação à pressão diastólica. O maior incremento da pressão sistólica com a idade em pretos pode ser decorrente da maior rigidez arterial existente neste grupo de raça/cor em relação aos brancos, conforme dados da velocidade da onda de pulso carotídeo-femoral [5,83(0,93) m/s vs 5,44(0,73) m/s; $p < 0.05$], com valor intermediário em pardos [5,55(0,75) m/s]. Os dados permitem concluir que valores ligeiramente maiores de rigidez arterial em pretos favoreçam incremento mais acelerado da pressão sistólica ao longo do crescimento. Portanto, a raça/cor constituiria um determinante da elevação pressórica ao longo do crescimento contribuindo para os valores mais altos da pressão arterial encontrados em adultos de raça/cor preta.</p>



Title	MELANOPSIN MAINTAINS SKIN HOMEOSTASIS AND MITIGATES UVA DAMAGE
Author	José Thalles Lacerda
Affiliations	Departamento de Fisiologia Geral- Universidade de São Paulo
Contact	thalles_lacerda2@hotmail.com
Abstract	<p>The presence of melanopsin (OPN4) in cultured melanocytes and its association with ultraviolet A radiation was previously demonstrated, suggesting that OPN4 serves as a critical protein hub in skin biology. Recently, we described the protective role of OPN4 in maintaining skin homeostasis and the heightened damage from UVA exposure in its absence. Using fragments of lumbar skin from sham and UVA irradiated male mice, we revealed changes in response to UVA irradiation through a proteomics approach (Label-free quantification) followed by gene ontology (GO) biological processes and signaling pathways (KEGG) enrichments. Our results identified a repertoire of differentially encoded proteins in the skin of Opn4 KO mice related to processes which, in WT animals, only were unveiled after UVA irradiation. One may infer that these events are OPN4 protein-dependent. We identified 3,402 proteins and observed a large difference in the number of proteins between genotypes: 2,398 proteins (non-irradiated WT mice); 2,378 (irradiated WT mice); 2,790 (non-irradiated Opn4 KO mice); and 2,840 (irradiated Opn4 KO mice). Meanwhile in Opn4 KO, the proteins are associated to proteolytic processing (PRSS1, SERPINA1E, S100A8), mRNA processing and splicing (SAFB2, SNRPD3), regulation of translation (NGD) and chromatin remodeling (DDX21) (Figure 9B). The proteins absent in the skin of Opn4 KO mice are associated with actin cytoskeleton organization, tight junction and keratinocyte differentiation and also indicate differences in the skin structure composition. Impairment of the components of the skin's physical barrier can contribute to more enhanced sensitivity to environmental antigens and failure to present foreign particles to the immune system, resulting in inflammatory conditions. Our data demonstrate that the lack of functional OPN4 protein promotes an impairment in the skin barrier function and increases sensitivity to environmental factors. The skin of Opn4 KO mice showed increased protein number related to lipid metabolic processes, response to oxidative stress and hydrogen peroxide, regulation of circadian rhythm, peroxisome function, ferroptosis, and actin filament severing/reorganization after UVA stimulus. It also increased proteins related to positive regulation of apoptosis and reduced those related to negative regulation, and proteins associated with keratinocyte differentiation were restored. Unexpectedly, UVA stimulus on Opn4 KO mice led to loss of proteins associated with DNA damage responses, when compared to non-stimulated Opn4 KO mice. These findings indicate that lack of OPN4 lead to photosensitization of the skin, which in turn promotes UVA-induced ROS accumulation and deleterious effects on DNA damage responses. Moreover, crosstalk pathways between ROS accumulation and inhibition/loss of DNA damage sensors have also been previously described. Having this in mind we decided to evaluate gene expression of Atm and Xpa; both showed higher expression in the absence of OPN4 than in the WT mice. Only in the KO animals, UVA reduced the expression of both genes. Our results strongly suggest an important and novel protective role of OPN4 in skin homeostasis. Financial Support: CAPES (88887.615662/2021-00 GZ); CNPq (305032/2023-2 to AMLC, 161118/2021-6 to CDSC and 167833/2023-5 to GZ); and FAPESP (grants 2017/24615-5 and 2018/14728-0 to AMLC, 2017/26651-9 MNM; scholarships 2018/23043-0 DDD, 2021/01659-2 to GZ and 2022/04584-6 to CDSC). Ethics Committee IBUSP 350/2019.</p>

Title	Treinamento físico, inflamação e sarcopenia
Author	Kelson Mauro De Castro Pinto
Affiliations	Departamento de Educação Física- UFOP
Contact	kelerson@ufop.edu.br
Abstract	<p>A sarcopenia é uma síndrome caracterizada pela perda de força e massa muscular que impacta diretamente na capacidade funcional e consequentemente na qualidade de vida dos idosos, produzindo vários resultados adversos, como por exemplo, maior probabilidade de queda, maior risco de hospitalizações e até mesmo de morte, comparados com indivíduos não sarcopênicos. Trata-se de uma síndrome multifatorial influenciada por doenças crônicas, deficiências nutricionais, baixos níveis de atividade física, alterações endócrinas e inflamatórias. O envelhecimento, é um processo de desenvolvimento maturacional natural, envolvendo alterações neurobiológicas estruturais, funcionais e químicas. Durante toda a vida do ser humano, seu sistema imune sofre continuamente mudanças morfológicas e funcionais, que atingem o pico da sua função na puberdade e um declínio gradual no envelhecimento. O termo imunossenescência refere-se à disfunção do sistema imunológico relacionado com a idade, associado ao progressivo declínio da função imunológica. Com isso, observa-se com o envelhecimento, níveis basais aumentados de citocinas inflamatórias, caracterizando um estado inflamatório crônico de baixo grau que impactaria na capacidade funcional e qualidade de vida dos mesmos, como por exemplo, favorecendo o desenvolvimento da sarcopenia. O perfil inflamatório crônico de baixo grau relacionado à idade foi reconhecido como importante fator da sarcopenia. Existem estudos que associam as citocinas inflamatórias a perda de massa muscular, estimulando, em última análise, o catabolismo proteico e suprimindo a síntese muscular. O treinamento físico e especialmente o treinamento de força vem sendo utilizado como estratégia para otimizar a prevenção e o tratamento da sarcopenia, além de estar relacionado com melhorias da condição inflamatória característica do envelhecimento. Em relação ao treinamento físico a resposta inflamatória é considerada um processo benéfico e necessário quando relacionado ao treinamento físico regular e sistematizado, uma vez que, em conjunto com outros mecanismos, torna-se responsável pela regeneração e reparo das estruturas danificadas. O equilíbrio entre as ações das citocinas inflamatórias e regulatórias, entre a atividade pró e antioxidante, contribuem para as adaptações ao treinamento. Estudos demonstram que o treinamento físico, tanto aeróbio quanto de força, proporciona uma redução de citocinas inflamatórias e aumento das citocinas regulatórias que contribuiriam para este equilíbrio, além de um aumento da capacidade antioxidante. É importante destacar que quando se fala em treinamento, estamos falando de exercícios pedagogicamente sistematizados e orientados, sendo realizados de forma contínua. As diferentes possibilidades de organização, dos diferentes parâmetros de treinamento, produzirão respostas adaptativas diferentes, o que dificulta muito a interpretação dos resultados de pesquisa, quando se trata de treinamento físico, porém justamente esse comportamento torna o estudo de exercício físico desafiador. Ainda existem lacunas a serem investigadas sobre as respostas adaptativas aos diferentes métodos de treinamento físico quando se analisa a relação sarcopenia e imunossenescência.</p>



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Title	Skeletal Muscle recovery after Physical Exercise: The Angiotensin-(1-7) Physiological Effects.
Author	Lenice Kappes Becker
Affiliations	Fisiologia do Exercício- UFOP- Universidade Federal de Ouro Preto
Contact	lenice@ufop.edu.br
Abstract	<p>Improving and accelerating the muscle recovery process after physical exercise is essential for athletes and exercise practitioners. Effective muscle recovery ensures better physical performance and greater adherence to exercise routines. Several strategies are applied to accelerate or improve muscle recovery among them are nutritional (carbohydrate and protein ingestion), mechanical (massage, compression garments), temperature immersion treatment (cold and heat), active recovery, and supplements. Various discoveries have shown that Angiotensin-(1-7) [Ang-(1-7)], a peptide traditionally recognized for its cardiovascular actions, plays a fundamental role in the control and maintenance of skeletal muscle. Different models of induced skeletal muscle mass loss or gain demonstrate a positive effect of Ang-(1-7) in maintaining lean mass and regenerating skeletal muscle. In the senescence model, the Ang-(1-7) delays the age-related decline in the function of skeletal muscle, in the animal muscular dystrophy model, the Ang-(1-7) has an important effect in decreasing the fibrosis and improving physical function. The mechanisms through which Ang-(1-7) modulates muscle function include improved glucose uptake by skeletal muscle cells, reduced inflammation, and decreased anti-atrophic pathways. Our research group aims to evaluate the effect of Ang-(1-7) on muscle recovery in both animal and human models related to physical exercise. Supporting the existing scientific literature, we observed that treatment with Ang-(1-7) reduces inflammation and fibrosis and increases anti-inflammatory cytokines in models of exercise-induced muscle injury and laceration. Treatment with Ang-(1-7) also reduces levels of classic muscle injury markers and decreases pain perception in the human model during different stages (days after injury), indicating an acceleration of the repair process. Double-blind crossover trials show that in the condition treated with Ang-(1-7), there is an increase in physical performance and better control of basal and post-exercise glucose and lactate levels. The data so far demonstrate the beneficial effects of Ang-(1-7) on muscle recovery and physical performance, suggesting a potential modulatory role in metabolic control mechanisms and skeletal muscle regeneration.</p>



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Title	Nicotine exposure and hypoglossal motor neuron development: relevance to breathing-related tongue muscle control
Author	Lila Buls Wollman
Affiliations	Department of Human Physiology- University of Oregon
Contact	lwollman@uoregon.edu
Abstract	<p>Disruption of nicotinic cholinergic signaling, as occurs with perinatal nicotine exposure, alters the development of the neural respiratory network, and is strongly associated with sudden infant death syndrome (SIDS). Infants and children born to mothers that smoked during and after pregnancy have abnormalities in hypoglossal motor neurons (XIIMNs), the neurons that innervate the tongue muscles, and increased incidence of obstructive apneas, which are considered a potential mechanism underlying SIDS. To model perinatal nicotine exposure, we exposed pregnant rats to chronic episodic nicotine through drinking water starting at embryonic day 5. This model (developmental nicotine exposure; DNE) results in fetal exposure by the placental circulation in utero, and through breast milk after birth, and produces plasma cotinine levels in the pups that are like what is found in infants born to mothers who are considered moderate smokers. We studied rat pups at postnatal days (P)1-5, and P10-12, which encompasses a critical period of postnatal brain development, and tested the hypothesis that DNE alters nicotinic acetylcholine receptor (nAChR) function and XIIMN intrinsic properties in vitro, and breathing-related tongue muscle function in vivo. At P1-5, DNE was associated with altered nAChRs on XIIMNs, including delayed recovery from desensitization (time to recovery = 97.05 sec for Control and 189.3 sec for DNE, 2-way ANOVA- time: $F = 52.39$, $p < 0.0001$; treatment: $F = 9.498$, $p = 0.006$). However, XIIMN firing properties and potassium currents were not different from control neurons. There was also no difference in breathing-related tongue muscle function in DNE pups compared to control pups at this age. At P10-12, nAChRs on XIIMNs continued to exhibit delayed recovery (time to recovery = 27.8 sec for Control and 88.5 sec for DNE, time: $F = 27.01$, $p < 0.0001$; treatment: $F = 26.52$, $p = 0.0009$), XIIMNs had lower peak firing frequencies in response to depolarizing current (~ 45 Hz in Control and ~ 30 Hz in DNE, $F = 4.805$, $p = 0.0392$), and larger whole cell potassium currents (sustained whole cell current, $F = 4.306$, $p = 0.0499$). These cellular changes were associated with a blunted and delayed tongue muscle response to nasal occlusion in vivo (time: $F = 38.38$, $p < 0.0001$; treatment: $F = 10.17$, $p = 0.0066$). Overall, these findings indicate that DNE produces changes to the intrinsic properties of XIIMNs at a critical developmental age, which may be an important mechanism underlying impaired breathing-related tongue muscle control and the pathophysiology of SIDS.</p>



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Title	Interação entre controle respiratório, comportamento e neuroinflamação em modelo animal de ansiedade.
Author	Luana Tenorio Lopes
Affiliations	Morfologia e Fisiologia Animal- UNESP
Contact	luana.tenoriolopes@gmail.com
Abstract	<p>De acordo com a OMS (2022), o transtorno de ansiedade generalizada (TAG) é um distúrbio caracterizado pelo medo irracional e preocupação excessiva, por período de pelo menos seis meses podendo ainda desencadear outros distúrbios como por exemplo, o transtorno do pânico. Recentemente, foi demonstrado que neurônios orexinérgicos presentes no hipotálamo dorsomedial (DMH) em animais previamente expostos a uma forma de estresse neonatal, são ativados de forma sexo-específica na fase adulta durante hipercapnia (teste de inalação de CO₂). A quimiossensibilidade aumentada ao CO₂ e prevalência sexo-específica são características observadas na fisiopatologia do TAG, porém pouco sabemos a esse respeito. Curiosamente, pesquisas apontam que a exposição a diversos tipos de estresse também causam disfunção na micróglia, células imunes inatas do sistema nervoso central (SNC). Micróglia são células altamente dinâmicas rapidamente ativadas em resposta a um desequilíbrio homeostático e respondem com precisão ajustando de maneira regulada sua morfologia, expressão gênica e comportamento funcional. Além de defenderem o SNC em situações patológicas, a micróglia contribui com o desenvolvimento encefálico e são sensíveis aos efeitos dos hormônios gonadais. Embora estudos mais recentes tenham apontado para o papel fundamental da micróglia na patogênese dos transtornos psiquiátricos, ainda não se sabe se as alterações na micróglia colaboram diretamente com o surgimento dessas doenças ou se contribuem para potencializar sintomas associados às patologias que já se encontram em curso. Assim, a combinação de protocolos experimentais que envolvem exposição prévia ao estresse, testes de inalação de CO₂ combinados com análises comportamentais e de parâmetros respiratórios, bem como investigações sobre ativação micrógliar e mensuração de citocinas inflamatórias periféricas são ferramentas que trazem implicações importantes para ampliar nosso entendimento sobre os mecanismos etiológicos e fisiopatológicos envolvidos nos transtornos de ansiedade. Essa compreensão é crucial para que possamos contribuir com o desenvolvimento de abordagens preventivas no âmbito da saúde pública e com a descoberta de novas estratégias terapêuticas seguras e eficazes para tratar o TAG.</p>



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Title	Impacto do estresse neonatal no controle neural da respiração: papel dos hormônios sexuais.
Author	Luana Tenorio Lopes
Affiliations	Morfologia e Fisiologia Animal- UNESP
Contact	luana.tenoriolopes@gmail.com
Abstract	<p>Embora a respiração seja uma função homeostática robusta, pesquisas usando modelos pré-clínicos e clínicos mostram que a exposição a diferentes formas de estresse na fase neonatal desregula o desenvolvimento e o funcionamento do núcleo paraventricular do hipotálamo, que por sua vez causará desregulação em todo o sistema hipotálamo-hipófise-adrenal (HPA) e simpático-adrenal-medular (SAM). Neste contexto, a separação materna neonatal (SMN) é um modelo amplamente usado no campo de Neurociências e é considerado um método simples e confiável capaz de interromper o desenvolvimento do eixo HPA. Embora existam variações do modelo de SMN descritas na literatura, os protocolos raramente se estendem além da segunda semana de vida neonatal, considerado período crítico de desenvolvimento do sistema nervoso e respiratório. Os efeitos desse desbalanço neuro-hormonal desencadeado pelo estresse neonatal, impactam os circuitos neurais respiratórios e desencadeiam comportamentos psicopatológicos na fase adulta dos animais. Esses comportamentos são comparáveis ao que é descrito em condições clínicas em pacientes com transtorno de pânico (TP). O fato de que ataques de pânico surgem na puberdade e a maior prevalência destes transtornos ocorra em mulheres, sugere fortemente que os hormônios sexuais contribuem com a fisiopatologia destas condições, impactando de forma direta o controle respiratório em situações de estresse. De forma interessante, o modelo pré-clínico de SMN gera diferenças sexo-específicas marcantes, sendo uma abordagem experimental importante para a investigação de mecanismos etiológicos que possam auxiliar pesquisadores na busca de novos alvos farmacológicos para tratamento dos sintomas respiratórios e comportamentais presentes no TP.</p>



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14 a 17 de Setembro de 2024
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Title	Pharmacological interventions and channelopathies in the development of respiratory control
Author	LUIS GUSTAVO ALEXANDRE PATRONE
Affiliations	MORFOLOGIA E FISILOGIA ANIMAL- UNESP
Contact	luispatrone@hotmail.com
Abstract	<p>The development of neural circuitry within respiratory system and their highly complex network of connections does not follow a rigidly predetermined genetic model. Instead, the structural development of physiological systems and the differentiation of neurons into specific functional phenotypes result from extremely complex interactions between genes, transcription and neurotrophic factors. Thus, pre- and postnatal period is a highly dynamic and plastic process that can be influenced by environmental, chemical, and even psychological factors, which may be responsible for remodeling ontogenetic development, leading to alterations in the CNS, including the network responsible for respiratory function. The normal functionality of ion channels is essential for maintaining membrane potential, homeostasis, and producing electrical signals, serving as key regulators of neuronal excitability. Thus, abnormalities in central respiratory control in pediatric patients and neonatal rodent models have been associated with neurologic channelopathies involving potassium channels. Chemoreception or central integration of respiratory control dysfunction are linked primarily to altered function of ion channels, including large-conductance calcium-activated K channel (BK channel). Furthermore, among various processes, the maturation of neurotransmission systems such as catecholaminergic, serotonergic, and endocannabinoid emerges as an important factor in the control and modulation of respiratory function. Disruptions of these neurotransmission systems during development has been associated with clinical disorders such as Rett syndrome, Sudden Infant Death Syndrome (SIDS), and Congenital Central Hypoventilation Syndrome (CCHS). Therefore, in this talk, I will highlight some short-, medium- and long-term consequences of the use of a synthetic cannabinoid, an anxiolytic and antidepressive drug used during pregnancy, as well as the consequences of BK channel mutations in the respiratory control system throughout development using rodents as a model. Financial support: FAPESP and CNPq.</p>



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Title	CONTROLE SIMPÁTICO DA NEOGLICOGÊNESE HEPÁTICA
Author	Luiz Carlos C. Navegantes
Affiliations	Fisiologia- FMRP-USP
Contact	navegantes@fmrp.usp.br
Abstract	<p>É bem estabelecido que a proteína ligante ao elemento responsivo de AMPc (CREB) associada ao seu coativador transcricional do tipo 2 (CRTC-2) exerce um papel chave na indução do programa gênico da neoglicogênese hepática, em resposta ao glucagon. Entretanto, muito pouco se conhece sobre o papel do Sistema Nervoso Simpático (SNS) na modulação deste complexo transcricional. Nesse contexto, investigamos a participação de CREB/CRTC-2 na ativação da neoglicogênese hepática induzida pela inervação simpática, durante o estresse térmico, em roedores. Para melhor compreender a arquitetura da inervação simpática do fígado de camundongos, utilizamos a técnica de 3DISCO e constatamos que as fibras simpáticas noradrenérgicas ficam restritas à vasculatura do tecido e não alcançam diretamente o hepatócito. Com o objetivo de investigar a função desta inervação, camundongos neonatais foram simpatectomizados (6-hidroxiopamina) e, após 8-10 semanas, foram expostos ao frio (4°C) ou mantidos em temperatura ambiente, por um período de 6 horas. Serão discutidos resultados que mostram que a estimulação simpática induzida pelo frio induz hiperglicemia acompanhada de maior atividade enzimática, conteúdo de proteínas e expressão de genes chaves da neoglicogênese, bem como ativação da sinalização de CREB/CRTC-2, sendo esses efeitos abolidos ou atenuados pela simpatectomia ou em animais nocautes de CRTC-2. Verificou-se também que o estresse térmico ou a Noradrenalina, em hepatócitos isolados, estimula as cascatas de sinalização do AMPc e do Ca²⁺ e que a simpatectomia só é capaz de modular proteínas relacionadas à via do Ca²⁺. Nossos dados demonstram a importância da via CREB/CRTC2 na mediação dos efeitos simpáticos na neoglicogênese hepática e contribuem para a melhor compreensão do controle neural da homeostase glicídica.</p>



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Title	On Spatiotemporal Patterns of the Brain's Functional Connectogram
Author	Márcio Flávio Dutra Moraes
Affiliations	Fisiologia e Biofísica- UFMG
Contact	marcionnc@gmail.com
Abstract	<p>Neuroscience is transitioning- a movement that started a couple of decades earlier- into adopting a new conceptual framework for brain architecture, in which time and thus temporal patterns play a central role in the neuronal representation and processing of sampled data from the world. Our understanding of the brain has evolved to acknowledge the importance of brain rhythms in the overall functional architecture of the nervous system and how long-range integration between neuronal substrates take place in a small-world network arrangement. The shift in view from functional anatomy and the integrate-and-fire paradigm of neuronal processing to a coincidence detector and parallel processing network is just beginning to substantially impact neuromodulation treatment and non-pharmacological therapeutic strategies. This seminar will explore evidence supporting this paradigm shift (i.e. the importance of temporal coding in neuronal processing) and our work involving both basic neurophysiology (e.g. sensory processing, neuronal representation and memory engram formation) and the application of such a new framework on new therapeutic strategies for neurological diseases, such as epilepsy. A neurociência está em transição- um movimento que começou há algumas décadas - para a adoção de uma nova estrutura conceitual para a arquitetura cerebral, na qual o tempo e, portanto, os padrões temporais desempenham um papel central na representação neuronal e no processamento de dados amostrados do mundo que nos cerca. Nossa compreensão do cérebro evoluiu para reconhecer a importância dos ritmos cerebrais na arquitetura funcional geral do sistema nervoso e como a integração de longo alcance entre substratos neuronais ocorre em um arranjo de rede de mundo-pequeno. A mudança de visão da anatomia funcional e do paradigma de integração-e-disparo do processamento neuronal para um detector de coincidências e uma rede de processamento paralelo está apenas começando a impactar substancialmente o tratamento de neuromodulação e as estratégias terapêuticas não farmacológicas. Este seminário irá explorar evidências que apoiam esta mudança de paradigma (ou seja, a importância da codificação temporal no processamento neuronal) e o nosso trabalho envolvendo tanto a neurofisiologia básica (por exemplo, processamento sensorial, representação neuronal e formação de engramas de memória) e a aplicação de tal nova estrutura em novas estratégias terapêuticas para doenças neurológicas, como a epilepsia.</p>



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14 a 17 de Setembro de 2024
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Title	Estado da arte da fisiologia no Brasil e propostas de interação com o setor produtivo e empresas estatais
Author	Márcio Flávio Dutra Moraes
Affiliations	Fisiologia e Biofísica- UFMG
Contact	marcionnc@gmail.com
Abstract	<p>Torna-se cada vez mais necessário e benéfico que os laboratórios de investigação básica interajam com o sector privado. Iniciativas desse tipo não apenas ampliam oportunidades de perfil dos egressos da academia, mas também são um elemento crucial para a prosperidade e o desenvolvimento das nações. No entanto, isto não pode ocorrer à custa de comprometer a investigação fundamental ou pura, movida pela curiosidade e pelo desejo de expandir o conhecimento, e não unicamente direcionado por uma aplicação prática específica ou objetivo comercial. Os laboratórios de fisiologia podem interagir com o setor privado de várias maneiras: desenvolvimento e testes de medicamentos, descoberta de biomarcadores, apoio a ensaios clínicos, desenvolvimento de dispositivos médicos (testes de protótipos, estudos de validação, pesquisa de biocompatibilidade, dispositivos de monitoramento de saúde), testes de desempenho para esportes, desenvolvimento de tecnologia vestível, estudos ergonômicos, pesquisas em fisiologia animal para agricultura e indústria alimentícia, serviços de saúde- seguros e diversas outras aplicações. Estas colaborações podem levar ao desenvolvimento de novos produtos, ao aprimoramento das tecnologias existentes e à melhor compreensão dos processos fisiológicos, beneficiando, em última análise, tanto o mundo acadêmico quanto o comercial. A questão não é tanto se queremos colmatar o fosso entre a investigação e o desenvolvimento, mas sim como o fazemos de forma a preservar os interesses destes mundos aparentemente em conflito. O objetivo é reconciliar estas diferenças e desenvolver uma estrutura que destaque os aspectos benéficos mútuos do trabalho conjunto.</p>



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Title	Desenvolvimento de ferramentas e modelos computacionais para estudos de ritmos biológicos na neurociência
Author	Márcio Flávio Dutra Moraes
Affiliations	Fisiologia e Biofísica- UFMG
Contact	marcionnc@gmail.com
Abstract	<p>Biological rhythms are essential patterns of physiological processes that occur at regular intervals, influencing behavior, cognition, and overall health. In neuroscience, these rhythms are crucial for proper brain functioning at the network level (i.e. ultradian rhythms) but also, at intervals within the circadian and infradian rhythms may regulate various bodily functions. Disruptions in these rhythms can lead to or be a consequence of several neurological and psychological disorders. This seminar will address a new conceptual framework for brain architecture, in which temporal coding within specific brain oscillations play a central role not only in generating the neuronal patterns our brain uses to encode the world that surrounds us but is also key in how long-range integration between neuronal substrates take place in a small-world network arrangement. We will show the design of new computational tools and models to study such temporal coding and measure temporal pattern formation. In addition, we will show that similar programs can be used to process data from conventional circadian Rhythms, in fact we developed an open-source Python library which encapsulates methods for chronobiological analysis and data inspection. We applied this toolkit in the analysis of Intellicage Data from experimental groups studying subthreshold insults in animal models of epilepsy. Os ritmos biológicos são padrões essenciais de processos fisiológicos que ocorrem em intervalos regulares, influenciando o comportamento, a cognição e a saúde geral. Na neurociência, estes ritmos são cruciais para o funcionamento adequado do cérebro ao nível da rede (ou seja, ritmos ultradianos), mas também, em intervalos dentro dos ritmos circadianos e infradianos, podem regular várias funções corporais. As perturbações nestes ritmos podem levar ou ser consequência de vários distúrbios neurológicos e psicológicos. Este seminário abordará uma nova estrutura conceitual para a arquitetura cerebral, na qual a codificação temporal dentro de oscilações cerebrais específicas desempenha um papel central não apenas na geração dos padrões neuronais que nosso cérebro usa para codificar o mundo que nos rodeia, mas também é fundamental na forma como o longo alcance a integração entre substratos neuronais ocorre em um arranjo de rede de mundo pequeno. Mostraremos o projeto de novas ferramentas e modelos computacionais para estudar essa codificação temporal e medir a formação de padrões temporais. Além disso, mostraremos que programas semelhantes podem ser usados para processar dados de ritmos circadianos convencionais; na verdade, desenvolvemos uma biblioteca Python de código aberto que encapsula métodos para cronobiológicos análise e inspeção de dados. Aplicamos este kit de ferramentas na análise de dados do Intellicage de grupos experimentais que estudam insultos subliminares em modelos animais de epilepsia.</p>



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Title	Temporally coded stimulation for the treatment of neurological dysfunctions
Author	Márcio Flávio Dutra Moraes
Affiliations	Fisiologia e Biofísica- UFMG
Contact	marcionnc@gmail.com
Abstract	<p>There are few alternatives to patients that have pharmacoresistant neurological diseases: resective surgery, nutritional therapy, genetic and genomic approaches among others. Another possible option is the use of neuromodulation devices, which have advanced significantly as neuroscience increases to advance in establishing a solid theoretical background explaining the mechanisms behind its therapeutic success (e.g. Parkinson's disease and epilepsy). Epilepsy is a brain disease that afflicts approximately 1% of the world population, with an alarming one-fourth of these patients not having seizures satisfactorily controlled by pharmacological treatment. Even resective surgery may not be an option to a significant percentage of drug-resistant epilepsy patients, these are the patients in which neuromodulation treatment may very well be a last resort. Our work has focused on how a new conceptual framework for brain architecture, based on coincidence-detector network processing and on temporally coded long-range communication, may help devise better neuromodulation protocols for treatment. We've shown that targeting the synchronization of hyper-coupled networks, even at the cost of increasing overall network excitability, produces much better results with very low frequency stimulation protocols. In addition, we suggest that several neurological diseases might have a common pathophysiological disfunction regarding abnormal coupling between brain substrates.</p> <p>Existem poucas alternativas para pacientes que apresentam doenças neurológicas farmacorresistentes: cirurgia ressectiva, terapia nutricional, abordagens genéticas e genômicas, entre outras. Outra opção possível é a utilização de dispositivos de neuromodulação, que têm avançado significativamente à medida que a neurociência aumenta para avançar no estabelecimento de uma base teórica sólida que explica os mecanismos por detrás do seu sucesso terapêutico (por exemplo, doença de Parkinson e epilepsia). A epilepsia é uma doença cerebral que atinge aproximadamente 1% da população mundial, sendo que um alarmante um quarto desses pacientes não apresenta crises convulsivas controladas satisfatoriamente por tratamento farmacológico. Mesmo a cirurgia ressectiva pode não ser uma opção para uma percentagem significativa de pacientes com epilepsia resistente a medicamentos; estes são os pacientes nos quais o tratamento de neuromodulação pode muito bem ser o último recurso. Nosso trabalho concentrou-se em como uma nova estrutura conceitual para a arquitetura cerebral, baseada no processamento de redes de detectores de coincidências e na comunicação de longo alcance codificada temporalmente, pode ajudar a desenvolver melhores protocolos de neuromodulação para tratamento. Mostramos que direcionar a sincronização de redes hiperacopladas, mesmo ao custo de aumentar a excitabilidade geral da rede, produz resultados muito melhores com protocolos de estimulação de frequência muito baixa. Além disso, sugerimos que diversas doenças neurológicas podem ter uma disfunção fisiopatológica comum em relação ao acoplamento anormal entre substratos cerebrais.</p>



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Title	Doenças Hepáticas: da Origem à Solução
Author	Maria De Fatima Leite
Affiliations	Fisiologia e Biofísica- UFMG
Contact	leitemd@ufmg.br
Abstract	Os casos de doenças hepáticas têm aumentado em todo mundo, sendo a 11ª causa de mortalidade e uma das principais causas de morbidade. Segundo dados da Organização Mundial da Saúde (OMS), cerca de 2 milhões de pessoas morrem por doenças no fígado por ano, correspondendo a 4% das mortes anuais. Esse cenário é extremamente alarmante e tem grande diversidade de perfis patológicos que ocasionam maiores gastos por parte dos sistemas de saúde e incluem o transplante de fígado como desfecho final comum para os casos graves. Nesta mesa redonda será discutido esse panorama a nível internacional (Dr Marlon Lemos, Instituto de Biofísica Carlos Chagas, UFRJ) e nacional (Dr. André Oliveira, Departamento de Fisiologia e Biofísica, UFMG), além de contar com a participação de um representante do Ministério da Saúde do Brasil (Rosângela Teixeira, CGDANT) que irá apresentar as políticas públicas de saúde voltadas ao combate do grave cenário de doenças hepáticas no país.



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Title	Electrophysiology of Dendritic Spines: Information Processing, Dynamic Compartmentalization and Synaptic Plasticity
Author	MARIA ELISA CALCAGNOTTO
Affiliations	Departamento de Bioquímica- UFRGS
Contact	elisa.calcagnotto@ufrgs.br
Abstract	<p>Dendritic spines, with their heterogeneous morphological, biochemical, and functional features, play a pivotal role as postsynaptic components in central nervous system synapses. These structures undergo dynamic morphological reorganizations throughout development, aging, and in response to behavioral cues. Dendritic spines not only integrate and filter signals to the soma, but they also facilitate diverse connections with axons from many different sources. Dendritic spines undergo geometric changes that can provide rapid adjustments to postsynaptic ionic balance, protein trafficking, and signaling events, ultimately regulating synaptic efficacy related to long-term plasticity. The cellular compartments of the synapse, including neuronal pre- and postsynaptic compartments plus glial cells such as astrocytes, NG2 cells, and microglia, together with a noncellular element, the functional scaffold extracellular matrix, named the tetrapartite synapse, are morphologically and functionally plastic and crucial for synapse development, physiology, and pathology. For a long time, the limitations of available methods prevented measuring electrical signals directly from the membrane of individual spines. However, important biophysical properties of dendritic spines have been recently unveiled. These advancements stem from the ongoing development of novel, integrated imaging and electrophysiological techniques that facilitate the assessment of functional dendritic characteristics. This includes the study of backpropagating action potentials, synaptic potentials mediated within dendritic and spine biochemical and electrical compartments, and the spatiotemporal dynamics of dendritic spines associated with synaptic plasticity. These discoveries actively contribute to our understanding of dendritic spine dynamics and neuronal behavior.</p>



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Title	PAPEL DAS MIOCINAS NO DANO MUSCULAR INDUZIDO PELO EXERCÍCIO
Author	MARIA FERNANDA CURY BOAVENTURA
Affiliations	Programa de Interdisciplinar em Ciências da Saúde- UNICSUL- UNIVERSIDADE CRUZEIRO DO SUL
Contact	maria.boaventura@cruzeirosul.edu.br
Abstract	<p>A fadiga muscular induzida pelo exercício ocorre devido a depleção de substratos, aumento de estresse oxidativo, depolarização da membrana muscular, depleção de potássio, hipertermia muscular, dano muscular, redução do suprimento de oxigênio e cálcio para o músculo e ativação da resposta inflamatória. O dano muscular e a inflamação são as causas mais relevantes de fadiga muscular, particularmente em corridas de longa-distância. As miocinas são um grupo de moléculas bioativas secretadas por diferentes órgãos que desempenham papéis vitais na coordenação do crosstalk interórgãos para manter o corpo na homeostase e inclui miocinas, cardiocinas, hepatocinas, adipocinas, e neurocinas. Mais de 650 miocinas foram descritas em resposta ao exercício e muitos pesquisadores têm investigado seus efeitos biológicos em diferentes tecidos. No tecido muscular as miocinas são responsáveis pela reparação e adaptação muscular cujas ações biológicas incluem miogênese, biogênese mitocondrial, mitofagia, autofagia; ativação de células satélites, proliferação de células musculares lisas vasculares; oxidação de gordura intramuscular, sensibilidade à insulina, captação de glicose, oxidação lipídica e resposta anti-inflamatória. Muitas dessas miocinas atuam em diversas vias de sinalização que culminarão na ativação do co-ativador de transcrição Coativador gama-receptor ativado por proliferador de peroxissoma (PGC)-1alfa e fator de transcrição PPAR-γ que modulam genes relacionados aos efeitos autócrinos/parácrinos musculares. As miocinas também possuem efeitos endócrinos sendo a maior parte dos estudos em coração e tecido adiposo, promovendo maior biogênese mitocondrial, sensibilidade à insulina e oxidação lipídica. Após exercício de endurance observamos aumento das citocinas clássicas como IL-8, IL-10, MCP1, assim como das miocinas GDF-15, BDNF, FSTL e FGF-21 logo após a maratona e redução de miostatina, musculina, IL-15, apelina e irisina principalmente no período de recuperação. Além disso, BDNF teve uma correlação negativa com o marcador de dano miocárdico, troponina. O BDNF é uma neurotrofina estimulada pelo estresse metabólico e maiores níveis de cálcio intracelular e atua na contração miocárdica diminuindo a apoptose dos cardiomiócitos e a disfunção mitocondrial; aumenta a neuro excitabilidade motora e a contração dos cardiomiócitos e melhorar o metabolismo lipídico e da glicose via ativação de p-AMPK e PGC-1α. O BDNF é expresso no cérebro e em tecidos periféricos como músculo, tecido adiposo, células imunes (linfócitos, eosinófilos e mastócitos), endoteliais e epiteliais. A contração muscular também leva a maior expressão de BDNF no tecido muscular para o processo de reparação do tecido, porém a secreção de BDNF para a circulação ainda vem sendo discutida. Mediadores antiinflamatórios clássicos (IL-10, IL-8 e IL-6) induzidos pelo exercício também foram associados à resposta das miocinas/hepatocinas como FGF-21, FSTL e musculina imediatamente após a corrida e no período de recuperação e podem afetar a dinâmica de reparo do tecido muscular.</p>



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Title	Unveiling the impact of advanced glaucoma on non-visual functions in mice: exploring the connexion between central and peripheral biological clocks in the regulation of metabolic and neuroendocrine process
Author	Maria Nathália Moraes
Affiliations	Departamento de Ciências Biológicas- Unifesp
Contact	Maria.nathalia@unifesp.br
Abstract	<p>The retinal ganglion cells (RGCs) expressing melanopsin, are intrinsically photosensitive in the mammalian eyes. The presence of melanopsin in the ipRGCs allows them to directly detect environmental light. These melanopsin-positive cells are crucial for light detection leading to the synchronization of central circadian timing system, located in the suprachiasmatic nucleus (SCN). Therefore, diseases that result in degeneration of RGC and/or retinohypothalamic tract could impair light transmission to the circadian system, consequently giving rise to secondary disorder. In fact, such disruption of the circadian rhythm can have implications for maintaining overall health and wellbeing and may even contribute to the development of various diseases. Glaucoma, a degenerative optic neuropathy, is one of the leading causes of irreversible blindness globally. One of the most risk factors for glaucoma is elevated intraocular pressure (IOP). The primary site of degeneration in glaucoma is the retinal ganglion cells, and we have demonstrated that mice with advanced glaucoma shows disrupted circadian rhythm of <i>Per1</i> and <i>Vip</i>, which are critical for processing photic light in the SCN. Glaucomatous mice exhibit alterations in SCN-driven circadian rhythms, including changes in circadian locomotor activity and core body temperature. These responses are linked with disrupted molecular clock component of central biological clock. Consequently, metabolic peripheral tissue of glaucomatous mice present altered diurnal rhythm of clock genes and tissue-specific genes. As a consequence, we found altered circadian rhythm of clock genes in the hypothalamic-pituitary-adrenal (HPA) axis and energy metabolism. This research opens a new avenue of investigation into the mechanisms underlying RGC degeneration and its systemic consequences. It may contribute to establishing the cause-and-effect relationship between chronodisruption and the development of diseases.</p>



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Title	In vivo and in vitro assessment of pathways involved in acute kidney injury.
Author	Maria Oliveira De Souza
Affiliations	Fisiologia- USP
Contact	souza@icb.usp.br
Abstract	<p>Introduction. Ischemia-reperfusion injury (IR) is one of the most common causes of acute kidney injury (AKI). In the schematic kidney, the injured epithelium presents depletion of adenosine triphosphate (ATP), mitochondrial dysfunction, disruption of apicobasal polarity and cell death by apoptosis or necrosis. However, cell signaling associated with tubulointerstitial injury processes is poorly understood. Therefore, the present study aims to investigate the contribution of the TLR4/p38MAPK signaling pathways related to the responses of tubulointerstitial injury to renal IR. To this end, we use in vivo and in vitro models to understand the cellular signaling responsible for such events. Methods. For in vivo study, anesthetized male C57BL/6J mice were used. The sham group underwent simulated surgery and IR group had renal flow interrupted by the use of mini-clamps on the both renal arteries for 30 minutes. Then, the mini-clamps were removed to allow renal reperfusion for 48 hours, when the animals were anesthetized, and cardiac puncture was performed to collect blood samples and the mice were euthanized by exsanguination. Next, the kidneys were removed for further analysis by RT-PCR, immunoblotting, immunofluorescence and histology. For in vitro study, the immortalized mouse proximal tubular (TKPTS) cells in culture were subjected to ischemia using antimycin A (5 μM) for 20 minutes, followed by reperfusion with standard culture medium for 60 minutes. After IR the cells were used to flow cytometry, immunoblotting and immunofluorescence analysis. The data were analyzed by unpaired t test with Welch's correction. Results. All results from the IR group were compared with the sham group. In the in vivo study, IR results in increased levels of creatinine and urea in plasma, albuminuria, increased renal weight, severe tubulointerstitial injury with significant loss of megalin, increased expression of Kim-1 mRNA and protein, as well as NGAL and Ki67, increased mRNA expression, for pro-inflammatory factors such as IL1B, IL12, CXCL1, CXCL4, CXCL10, MCP1 and TNFα, as well as pro-fibrotic factors such as TGFβ, αSMA, collagens 1, 3 and 4. In the in vitro study, IR in cells TKPTS resulted in apoptosis regulated by the phospho P38MAPK/caspase 8 pathway. Conclusion. IR induces relevant tubulointerstitial injury with subsequent activation of the phospho P38MAPK/caspase 8 signaling pathway that culminates in the apoptosis of proximal tubule cells. Financial Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) e Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES).</p>



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Title	Seeking for non-canonical photoreceptors and light-inducible molecules in the inner retina of diurnal vertebrates
Author	Mario Eduardo GUIDO
Affiliations	Química Biológica Ranwel Caputto- Universidad Nacional de Cordoba, Argentina
Contact	mario.guido@unc.edu.ar
Abstract	<p>Photic detection is required for vision and image-forming activities but also for a number of essential non-visual tasks such as adjusting the circadian clock, pupil reflexes or melatonin inhibition, among others, occurring all of them, in the vertebrate retina. The retina is a multilayer-organized tissue that is part of the central nervous system composed of visual photoreceptors (PRCs) (cones and rods) responsible for diurnal/color and nocturnal vision respectively, and a group of non-canonical photoreceptors present in the inner retina for blue and UV light detection. Among them, the first ones to be described in mammals and then, in the avian retina (results from my lab), were the intrinsically photosensitive retinal ganglion cells (ipRGCs) expressing the photopigment melanopsin (Opn4). The ipRGCs are involved in the synchronization of the biological clock by light, the pupillary light reflexes and other non-image forming tasks through their projections to different brain areas. This intrinsic photosensitivity works even in the absence of vision, as we found in the GUCY1 chickens suffering blindness since hatching. Also, we found that another inner retinal cell population, the horizontal cells (HCs) were also photosensitive and such photosensitivity in the blue region was conferred by the photopigment Opn4x (the Xenopus ortholog). My laboratory was the first to characterize the photocascade taking place in these two Opn4-expressing cells (ipRGCs and HCs) which involved a Gq protein, the activation of phospholipase C, Ca²⁺ mobilization, depolarization, and GABA release by HCs. IpRGCs also express the photoisomerase RGR that is responsible for regulating the pool of retinoids in light to provide the chromophore required for Opn4 through an alternative visual cycle. More recently, we have identified that the Muller glial cells (MGCs), the most abundant and multitasking glial cells of the retina, expressed the non-visual photopigments Opn3 (encephalopsin) and Opn5 (neuropsin) in the blue/UV region and respond to light by increasing Ca²⁺ and AMPc levels. This is the first report to demonstrate that a glial cell in the retina can be photosensitive, although its role is still unknown. In addition, we found that different retinal cell types contain autonomous circadian clocks regulating diverse metabolic and physiological functions. Among the metabolic processes investigated, we first demonstrated rhythms in the metabolic labeling and glycerophospholipid synthesizing enzyme activities in different retinal cell layers synchronized by light/dark cycles. In addition, we observed antiphasic rhythms in melatonin synthesis and expression and activity of AANAT (serotonin-acetyl transferase), the key regulatory melatonin enzyme, between PRCs and RGCs. Indeed, in PRCs melatonin levels and AANAT expression was high during the night whereas in RGCs, they were high during the day. All these findings together support the idea that non-visual photoreceptors and clocks converge together in the same cell populations to finely regulate retinal function and physiology for the entire organism according to the illumination and environmental/time conditions.</p>





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Title	Speaker Abstract: The Baroreceptor Reflex: Breakthrough Discoveries and Future Directions`
Author	MARK W CHAPLEAU
Affiliations	Division of Cardiovascular Medicine- The University of Iowa
Contact	elisardo.vasquez@uvv.br
Abstract	The baroreceptor reflex is well established as a major regulator of arterial blood pressure and cardiovascular function. I will provide an overview of breakthrough discoveries past and present, with emphasis on the molecular determinants of baroreceptor activation, adaptation and modulation. The roles of acid-sensing ion channel 2 (ASIC2) and the Nobel-prize winning PIEZO channels will be highlighted. I will touch on baroreflex interactions with other organ systems (e.g., pain, sleep) and end with future directions for research discovery and therapeutic targeting of baroreflex dysfunction in disease.



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Title	Bioengenharia de arcabouços hepáticos: contribuições para o avanço da medicina regenerativa
Author	Marlon Lemos Dias
Affiliations	Centro de Pesquisas em Medicina de Precisão- Universidade Federal do Rio de Janeiro
Contact	marlonlemons@biof.ufrj.br
Abstract	<p>O transplante hepático é o único tratamento definitivo para a falência hepática. No entanto, problemas como a escassez de órgãos e a imuno rejeição resultam em longas filas de espera e elevadas taxas de intercorrências pós cirúrgicas. Frente a este cenário, a bioengenharia de órgãos e tecidos surge como uma alternativa promissora através da obtenção de arcabouços acelulares (órgãos descelularizados) pela técnica de descelularização. Arcabouços hepáticos acelulares tem sido explorados com sucesso na medicina regenerativa, no entanto, pouco se sabe a respeito dos mesmos após o transplante em fígados cirróticos. Ainda é desconhecido se o arcabouço transplantado pode ser afetado pelo fígado cirrótico que o recebeu, tornando-se cirrótico, ou permanecendo como um arcabouço saudável para o crescimento de células saudáveis. Assim, o objetivo desta palestra é apresentar o uso de arcabouços hepáticos acelulares como uma nova alternativa ao transplante hepático capaz de eliminar completamente os dois maiores problemas relacionados ao transplante: as longas listas de espera e o potencial de imuno rejeição. Para isso, serão apresentados os principais resultados obtidos após análises de arcabouços hepáticos acelulares transplantados em animais receptores com cirrose hepática. Os principais achados que demonstram que arcabouços hepáticos acelulares podem ser transplantados em fígados cirróticos, tornando-se completamente recelularizados em trinta dias após o transplante serão apresentados. Além disso, evidências de que os arcabouços hepáticos acelulares induzem regeneração hepática, atenuam a cirrose e contribuem para melhora funcional do fígado após o transplante serão apresentadas. Portanto, em um contexto translacional, esta palestra vai demonstrar que os arcabouços hepáticos acelulares podem ser utilizados como um fígado bioartificial servindo como suporte auxiliar ou transplantados em pacientes com doença hepática submetidos a procedimentos de hepatectomia. Além disso, essa palestra vai confirmar que os produtos de engenharia de tecidos oferecem uma nova abordagem terapêutica para o tratamento de doenças hepáticas agudas e crônicas em seres humanos.</p>



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Title	Atividade física e hipertensão arterial sistêmica: da redução pressórica aos mecanismos adaptativos.
Author	Mateus Camaroti Laterza
Affiliations	Fundamentos da Educação Física- Universidade Federal de Juiz de Fora
Contact	mateus.laterza@ufjf.br
Abstract	<p>A hipertensão arterial sistêmica é caracterizada por níveis pressóricos elevados e sustentados cronicamente, justificados em parte, por alterações autonômicas e vasculares. Considerada com um dos principais fatores de risco para o surgimento do infarto agudo do miocárdio e do acidente vascular encefálico, a hipertensão arterial sistêmica atinge aproximadamente 50% da população brasileira. Desta forma, diferentes estratégias farmacológicas e/ou não farmacológicas são adotadas para prevenção e tratamento desta patologia. Nesse sentido, a prática regular de atividades físicas ganha importante destaque. Pessoas fisicamente ativas possuem menor probabilidade de desenvolvimento hipertensivo quando comparadas as pessoas fisicamente sedentárias. Já nas pessoas com hipertensão arterial sistêmica o treinamento físico parece promover importante redução pressórica. Esse fenômeno é acompanhado de importantes desfechos clínicos, incluindo a melhora da qualidade de vida. Sem dúvida, todos esses efeitos positivos do treinamento físico são mediados por adaptações fisiológicas. Por exemplo, a redução da hiperatividade simpática e o remodelamento cardíaco e vascular são adaptações fisiológicas presentes em pessoas com hipertensão arterial sistêmica após período de treinamento físico. Deste modo, a referida palestra versará sobre os efeitos do treinamento físico na pressão arterial e os mecanismos fisiológicos envolvidos neste processo.</p>



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Title	Alterações cardiovasculares e respiratórias durante a inflamação sistêmica
Author	Mateus Ramos Amorim
Affiliations	Anesthesiology and Critical Care Medicine- The George Washington University
Contact	amorimmr@hotmail.com
Abstract	<p>Embora a inflamação seja uma característica evolutiva dos organismos multicelulares ao desafio imune, a produção e liberação exacerbada de citocinas pró-inflamatórias durante a inflamação sistêmica contribui para a disfunção de múltiplos órgãos. Considerando a gravidade da sepse e suas complicações fisiopatológicas, diferentes grupos de pesquisa têm se dedicado ao estudo das repercussões da inflamação sistêmica em busca de estratégias terapêuticas para o tratamento desta condição. Algumas semelhanças com a sepse humana são compartilhadas com modelos experimentais. Neste cenário, a administração sistêmica de endotoxina (lipopolissacarídeo – LPS) vem sendo amplamente utilizada em modelos animais para estudar as alterações fisiopatológicas observadas durante a inflamação sistêmica, tais como hipotensão, taquicardia e febre. Estas respostas hemodinâmicas e termorregulatórias frente ao LPS são similares às aquelas observadas em seres humanos com sepse. Durante a inflamação sistêmica induzida por LPS há também o surgimento de alterações respiratórias significativas em ratos e humanos. Pretendemos abordar os aspectos neurais envolvidos no controle cardiovascular e respiratório bem como as interações complexas entre o sistema nervoso central e periférico durante a inflamação sistêmica.</p>



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Title	Astrócitos como elementos osmosensíveis do Núcleo Supraoptico
Author	MELINA PIRES DA SILVA
Affiliations	Biofísica- Escola Paulista de Medicina
Contact	melina.silva@unifesp.br
Abstract	<p>Uma característica fantástica das redes neurais é sua capacidade de passar por mudanças estruturais e funcionais rápidas em resposta a desafios para manter sua função. No núcleo supraóptico (SON), que representa um dos núcleos recrutados durante distúrbios hidroeletrólíticos, sabe-se que remodelações estruturais significativas resultam em mudanças na morfologia, atividade e função das células que abrigam esse núcleo. No entanto, do ponto de vista elétrico, as consequências de tais mudanças ainda são pouco exploradas, especialmente no que diz respeito à comunicação entre astrócitos e neurônios magnocelulares. Nesse sentido, interessa-nos entender se as células da glia, particularmente os astrócitos, interferem nas propriedades elétricas dos neurônios magnocelulares durante a hipertonicidade aguda de curto prazo. Portanto, combinando a técnica de patch-clamp de célula única e duplo registro em animais geneticamente modificados, investigamos a contribuição dos astrócitos para a excitabilidade dos neurônios magnocelulares durante aumentos na osmolalidade plasmática. Observamos que os astrócitos por si só são sensíveis à estimulação hipertônica de curto prazo e que os registros de patch duplo (neurônio e astrócito) revelou que a despolarização do potencial de membrana em repouso dos astrócitos precede o aumento na atividade dos neurônios SON magnocelulares. Oscilações de cálcio também foram observadas nos astrócitos SON durante o estímulo hipertônico, indicando um possível mecanismo de despolarização da membrana dessas células. Os resultados obtidos até agora forneceram insights sobre a contribuição dos astrócitos no controle da excitabilidade dos neurônios magnocelulares durante a hipertonicidade, bem como os mecanismos sinápticos e biofísicos envolvidos nesse processo.</p>



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Title	Intrinsically photosensitive Müller glial cells: a novel mechanism for the regulation of retinal functions by non-visual opsins
Author	Natalia Andrea
Affiliations	Quimcia Biológica Ranwell Caputto- FCQ-UNC- Universidad Nacional de Córdoba
Contact	natalia.marchese@unc.edu.ar
Abstract	<p>In vertebrates, the retina process light stimuli for visual and non-visual purposes. In this complex structure different types of neuronal and glial cells are linked in an ordered and layered anatomical arrangement where light information flows vertically and horizontally. To direct functions beyond image formation, the retina has developed over the course of evolution the capacity for photodetection in the blue-UV light range. Müller glial cells (MCs), derived from neuronal precursors and the most abundant retinal glial cell type, have been shown to express different blue- and UV-sensitive opsins (Opn3 and Opn5) and the photoisomerase retinal G protein-coupled receptor (RGR). Indeed, pioneering evidence from this group identified a stepwise increase in Opn3 levels throughout development until the time of birth, coinciding with the increase in classical glial markers. Moreover, Opn3 expression in CM is photic regulated, by increasing its expression and modifying its cellular localization after 1 hour of light exposure, where both events are part of the same response that is dependent on protein synthesis. Subsequently, we identified for the first time a direct photic response by MCs specifically to a blue light pulse, observed as a significant increase in intracellular calcium levels sustained for several minutes. Notably, this response is observed in a subpopulation of cultured CMs (50% of the cells analyzed) and is dependent on opsin activation. In fact, intrinsic cellular responses in primary cultures of avian MCs elicited by blue light stimulation (peak at 480 nm), activates mixed intracellular responses implying two signaling pathways: calcium release from internal stores and cAMP elevated levels. The complex output in MCs intrinsic photosensitivity, involving calcium and cAMP signaling, remains to be elucidated; considering their multiple described functions, including a prominent regenerative potential in the retina in non-mammalian vertebrates, our results suggest a higher level of complexity for light sensing in the retina, involving photic activation of MCs in light-regulated circuits and pathways.</p>



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Title	Efeito do agonista (G-1) do receptor de estrogênio acoplado a proteína G (GPER) em artérias mesentéricas de resistência
Author	Nathalie Tristão Banhos Delgado
Affiliations	Ciências Fisiológicas- Universidade Federal do Espírito Santo
Contact	nathalie.tristao@gmail.com
Abstract	<p>O efeito protetor do estrogênio sobre o sistema cardiovascular é classicamente descrito e não pode ser explicado apenas por suas ações sobre os receptores de estrogênio clássicos (ER-α e ER-β). Um terceiro grupo de receptores foi recentemente descrito: os receptores de estrogênio acoplados à proteína G (GPER), responsáveis pelas respostas rápidas do estrogênio, e que também podem estar envolvidos nessa proteção. A cessação desses hormônios após a menopausa está associada à hipertensão e doenças cardiovasculares. Ademais, após resultados negativos da terapia de reposição hormonal na década de 90, novas terapias começaram a ser exploradas. Entre as mais promissoras está a descrição dos efeitos do GPER no sistema cardiovascular utilizando o G-1, seu agonista seletivo, considerado uma importante ferramenta farmacológica para estudar os efeitos provenientes da ativação do GPER e um potencial fármaco nas doenças cardiovasculares. No início da década de 90, foram clonados a partir de células B linfoblásticas humanas, GPCR órfãos, ou seja, receptores que não apresentavam ligante endógeno ou exógeno descrito. Estes receptores foram inicialmente designados como GPR30 devido à numeração consecutiva de receptores órfãos GPCR informados na literatura. No entanto, somente em 1997 foram descritos os primeiros indícios de que o GPR30 poderia estar relacionado à responsividade ao estrogênio. Também em 1997, foi relatado o primeiro estudo que indicou o papel desses receptores em células endoteliais, demonstrando a participação dos GPCR na resposta dos vasos ao shear stress, embora nenhum ligante específico tenha sido descrito na época. Somente em 2005, em células tumorais de mama, foi estabelecido o conceito de que o GPR30 é um receptor de estrogênio, levando à sua descrição como GPER. A ativação do GPER promove a manutenção da glicemia e apresenta ações antiaterogênicas. Ademais, a ausência de GPER provoca alterações em parâmetros metabólicos associados à obesidade e diabetes, tais como: aumento da adiposidade, piora no perfil lipídico, intolerância à glicose, resistência à insulina e elevação nos níveis de citocinas pró-inflamatórias. Promove também disfunção cardíaca por meio do aumento do estresse oxidativo. Por fim, o comprometimento da função do GPER pode estar associado ao aumento da pressão arterial e ao risco de hipertensão. Presente em diversos sistemas, no cardiovascular o GPER está amplamente distribuído e sua ativação promove o relaxamento de segmentos arteriais de diferentes tipos, leitos e espécies de animais. O GPER é encontrado tanto em células endoteliais quanto no músculo liso vascular de segmentos arteriais mesentéricos de ratos de ambos os sexos. Em ratos normotensos, a ativação do GPER promove o relaxamento de artérias mesentéricas de resistência de forma similar entre os sexos, com a participação endotelial e a ativação da via fosfatidilinositol-3-quinase/proteína quinase B/óxido nítrico sintase endotelial (PI3K-Akt-eNOS). Na deficiência endógena de hormônios sexuais, a ativação do GPER também promove relaxamento parcialmente dependente do endotélio em ambos os sexos, com maior participação do óxido nítrico (NO) proveniente de todas as três isoformas da NOS, sendo a induzível (iNOS) mais expressiva nos machos. Além disso, a via de sinalização rápida PI3K-Akt-eNOS é evidenciada nos machos, enquanto a via proteína quinase ativada por mitógeno/quinase regulada por sinal extracelular (MEK-ERK-eNOS) é evidenciada nas fêmeas. Na hipertensão, a ativação do GPER promove uma resposta de relaxamento similar em ratos de ambos os sexos, embora com a participação de distintos mediadores endoteliais. Nos machos, há uma dependência maior da via do NO, seguida pela via do peróxido de hidrogênio (H₂O₂), enquanto nas fêmeas, a resposta de relaxamento é mais dependente do endotélio com participação da via dos prostanoídeos (PNs) e do H₂O₂. De fato, a ativação do GPER aumenta a produção do H₂O₂ nesses segmentos arteriais. A presença do GPER no músculo liso vascular indica que a sua ativação pode induzir respostas de relaxamento mediante ações diretas sobre esse tecido. Essas ações podem ocorrer por modulação da atividade dos canais para K⁺ ou por ações sobre a mobilização do Ca²⁺ nessas células. Além disso, a ativação do GPER pode reduzir a sensibilidade do miofilamento ao Ca²⁺. Dessa forma, as informações geradas aqui poderão contribuir para uma melhor compreensão do papel do GPER no sistema cardiovascular e para o desenvolvimento de terapias mais eficazes para a pós-menopausa ou hipogonadismo em adultos (anteriormente conhecido como andropausa) associados à hipertensão essencial.</p>



Title	Contribution of renin-angiotensin-aldosterone and kallikrein-kinin systems to metabolic alterations associated to childhood obesity
Author	Nayara Azinheira Nobrega Cruz
Affiliations	Departamento de Medicina- Universidade Federal de São Paulo
Contact	azinheira.nayara@unifesp.br
Abstract	<p>Introduction: Overweight and obesity during childhood and adolescence is a major global public-health challenge as it has been associated with the early development of cardiometabolic diseases and premature mortality in adults. The rising prevalence of pediatric obesity worldwide has impacted on the prevalence of dyslipidemia secondary to obesity (DSO) which has superseded primary causes of dyslipidemia among children and adolescents. In this context, guidelines to treat and manage cardiovascular risk factors, including dyslipidemia, in pediatric patients are lagged. In addition, there is a knowledge gap on the mechanisms that may be triggered in DSO contributing to higher cardiovascular risk. Renin-angiotensin system (RAS) is an important hormonal system controlling blood pressure (BP) and electrolytic balance along with kallikrein-kinin system (KKS). Angiotensin-converting enzyme (ACE) is a component of RAS notorious for biosynthesizing Angiotensin (Ang) II, an active peptide that promotes vasoconstriction, cell growth and proliferation, oxidation, and inflammation. Besides, ACE is a metabolic pathway for Ang 1-7 and bradykinin (BK) catabolism. Ang 1-7 is a peptide of RAS that has counterregulatory effects on Ang II, and BK is an effector of KKS with potent vasodilatory effect. Recently, our group found that ACE expression is augmented in obese children and that ACE activity correlates with lipoprotein levels, lower levels of Ang 1-7 and BK were also observed suggesting that there is a relationship between ACE activity and pediatric dyslipidemia once the ACE activity can modulate Ang II, Ang 1-7, and BK levels. Objective: This study aimed to evaluate the enzymatic activity of the angiotensin-converting enzyme (ACE) in children and adolescents to investigate their relationship with dyslipidemia and other cardiometabolic alterations. Methods: Anthropometric measurements, blood pressure (BP), and fasting lipid concentrations were taken from 360 subjects aged 6 to 18 years from both sexes. Categorization was done according to the levels of each lipoprotein (total cholesterol, triglycerides (TG), LDL-C, HDL-C, and non-HDL-C) into three groups: normolipidemic (NL), borderline (BL), and dyslipidemic (DL). Enzymatic activity in urine was measured using the substrates Z-FHL-OH and hippuryl-HL-OH (h-HL-OH) and the ACE activity ratio (Z-FHL-OH/h-HL-OH) was calculated. Results: Dyslipidemic levels of HDL-C, TG, and LDL-C were observed in 23%, 9%, and 3% of the participants, respectively, and were more frequent in obese children (Chi-square, $p < 0.001$). ACE activity ratio was augmented in BL(HDL-C) when compared to NL(HDL-C) (5.06 vs. 2.39, $p < 0.01$), in DL(LDL-C) in comparison to BL(LDL-C) and NL(LDL-C) (8.7 vs. 1.8 vs. 3.0, $p < 0.01$), and in DL(non-HDL-C) than in BL(non-HDL-C) and in NL(non-HDL-C) (6.3 vs. 2.1 vs. 2.9, $p = 0.02$). The groups with impaired HDL-C and TG levels presented an increased diastolic BP percentile, and a higher systolic BP percentile was observed in BL(TG) and DL(TG). The carotid-femoral pulse wave velocity (cfPWV) was higher in the groups with DL levels of TG and LDL-C than in NL groups. Hypertriglyceridemia was associated with higher cfPWV. Conclusion: No direct impact of the ACE activity on BP values was observed in this cohort, however, there was an association between hyperlipidemia and ACE upregulation which can trigger mechanisms driving to early onset of hypertension and cardiovascular disease. Compliance with Ethical standards: All procedures were approved by the institutional ethics committee on human experimentation from UNIFESP (nº 83298217.1.0000.5505) and UFES (nº 83298217.1.3001.5060).</p>



Title	Estudo da vulnerabilidade do rim remanescente em decorrência de nefrectomia unilateral, quando submetido à nefropatia cristalina
Author	Neydiana Belize De Pina Lopes
Affiliations	Fisiologia e Biofísica- Universidade de São Paulo
Contact	neydianalopes@icb.usp.br
Abstract	<p>Introdução: A incidência de doença renal progressiva é um problema sério de saúde pública e o transplante renal é a melhor alternativa para pacientes em fase terminal. Entretanto, no doador, a nefrectomia unilateral (NU) pode resultar na sobrecarga do rim remanescente, podendo se tornar um fator relevante no desenvolvimento de injúria renal aguda (IRA) e aumentar a vulnerabilidade do rim remanescente à doença renal crônica (DRC). Portanto, o presente estudo tem como objetivo investigar a função do rim remanescente após a NU, sua resposta à nefrolitíase e os possíveis fatores e mecanismos envolvidos no seu estado de vulnerabilidade. Métodos: Camundongos C57BL/6J com oito semanas (n=23) foram divididos em quatro grupos: sham, submetidos a NU, oxalato de sódio (injeção intraperitoneal de 9 mg/100 g de NaOx para induzir nefrolitíase, 24 horas antes da eutanásia) e NU tratado com oxalato de sódio (NU/NaOx). Seis dias após a cirurgia sham ou NU e 24 horas antes da eutanásia, os camundongos foram tratados de acordo com o respectivo grupo e colocados em gaiolas metabólicas para o monitoramento de parâmetros metabólicos e da função renal. Ao final das vinte e quatro horas, os animais foram submetidos à anestesia com isoflurano (0,8 L/min/taxas de 5%), coleta de sangue e urina, remoção do rim esquerdo e eutanásia por exsanguinação, conforme protocolo aprovado pelo comitê de ética (CEUA-ICB/USP, nº 4550140422). Resultados: Uma semana após a cirurgia, os animais NU apresentaram um aumento significativo no fluxo urinário ($p < 0,04$), na relação peso do rim/peso corporal ($p < 0,003$) e na creatinina plasmática ($p < 0,004$) quando comparados aos animais sham. Também apresentaram um aumento significativo na expressão de RNAm para Mki-67 ($p < 0,02$), um biomarcador da regeneração tubular e reparo renal após a IRA. Ainda nesse grupo, observamos um aumento na expressão de RNAm para Col1A1 ($p < 0,05$) e Col4A1 ($p < 0,05$) e na expressão proteica de um marcador específico de macrófagos, F4/80 ($p < 0,004$). Diante do insulto com NaOx, os animais NU/NaOx apresentaram hipertrofia renal mais pronunciada ($p < 0,02$), maior acúmulo de creatinina no plasma ($p < 0,003$) e maior expressão de RNAm para fatores de injúria tubular, como Havcr1 (Kim-1) ($p < 0,006$) e LCN2 (NGAL) ($p < 0,0006$) e expressão proteica de Kim-1 ($p < 0,003$), quando comparados aos animais NaOx. Conclusão: Nossos achados indicam que o rim remanescente apresenta vulnerabilidade, o que afetou sua resposta ao insulto e pode potencialmente dificultar a melhora e contribuir para o desenvolvimento da DRC.</p>



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Title	Consequências do hipotireoidismo na ritmicidade central e periférica do metabolismo
Author	Paula Bargi De Souza
Affiliations	Departamento Fisiologia e Biofísica- Universidade Federal de Minas Gerais
Contact	bargisouzap@gmail.com
Abstract	<p>A ritmicidade é fundamental para a manutenção da homeostasia do organismo frente às demandas do dia a dia. Em mamíferos, a ritmicidade circadiana já foi descrita em diversos parâmetros fisiológicos e comportamentais como atividade locomotora espontânea, temperatura corporal, ciclo sono-vigília, síntese e secreção hormonal, dentre outros. A dessincronização destes processos rítmicos está associada à maior prevalência de cânceres, doenças cardiovasculares, distúrbios endócrinos e metabólicos, como as desordens tireoidianas e o câncer de tireóide. Os hormônios tireoidianos, tetraiodotironina (T4) e triiodotironina (T3) agem basicamente em todos os tecidos por meio de ações genômicas ou não genômicas, regulando diversas funções das quais destacam-se o metabolismo basal e a manutenção da temperatura corporal, que apresentam ritmicidade circadiana bem definida. Em contrapartida, as disfunções tireoidianas, como o hipotireoidismo está associado a alterações na maquinaria molecular dos relógios biológicos central, localizando no núcleo supraquiasmático do hipotálamo e de órgãos alvos periféricos como a glândula adeno-hipófise, componente central dos eixos endócrinos, o coração e o intestino proximal. Assim, a dessincronização dos relógios circadianos central e periféricos pode explicar, ao menos em parte, a ampla variedade de alterações metabólicas e sintomas em decorrência do hipotireoidismo e a sua associação com diabetes mellitus, síndrome metabólica e prejuízos cognitivos.</p>



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 Hotel Glória Caxambu Resort & Convention

Title	Ritmos da Vida: do controle molecular ao comportamento
Author	Paula Bargi De Souza
Affiliations	Departamento Fisiologia e Biofísica- Universidade Federal de Minas Gerais
Contact	bargisouzap@gmail.com
Abstract	<p>A vida na Terra evoluiu sob condições cíclicas de alternância entre dia e noite gerado pelo padrão rotacional do planeta. A alternância rítmica da presença ou ausência de luz com duração de cerca de 24 h está associada ao padrão de evolução convergente dos ritmos circadianos, ou seja, diferentes espécies desenvolveram mecanismos semelhantes para sincronizar seus processos biológicos com os ciclos ambientais de aproximadamente 24 horas, independente do padrão de atividade das espécies. A geração da ritmicidade endógena apoia-se na atividade de um conjunto de genes e seus produtos proteicos, que por meio de alças positivas e negativas e ações transcricionais e pós transcricionais, se autorregulam e também modulam a ritmicidade de diversos componentes celulares. Este mecanismo endógeno oscilatório, conhecido como o relógio biológico, está presente em todas as células e tecidos e possibilita a antecipação e adaptação do organismo às mudanças diárias no ambiente interno e externo, sendo tal característica fundamental para a sobrevivência de muitas espécies. De maneira geral, a atividade rítmica do mecanismo oscilatório endógeno sincroniza a expressão e atividade de componentes e vias intracelulares envolvidas na geração e/ou utilização de substratos energético de acordo com a fase de atividade do organismo, otimizando as respostas celulares, fisiológicas e comportamentais ao longo das 24 h. Deste modo, a ritmicidade circadiana pode ser observada em basicamente todos os tipos de comportamentos como ingestão alimentar e hídrica, atividade e repouso, reprodutivo, bem como no metabolismo energético, frequência cardíaca e respiratória, temperatura corporal, dentre outros. Embora este mecanismo seja autossustentável, diversos estímulos e fatores ambientais como a luz, a temperatura, a disponibilidade e tipo de nutrientes e diversos hormônios fornecem pistas temporais, atuando em conjunto na sincronização das respostas metabólicas celulares. Assim, o entendimento da regulação e sincronização do relógio biológico e seu controle sobre o metabolismo e função celular é de extrema importância para a compreensão dos mais variados tipos de comportamentos rítmicos encontrados nos seres vivos, enriquecendo nossa compreensão da evolução e da fisiologia, mas também com implicações significativas para áreas como medicina e cronoterapia. Nesta aula do curso, os mecanismos moleculares transcricionais e pós transcricionais envolvidos na geração e manutenção da ritmicidade circadiana serão abordados.</p>



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Title	Eletrônica básica: construindo circuitos para o ensino de Fisiologia
Author	Paulo Fernando Guedes Pereira Montenegro
Affiliations	Departamento de Sistemática e Ecologia- UFPB- UNIVERSIDADE FEDERAL DA PARAÍBA
Contact	pmonte@dse.ufpb.br
Abstract	<p>Processos fisiológicos envolvem sequência de eventos complexos, e seu aprendizado pode se tornar difícil caso não haja motivação dos estudantes. Uma das formas de gerar esse envolvimento é a utilização de metodologias ativas de aprendizagem, representadas por um conjunto de estratégias didáticas que colocam o aluno como protagonista do processo de aprendizagem, estimulando sua autonomia e contribuindo para a construção do conhecimento. O uso de modelos físicos é um exemplo de metodologia ativa, pois envolve os alunos no mapeamento de atributos entre o modelo e o processo de interesse. Modelos físicos são objetos concretos utilizados como modelos analógicos para representar uma estrutura, fenômeno ou conceito, e permitem experiências ativas de manipulação, contribuindo para o desenvolvimento de domínios cognitivos complexos. Circuitos eletrônicos são um interessante modelo físico porque podem simular facilmente processos fisiológicos simples de estímulo-resposta. Nesta palestra iremos apresentar relatos de experiência na construção e utilização de modelos físicos baseados em circuitos eletrônicos simples, utilizados como recurso didático nas aulas de fisiologia humana e animal comparada para os cursos de licenciatura e bacharelado em Ciências Biológicas da Universidade Federal da Paraíba – Campus I (João Pessoa). Serão discutidas as potencialidades no uso desses recursos e os desafios para a sua implementação em sala de aula.</p>



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Title	Uso de nanopartículas em terapias avançadas
Author	Pedro Pires Goulart Guimaraes
Affiliations	Fisiologia e Biofísica- Universidade Federal de Minas Gerais
Contact	ppiresgo@gmail.com
Abstract	<p>Com o avanço da tecnologia de entrega de ácidos nucleicos, novas plataformas de nanopartículas lipídicas (LNPs) estão sendo desenvolvidas. A entrega de mRNA para expressão gênica destacou-se recentemente devido à produção das vacinas para COVID-19. No entanto, a entrega de RNA de silenciamento (siRNA) utilizando LNPs já foi aprovada pelo FDA como uma terapia inovadora para edição gênica em doenças hereditárias. Esses avanços possibilitam o desenvolvimento de novas plataformas de ácidos nucleicos que podem ser produzidas e comercializadas a um custo menor em comparação com a tecnologia de mRNA. Nesse contexto, nosso grupo trabalha no desenvolvimento de plataformas de nanoformulações para terapias avançadas, incluindo formulações para tratamento do câncer e vacinas contra doenças infecciosas, com demonstração de eficácia em modelos pré-clínicos. O desenvolvimento dessas plataformas para entrega de ácidos nucleicos, que será abordado no simpósio, abre caminho para novas abordagens que exigem a entrega intracelular de DNA, mRNA ou siRNA.</p>



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Title	Liver glucose output contributes to hyperglycemia in non-obese diabetic rats
Author	Priscila Cassolla
Affiliations	Ciências Fisiológicas- Universidade Estadual de Londrina
Contact	pricassolla@uel.br
Abstract	<p>The liver is essential for maintaining glycemia due to the flow of metabolic pathways in this organ, especially carbohydrate metabolism. Changes in hepatic metabolism are associated with several diseases, like as Diabetes mellitus (DM). DM is a chronic disease of global proportions resulting from defects in the production, secretion, and/or action of insulin. In general, type 2 DM (DM2), which is the most prevalent, has been associated with obesity, however, especially in East Asia, a portion of the diabetic population is eutrophic or has a low body mass index. Despite the increasing number of cases of non-obese DM2, the pathophysiological mechanisms of these cases are not yet completely elucidated. Thus, it is interesting to study the hepatic metabolism of Goto-Kakizaki (GK) rats, an isogenic lineage with spontaneous insulin resistance without obesity, which presents a chronology of the disease very similar to that of humans. GK animals present moderate hyperglycemia, glucose intolerance, insulin resistance, dyslipidemia, inflammation, and oxidative stress. There are discrepancies in the literature regarding gluconeogenesis and glycogenolysis in adult GK rats, and there is a lack of studies on the onset of metabolic changes in this experimental model. Therefore, this lecture aims to present the history of the art and news about the contribution of liver gluconeogenesis and glycogenolysis to chronic hyperglycemia at the beginning of the development of DM2 in GK rats.</p>



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Title	Efeito da suplementação com óleo de peixe sobre a função renal de ratos e camundongos obesos
Author	RICARDO FERNANDEZ PEREZ
Affiliations	FISIOLOGIA- UNIVERSIDADE FEDERAL DO PARANÁ- UFPR
Contact	ricfer@ufpr.br
Abstract	<p>A obesidade e o excesso de peso são considerados uma pandemia em crescimento, afetando cerca de 2 bilhões de pessoas. A obesidade gera distúrbios metabólicos sistêmicos e teciduais, como resistência à insulina, dislipidemia, hipertensão e doenças cardiovasculares e renais. A doença renal crônica, que atinge 10% da população adulta, é relacionada na maioria dos casos com a obesidade, resistência à insulina e hipertensão e resulta em progressivo declínio da função renal com aumento da morbimortalidade. A obesidade infantil persiste na vida adulta junto com as comorbidades a ela relacionadas, incluindo alterações na função renal. O óleo de peixe, rico em ácidos graxos n-3, é considerado um modulador do sistema imune, do metabolismo lipídico e energético. Nos últimos anos nosso laboratório tem estudado o efeito da obesidade na função renal e metabólica utilizando dois modelos de obesidade em roedores: ingestão crônica de uma dieta hiperlipídica em camundongos e sobrenutrição perinatal em ratos, avaliando o efeito da suplementação por 30 dias com óleo de peixe (OP) sobre estes parâmetros. No primeiro estudo foram utilizados camundongos Swiss adultos que consumiram por 8 semanas ração rica em lipídeos (HF) ou ração padrão (S) (26 e 63% de carboidratos; 15 e 26% de proteínas; 59 e 11% de lipídeos, respectivamente). A indução do modelo foi avaliada acompanhando o ganho de peso e a intolerância à glicose pelo teste de tolerância intraperitoneal à glicose (TTIG) e área sob a curva (AUC) do TTIG. No período de indução, a dieta HF gerou aumento da intolerância à glicose e do ganho de peso. A dieta HF reduziu a filtração glomerular, fluxo urinário e a uremia. Esta dieta elevou também a albuminúria e a concentração de TNF-α renal e reduziu a expressão proteica de COX-2, efeito revertido pela suplementação com OP. A dieta HF alterou o manejo tubular de sódio, com redução da fração de excreção de Na⁺, efeito revertido pela suplementação com OP. O OP reduziu a marcação de vimentina nos túbulos, de pJNK nos glomérulos e de α-SMA glomerular e tubulointersticial; ainda, elevou a adiponectinemia com redução da concentração de TNF-α no plasma e rim. No modelo de sobrenutrição perinatal neonatos da linhagem Wistar machos foram randomizadas em ninhadas de 10 animais, formando o grupo controle (CTL) e ninhadas reduzidas para 3 animais ao terceiro dia pós-natal, formando o grupo obeso (OBS). Os animais foram acompanhados durante 180 dias, sendo suplementados nos últimos 30 dias com OP por via oral. Ao longo do experimento longitudinal, o grupo OBS teve maior ganho de peso bruto que o grupo CTL. Apesar disso, a ingestão de comida não foi diferente entre os grupos, mas a ingestão de água e a diurese foram reduzidas no grupo OBS. O clearance de creatinina caiu significativamente no grupo OBS aos 150 dias, demarcando o início das alterações renais causadas pelo modelo de obesidade. Além disso, uma maior excreção de albumina na urina ocorreu aos 90 e 120 dias no grupo OBS. Aos 180 dias, o grupo OBS teve maior peso que o grupo CTL, a ingestão de comida permaneceu igual entre os grupos, mas a ingestão de água e a diurese foram reduzidas nos grupos OBS e OBS suplementado (OBS-S). O grupo OBS teve maior peso da gordura mesentérica em relação ao grupo CTL e o grupo OBS-S teve redução neste parâmetro em relação ao grupo OBS. Os animais do grupo OBS e CTL não apresentaram diferenças na glicemia basal, na tolerância a glicose e ou perfil lipídico. No entanto, a suplementação reduziu o colesterol total nos grupos CTL-S e OBS-S. O clearance de creatinina foi reduzido nos grupos OBS e OBS-S e estes grupos tiveram maior albuminúria. O manejo de Na⁺ não foi modulado pela obesidade, mas foi aumentado no grupo CTL-S. Apesar disso, os grupos OBS e OBS-S tiveram maior excreção bruta de Na⁺. A concentração de adiponectina plasmática não diferiu entre os grupos, mas a suplementação tendeu a aumentar este parâmetro no grupo CTL-S. A concentração de TNFα no tecido renal foi aumentada nos grupo obesos. A concentração urinária de TXB2 foi reduzida nos grupos obesos, e a suplementação reduziu a concentração urinária de metabólitos da PGE2 na urina. Portanto, a obesidade gerada nestes modelos provocou inflamação e redução da função renal. O OP atuou com efeito anti-inflamatório sistêmico e renal, revertendo parcialmente às alterações geradas pela obesidade.</p>





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Title	Hepatic parenchymal heterogeneity and insulin resistance
Author	ROBERTO BARBOSA BAZOTTE
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas- UEM- Universidade Estadual de Maringá
Contact	rbbazotte@gmail.com
Abstract	States of insulin resistance are generally characterized by chronic hyperinsulinemia, often associated with excess weight and potentially manifesting as prediabetes or type 2 diabetes mellitus. In insulin resistance, it is observed that hepatic glucose production (inhibited by insulin) and lipid synthesis (stimulated by insulin) can simultaneously intensify. This suggests that a state of insulin deficiency or excess can coexist in this context. The possibility that insulin can act insufficiently or excessively in different organs and tissues or within the same organ or tissue has various physiological and pathophysiological implications. Based on the concept of metabolic compartmentalization in the liver, we propose that the process of insulin resistance accentuates the differences between periportal and perivenous hepatocytes, particularly in periportal glucose production and perivenous lipid synthesis. Thus, the coexistence of glucose overproduction and lipid accumulation could occur in the liver of individuals with insulin resistance. In this conference, we propose to present an integrated view of the mechanisms by which excessive glucose production in periportal hepatocytes and lipid accumulation in perivenous hepatocytes interact in states of insulin resistance.



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Title	Aspectos cronobiológicos e suas implicações para o delineamento experimental de estudos de Fisiologia
Author	Rodrigo Antonio Pelliciar Garcia
Affiliations	Departamento de Ciências Biológicas- UNIFESP
Contact	rodrigousp@gmail.com
Abstract	<p>A ritmicidade circadiana é fundamental para a manutenção da homeostasia do organismo frente às demandas diárias, sendo gerada por um grupo de genes que se autorregulam ao longo do período de 24 h. A luz é um dos principais fatores que sincronizam a oscilação dos chamados relógios biológicos, no entanto, outros fatores como a temperatura, atividade física e até mesmo certos tipos de comportamentos, como o padrão diário de ingestão alimentar também interferem na dinâmica temporal dos mecanismos geradores de ritmicidade. Contudo, os padrões modernos da sociedade e a excessiva exposição à luz artificial durante a noite resultam em condições constantes de dessincronização dos processos rítmicos biológicos, não apenas dos seres humanos mas em diversos seres vivos. A dessincronização dos ritmos biológicos está associada ao desenvolvimento de vários distúrbios e patologias como obesidade, síndrome metabólica, diabetes e cânceres. Dessa forma, um dos grandes desafios nos estudos de Fisiologia está relacionado à utilização de abordagens cronobiológicas para a avaliação de parâmetros diversos e na manutenção dos processos rítmicos nos modelos experimentais utilizados em laboratórios, respeitando as fases de atividade e repouso dos animais de acordo com os hábitos de cada espécie. Nessa discussão iremos abordar estratégias experimentais in vivo e in vitro que podem ser utilizadas levando em consideração a sincronização da ritmicidade biológica. Tais abordagens irão indubitavelmente ampliar o conhecimento acerca da sincronização dos processos fisiológicos permitindo a realização de protocolos experimentais que buscam mitigar os efeitos deletérios da dessincronização da ritmicidade biológica.</p>



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Title	Atualizando o conhecimento sobre a ação dos hormônios sexuais e a função vascular
Author	Roger Lyrio Dos Santos
Affiliations	Ciências Fisiológicas- UFES
Contact	rogerlyrio@hotmail.com
Abstract	<p>Como esteroides, os hormônios sexuais podem agir sobre as células dos vasos sanguíneos atravessando a membrana plasmática e interagir com receptores intracelulares para exercerem efeitos diretos sobre sequências específicas do DNA. Além disso, podem ativar vias de sinalização intracelulares já existentes, sem a necessidade de ativação gênica ou de síntese proteica. As ações sobre o DNA são conhecidas como ações genômicas, nucleares, clássicas ou canônicas, enquanto as ações que ocorrem por ativação rápida de vias de sinalização intracelulares são conhecidas como ações não-genômicas, extra-nucleares, não clássicas ou não canônicas. Tanto as ações genômicas quanto as não genômicas são mediadas por receptores específicos (embora alguns receptores possam responder a mais de um tipo de hormônio sexual). As ações genômicas da progesterona são mediadas pelos receptores PR-A, PR-B e PR-C, enquanto as ações não genômicas pelos receptores de membrana (mPRs): mPRα, mPRβ, mPRγ, mPRδ e mPRϵ. Para os estrogênios, as ações genômicas são mediadas pelos receptores ER-α ou NR3A1 e ER-β ou NR3A2, enquanto as ações não genômicas estão associadas principalmente à ativação do receptor de estrogênio acoplado à proteína G (GPER). Em relação à testosterona, as ações genômicas são mediadas pelos receptores AR-A e AR-B, enquanto as ações não genômicas ocorrem por modulação de íons através da membrana plasmática e aumento de segundos mensageiros de sinalização celular após a ativação dos GPCR, como o GPRC6A e o TRPM8. As ações vasculares dos hormônios sexuais ocorrem graças a presença de receptores nas diferentes camadas dos vasos sanguíneos. De fato, a descoberta de receptores de progesterona tanto no endotélio quanto no músculo liso, é um indicativo de seu importante papel para a regulação da homeostase vascular. No endotélio, a progesterona exerce uma influência significativa, estimulando a síntese e liberação de mediadores como óxido nítrico (NO), prostanoídes (PNs) e outras substâncias vasoativas. Já em relação ao músculo liso vascular (MLV), a ação da progesterona inclui a regulação negativa sobre os canais para Ca²⁺ tipo L dependentes de voltagem (LTCCs), resultando na redução do influxo de Ca²⁺ em diversos tipos de vasos, como anéis de aorta, coronárias, artéria basilar e carótida interna. Além dessas, a incubação com progesterona em células do MLV de aorta de ratas promove aumento na produção de peróxido de hidrogênio (H₂O₂). No que se refere aos estrogênios e suas ações sobre o endotélio, o estradiol (E₂), por exemplo, possui uma participação efetiva no controle do tônus vascular e na liberação de agentes vasoativos, por estimular a produção e liberação dos fatores de relaxamento derivados do endotélio (EDRFs), como o NO e os PNs, bem como e a hiperpolarização dependente do endotélio (EDH). Em relação às ações sobre o MLV, os estrogênios promovem diminuição na [Ca²⁺]_i, por agirem diretamente sobre os LTCCs no MLV, reduzindo sua probabilidade de abertura e consequentemente o influxo de Ca²⁺ por esses canais. Além disso, o E₂ promove aumento na recaptação de Ca²⁺ pelo retículo sarcoplasmático, aumento da probabilidade de abertura dos BKCa, e atenua a contração induzida pelo K⁺ e a fosforilação da cadeia leve de miosina (MLC) produzindo relaxamento rápido e sem diferença entre os tipos de segmentos vasculares (artéria femoral ou veia porta) e sexo. A testosterona, por sua vez, atua sobre o endotélio modulando a expressão da enzima óxido nítrico sintase (NOS), enzima que atua na formação de NO. A testosterona também estimula a síntese de PNs no endotélio, e estimula a via de EDH. Sobre o MLV, a testosterona atua sobre os canais para K⁺, aumentando a sua probabilidade de abertura e também pode atuar como antagonista dos canais para Ca²⁺, promovendo menor influxo de Ca²⁺ e consequente vasodilatação. Cabe ressaltar, que as ações de todos os hormônios sexuais variam de acordo com o leito vascular, o sexo e a espécie estudada. Por fim, a caracterização das ações dos hormônios sexuais sobre o sistema vascular permite não apenas uma melhor compreensão da ação desses hormônios, mas também pode contribuir para o desenvolvimento de melhores formas de terapia em situações em que ocorre deficiência endógena de hormônios sexuais, como na pós-menopausa e no hipogonadismo tardio, ou ainda em situações de hipersecreção de tais hormônios.</p>





Title	As contribuições da Cronobiologia para Educação
Author	Rubia A. Pereira De Carvalho Mendes
Affiliations	Departamento de Estudos Culturais- Universidade de São Paulo
Contact	rpcmendes@gmail.com
Abstract	<p>A Cronobiologia é o estudo da organização temporal dos seres vivos, especialmente os ritmos biológicos, entre os quais o ciclo sono/vigília tem sido frequente objeto de análises. Os estilos de vida predominantes nas sociedades contemporâneas ocidentalizadas interferem, em grande parte, na manifestação rítmica do ciclo sono/vigília no ser humano em favor de ritmos sociais muitas vezes hostis, que atendem prioritariamente aos interesses do capital econômico. Ambientes físicos e virtuais exigem cada vez mais tempo para o trabalho e para o consumo, e o tempo para o descanso torna-se mais restrito. Uma das consequências desse fenômeno está caracterizada pela irregularidade e/ou fragmentação do ciclo sono/vigília ao longo da semana (restrição do tempo de sono nos dias úteis por conta dos compromissos sociais e extensão nos finais de semana e feriados). Esse padrão, que com o tempo ocasiona comprometimento na saúde das pessoas, é verificado no público escolar e tem se tornado uma grande preocupação para profissionais da educação e saúde. Um exemplo que contribui para a manifestação deste padrão é o uso de aparelhos eletrônicos à noite para atividades de estudo e lazer, pois a luz azul emitida por estes aparelhos ocasiona o atraso no início da fase de sono e os estudantes que precisam acordar cedo no dia seguinte para ir à escola também acabam manifestam cochilos em sala de aula. A estrutura educacional não está preparada para auxiliar esses estudantes quanto a sua organização temporal, nem para considerar as preferências de horários para realização das atividades. Educadores geralmente não sabem como lidar com o sono na sala de aula, pois em muitos casos esse sono é confundido com desinteresse e isso cria estigmas na relação professor/aluno, sendo que o ideal seria os professores serem capacitados, por exemplo, para informar os estudantes sobre o uso da luz artificial à noite, bem como promover uma “consciência de liberdade” no que se refere ao conhecimento do próprio corpo por meio do respeito aos ritmos biológicos. Coisas simples, como observar os horários de sono, alimentação, o momento do dia de maior atenção e desempenho para realizar atividades, podem contribuir muito para qualidade de vida e desempenho acadêmico. Atualmente o ensino de Cronobiologia é oferecido somente em alguns cursos de graduação e pós-graduação, em geral nos currículos dos cursos de biologia e áreas afins. Não há uma sistematização destes conhecimentos para os profissionais da educação em geral, embora temas relacionados a eles constem na Base Nacional Comum Curricular (BNCC), que é o documento orientador da educação básica. Como consequência, o professor acaba não conseguindo identificá-los nas habilidades e competências propostas no documento e consequentemente os conhecimentos de Cronobiologia não são abordados em sala de aula. Além disso, essa reflexão interdisciplinar entre as áreas do conhecimento se faz cada vez mais necessária e urgente. Situação que exige uma revisão dos programas de ensino superior relacionado à formação de educadores. Desse modo, gostaria de compartilhar algumas experiências que tenho vivenciado juntamente com o Grupo Multidisciplinar de Desenvolvimento e Ritmos Biológicos (GMDRB) por meio do oferecimento de cursos de extensão para educadores. Os cursos foram realizados pela Escola de Artes Ciências e Humanidades da Universidade de São Paulo (EACH-USP) e tem como objetivo situar a Cronobiologia dentro dos parâmetros curriculares, com o intuito de demonstrar as possibilidades de trabalhar seus conceitos na Educação Infantil, Ensino Fundamental e Médio, bem como trazer exemplos de atividades que podem ser trabalhadas dentro de sala de aula. Assim, poderemos promover às futuras gerações uma escolha consciente dos caminhos a seguir em relação a atender ou não as necessidades do organismo, mais precisamente com relação aos ritmos biológicos, bem como conhecer as medidas que podem ser tomadas para amenizar os efeitos da má qualidade do sono. A principal ferramenta de divulgação do trabalho do grupo é uma animação denominada “Tempo na vida”, disponível no site da EACH-USP (http://www.each.usp.br/crono/home), que pode ser utilizada por professores em sala de aula. Portanto, deixo o convite para que mais pessoas possam refletir sobre o assunto e até mesmo compartilhar estes desafios.</p>



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Title	Integração do metabolismo durante o exercício físico
Author	Sandro Massao Hirabara
Affiliations	Programa de Pós-graduação Interdisciplinar em Ciências da Saúde- Universidade Cruzeiro do Sul
Contact	sandromh@yahoo.com.br
Abstract	<p>Durante o exercício físico, os músculos em atividade devem constantemente produzir ATP para fornecer a energia necessária para a contração muscular. As fibras musculares dispõem de três vias geradoras de ATP principais: a) sistema ATP-fosfocreatina, b) via glicolítica e c) sistema oxidativo, os quais são diferencialmente utilizados para atender as demandas energéticas conforme cada tipo de exercício físico. Uma série de alterações metabólicas ocorrem e são necessárias para atender essa demanda energética. A glicose e os ácidos graxos são os principais substratos energéticos, enquanto os aminoácidos têm contribuição menor, porém podem ter sua contribuição significativamente maior em determinadas condições. O sistema ATP-fosfocreatina utiliza a fosfocreatina, uma forma de armazenamento de ATP, para a geração de energia imediata no início do exercício físico. Entretanto, a reserva intracelular de fosfocreatina é muito limitada, suportando a geração de ATP por poucos segundos (3-5 s) em uma atividade de alta intensidade. A via glicolítica utiliza a glicose proveniente da corrente sanguínea ou do estoque de glicogênio intracelular. Quanto maior a intensidade do exercício físico, maior a geração do ácido láctico por essa via, o que é necessário para a reciclagem de NAD⁺, permitindo sua reutilização pela via glicolítica. Devido a sua baixa eficiência energética, a via glicolítica suporta atividades de alta intensidade por poucos minutos. O sistema oxidativo é mais versátil e complexo. Apesar da velocidade de geração de ATP ser relativamente muito mais lenta que nos demais sistemas e da necessidade de oxigênio, sua alta eficiência garante a produção da energia necessária para a execução de atividades leves a moderadas de longa duração (várias horas). Diversos fatores estão envolvidos na regulação do metabolismo energético durante o exercício físico, incluindo fatores neurais, humorais e hormonais, os quais agem em diferentes tecidos-alvo para a homeostase metabólica de forma integrada. Além disso, o exercício físico causa, principalmente a médio e longo prazo, várias adaptações fisiológicas que melhoram a eficiência energética por vias específicas, de acordo com as características de cada tipo de exercício físico. Todas as alterações e adaptações induzidas pelo exercício físico são integradas com difentes órgãos e tecidos, de forma a garantir a funcionalidade muscular nessa condição.</p>



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Title	Efeitos da progesterona sobre a reatividade vascular em fêmeas
Author	TAGANA ROSA DA CUNHA
Affiliations	Ciências Fisiológicas- UFES
Contact	taganarosa@gmail.com
Abstract	<p>Apesar dos significativos avanços nas pesquisas envolvendo a progesterona e nas descobertas de suas ações sobre diversos sistemas, incluindo o cardiovascular, os estudos que exploram a progesterona em contextos além do sistema reprodutor ainda são recentes e escassos, especialmente quando comparados aos estudos sobre outros hormônios sexuais. Este cenário decorre, em parte, devido a publicação no final da década de 1990 de resultados negativos associados à terapia de reposição hormonal (TRH) com estrogênio e acetato de medroxiprogesterona, um progestágeno sintético. Esses resultados culminaram em uma redução significativa na utilização da TRH clássica e o início de uma nova fase, onde outras formas de terapia passaram a ser testadas. Entre essas novas abordagens, destaca-se a investigação dos efeitos da progesterona bioidêntica sobre o sistema cardiovascular, especialmente quando administrada na forma de progesterona micronizada. Os efeitos dessa forma de progesterona diferem significativamente daqueles típicos dos progestágenos sintéticos, conhecidos como progestinas. A progesterona é um dos hormônios sexuais femininos, e a presença de receptores de progesterona nos vasos sanguíneos destaca a relevância desse hormônio na regulação da homeostase no sistema vascular. Pesquisas recentes têm demonstrado que a progesterona possui ação independente do estrogênio na prevenção de doenças cardiovasculares, fornecendo cardioproteção, particularmente para as mulheres. Este efeito benéfico da progesterona se deve à sua influência sobre diversos fatores de risco cardiovascular, dentre estes fatores podemos destacar a modulação da pressão arterial, uma vez que a progesterona diminui a pressão arterial em homens hipertensos e em mulheres na pós-menopausa. A progesterona também é capaz de diminuir a resistência vascular sistêmica em mulheres normotensas. Esses benefícios da progesterona sobre a pressão arterial têm relação com a sua ação direta sobre os vasos sanguíneos. Estudos recentes do nosso grupo de pesquisa demonstraram efeitos benéficos da progesterona bioidêntica, sobre o sistema vascular. De fato, a progesterona promove vasodilatação direta em artérias coronárias, mesentéricas, e aorta, assim como pode melhorar a vasodilatação dependente do endotélio de animais normotensos e hipertensos no leito coronariano. A ação da progesterona sobre o endotélio vascular tem relação com o aumento da síntese de mediadores como óxido nítrico (NO) e prostanoídes, e atualmente trabalhos têm demonstrado que a progesterona exerce efeito modulatório sobre a hiperpolarização dependente do endotélio (EDH), contribuindo para um efeito vasodilatador. No músculo liso vascular, a progesterona induz relaxamento por meio da regulação negativa dos canais de cálcio, diminuindo o influxo de cálcio em diferentes tipos de vasos. Também influencia a atividade de enzimas antioxidantes e a expressão de proteínas relacionadas à contração muscular, proporcionando efeitos benéficos na fisiologia vascular, além de inibir a proliferação de células musculares lisas vasculares e a agregação plaquetária, dessa forma, protege os vasos do desenvolvimento de aterosclerose. O conjunto de evidências aqui apresentado destacam a importância da progesterona na regulação vascular e na prevenção de distúrbios cardiovasculares, e é de grande importância, podendo ser utilizado no futuro para o desenho e aprimoramento de terapias e tratamentos clínicos.</p>





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Title	Variabilidade glicêmica e ritmicidade da glicemia como ferramenta do estudo do ritmo do comportamento alimentar
Author	Tatienne Neder Figueira Da Costa
Affiliations	Curso de Nutrição- Universidade Federal do Tocantins-UFT
Contact	tatienne_neder@outlook.com
Abstract	<p>Da bancada ao leito, investigar e adotar estratégias de manejo terapêutico que visam um melhor controle glicêmico, especialmente em indivíduos diabéticos, é de fundamental importância, a fim de evitar/retardar as diversas complicações associadas ao diabetes mellitus. Dentre os biomarcadores bioquímicos comumente relacionados ao controle glicêmico destacam-se a glicemia de jejum, insulina basal, teste oral de tolerância à glicose, hemoglobina glicada e índices relacionados à resistência à insulina, como o HOMA-IR. Contudo, tais parâmetros apresentam limitações, uma vez que são incapazes de detectar, de maneira contínua, variações intra e interdía da glicemia que ocorrem em resposta a estímulos como padrão temporal da ingestão alimentar e do ciclo sono/vigília, bem como o impacto da inter-relação entre esses componentes no padrão da variabilidade glicêmica. A partir de dados obtidos de sujeitos diabéticos e de indivíduos cegos que vêm sendo estudados no Laboratório de Neurobiologia e Ritmicidade Biológica (LNRB) da UFRN, o estudo da variabilidade glicêmica tem mostrado ser uma importante ferramenta de avaliação do ritmo alimentar. A investigação de fatores que possam minimizar a variabilidade glicêmica é de grande relevância clínica, dado que grandes variabilidades glicêmicas têm sido associadas a maior risco de complicações micro e macrovasculares do diabetes.</p>



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Title	AULA 2- Variabilidade Glicêmica: A homeostasia rítmica no controle da glicemia
Author	Tatienne Neder Figueira Da Costa
Affiliations	Curso de Nutrição- Universidade Federal do Tocantins-UFT
Contact	tatienne_neder@outlook.com
Abstract	A variabilidade glicêmica, isto é, as oscilações nos níveis de glicose no sangue que ocorrem ao longo do dia, bem como as flutuações na glicemia que ocorrem em um mesmo tempo em diferentes dias representa um fenômeno fisiológico, que é resultado não apenas do ritmo circadiano dos hormônios envolvidos na regulação do metabolismo da glicose, mas também da elevação pós-prandial da glicemia em resposta ao consumo de carboidratos e sua queda nos períodos interdigestivos. Nesta aula, serão abordados os mecanismos envolvidos na regulação rítmica da glicemia, bem como alguns fatores que podem prejudicar essa homeostase rítmica, podendo, desta forma, contribuir para um risco aumentado do desenvolvimento do diabetes mellitus e suas diversas complicações associadas.



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Title	Algorithms and Neural Circuits in Olfaction
Author	Venkatesh N Murthy
Affiliations	Moe- N/A
Contact	vnmurthy@fas.harvard.edu
Abstract	The olfactory system senses chemicals in the environment to guide behavior in animals. Fluctuating mixtures of chemicals, transported in fluid environments, are detected by an array of olfactory sensors and parsed by neural circuits to recognize odor objects, which then inform behavioral decisions. Some key questions for chemical sensing systems include how they can detect relevant molecules that are embedded in a sea of distractors, and how they use sparse intermittent stimuli to navigate. We work with theorists to frame these questions quantitatively and use experiments in mice to address them. I will present some examples from our recent and ongoing work.



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Title	Mesa Redonda- Inovação em Fisiologia: Conhecimento e Impacto na Sociedade
Author	Walker Magalhães Lahmann
Affiliations	ACFB- Eurofarma
Contact	wlahmann@icloud.com
Abstract	Discutir o processo de desenvolvimento tecnológico e de produtos a partir do conhecimento em fisiologia, abordando os passos necessários para sair do ambiente acadêmico e alcançar a entrega de soluções para a sociedade. Explorar também os aspectos legislativos e das agências de fomento que podem impulsionar o sistema, bem como oportunidades nas empresas, e como os fisiologistas podem se adaptar ao mundo da inovação, contribuindo não só com a importante pesquisa básica, mas também para a entrega de produtos e tecnologias aplicáveis, fomentando o empreendedorismo e a inserção de mestres e doutores nas empresas.



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Title	Hormônios sexuais masculinos e reatividade vascular: uma avaliação temporal em artérias mesentéricas de resistência
Author	Wender Do Nascimento Rouver
Affiliations	Departamento de Ciências Fisiológicas- Universidade Federal do Espírito Santo
Contact	wrouver@gmail.com
Abstract	<p>As doenças cardiovasculares são a principal causa de morte em todo o mundo e os homens são mais suscetíveis a desenvolvê-las quando comparados às mulheres em idade reprodutiva. No entanto, o papel dos hormônios sexuais masculinos na reatividade vascular ainda é controverso, principalmente no que diz respeito às suas ações relacionadas à idade. Neste sentido, o objetivo deste trabalho foi realizar uma avaliação temporal da reatividade vascular das artérias de resistência de ratos machos jovens, a fim de compreender como os hormônios sexuais masculinos podem influenciar a função vascular desses animais. Todos os procedimentos realizados neste trabalho foram aprovados pela Comissão de Ética no Uso de Animais da Universidade Federal do Espírito Santo (CEUA-UFES) sob protocolo nº 07/2016. Para atender o objetivo proposto, foram utilizadas artérias mesentéricas de terceira ordem de ratos machos com 10, 12, 16 e 18 semanas (de idade). Curvas concentração-resposta à acetilcolina (ACh, 0,1 nM–10 µM) foram obtidas em artérias previamente contraídas com fenilefrina (PE, 3 µM), antes e após o uso de inibidores da óxido nítrico sintase ou da ciclooxigenase. Curvas concentração-resposta de PE (1 nM – 100 µM) também foram obtidas. Os níveis de óxido nítrico vascular (NO), ânion superóxido (O₂•⁻) e peróxido de hidrogênio (H₂O₂) foram avaliados por microscopia de fluorescência. Análise histomorfológica e densidade de colágeno foram avaliadas. Microscopia eletrônica de varredura também foi realizada. Todos os dados são expressos como média ± SEM. Uma vez confirmada a normalidade, as alterações na reatividade vascular foram avaliadas por two-way ANOVA seguida pelo teste post hoc de Bonferroni. A área sob a curva (AUC) e a intensidade de fluorescência foram avaliadas por meio de one-way ANOVA seguida de teste post hoc de Tukey ou teste t de Student não pareado quando apropriado. Para análise dos parâmetros histomorfológicos (dados não gaussianos), utilizou-se o teste de Mann-Whitney. P < 0,05 foi adotado. Foi observado que o grupo com 18 semanas apresentou relaxamento dependente do endotélio prejudicado. Além disso, foi observada resposta vasodilatadora independente de prostanóides e dependente de NO nos grupos: 10 semanas e 18 semanas. A dependência do NO foi confirmada pela inibição simultânea das vias do NO e dos prostanóides nestes grupos. Em relação à resposta contrátil, os grupos 16 semanas e 18 semanas apresentaram respostas maiores em comparação aos grupos 10 e 12 semanas. A análise de microscopia de fluorescência revelou que o grupo com 18 semanas apresentou menor intensidade de fluorescência ao NO e H₂O₂, além de maiores níveis de O₂•⁻ quando comparado ao grupo com 10 semanas. Além do comprometimento funcional das artérias de resistência, os animais com 18 semanas apresentaram diferenças morfológicas nas artérias mesentéricas de terceira ordem, caracterizadas pelo aumento do lúmen, redução na área de secção transversa, redução da parede arterial e menor deposição de fibras colágenas quando comparado ao grupo de 10 semanas. A exposição aos hormônios sexuais masculinos ao longo do tempo parece promover alterações morfológicas e funcionais nas artérias mesentéricas de resistência que explicam o comprometimento vascular, tanto funcional quanto morfológico, encontrado no presente estudo. Assim, acreditamos que os hormônios sexuais masculinos podem estar envolvidos no desenvolvimento de alterações vasculares, mesmo em idade jovem, que podem participar do aparecimento de doenças cardiovasculares relacionadas à idade em homens.</p>





14 a 17 de Setembro de 2024
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Title	Into thin air: avian cardiorespiratory adaptations for life at altitude
Author	William K. Milsom
Affiliations	Department of Zoology- University of British Columbia
Contact	glaubersfs.ufmg@gmail.com
Abstract	High-altitude life poses physiological challenges for all animals arising from the ubiquitous presence of decreased environmental oxygen (O ₂) availability (hypoxia) and cold. Supporting the high metabolic rates and body temperatures of birds and mammals with limited O ₂ availability is challenging. Many birds, however, thrive at altitude. The O ₂ -transport cascade is the series of steps moving O ₂ from the environment to the tissues encompassing: 1) ventilation, 2) pulmonary O ₂ diffusion, 3) circulation, 4) tissue O ₂ diffusion, and 5) mitochondrial O ₂ use for ATP production. Shared avian traits such as rigid lungs with cross-current gas exchange and unidirectional airflow through the lungs aid in O ₂ acquisition and transport in all birds. Many high-altitude birds, however, have evolved enhancements to some or all steps in this cascade. In this presentation, I will summarize our current work on high-altitude avian gas exchange and O ₂ transport providing an overview of the O ₂ -transport cascade in high-altitude birds comparing high altitude migrants with high altitude residents to understand tempo and mode in the evolution of high altitude tolerance.



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Title	Cardioprotective activity by humoral factors with molecular weight < 3 kDa released during ischemic preconditioning
Authors	CAROLINE DA SILVA MORAES, DAHIENNE FERREIRA DE OLIVEIRA, JOSE HAMILTON MATHEUS NASCIMENTO, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Departamento de Fisiologia, Universidade Federal do Rio de Janeiro
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ischemic preconditioning (IPC) is an endogenous protective mechanism against ischemia and reperfusion injuries. Therefore, it is important to elucidate the mechanisms of PCI to explore its possible pharmacological use. Objective: To evaluate the cardioprotection induced by the <3kDa fraction of coronary effluent preconditioned by ischemia, and to investigate the pathways involved in this cardioprotection. Methods: Ceua-UFRJ (154-21). Hearts from male Wistar rats (<i>Rattus norvegicus</i>) were perfused with Krebs-Henseleit (KHB) solution in an isolated heart system at a constant flow rate of 10 ml/min. A latex balloon was inserted into the left ventricle and connected to a pressure transducer to record intraventricular pressure, to measure end-diastolic pressure (LVEDP) and developed pressure (LVEDP). Experimental groups (n=5 in each group): Control: subjected to 30 min. of ischemia and 60 min. reperfusion (I/R); PCI: subjected to 3 cycles of 5 min. of ischemia and 5 min. reperfusion, before I/R; RECEP: perfusion of effluent collected during PCI, for 15 min before I/R; <3kDa: perfusion of the <3 kDa fraction of the collected effluent (fractionation on AMICON membranes, cutoff 3kDa), for 15 min before I/R; <3kDa + antagonists: infusion for 15 min before I/R, of the <3kDa fraction plus 20 nM DPCPX (adenosine A1 receptor antagonist), 10 nM naloxone (opioid receptor antagonist; or ATP-sensitive K⁺ channel blockers , sarcolemmal (10 μM glyburide) and mitochondrial (100 μM 5HD) At the end of reperfusion, the hearts were sectioned and incubated with triphenyltetrazolium (1%), for planimetric determination of the infarct area (AI). Results: The PCI, RECEP and <3kDa groups had a smaller infarct area (PCI:7.08 ± 1.0%, RECEP 10.07 ± 1.74% and <3kDa: 12.09 ± 1.1%; p < 0.001), lower PDFVE (PCI:19.92 ± 2.7mmHg, RECEP: 43.45 ± 2.4 mmHg and <3kDa: 46.8 ± 4.8 mmHg; p < 0.001) and a higher percentage of post-ischemic recovery from PDVE (PCI: 89.4 ± 2.6%, RECEP 70.43 ± 10.05% and <3kDa: 65.54 ± 7.32%; p < 0.001), compared to the Control group (AI:38.01 ± 2.3%; PDFVE:69.8 ± 2.0 mmHg; PDVE:21.2 ± 4.5%).The protective effect induced by the <3kDa fraction was inhibited by DPCPX antagonists (AI:36.38 ± 8.09%; PDFVE:71.65 ± 63.6 mmHg; PDVE:25.45 ± 6.34%), naloxone (AI:42.65 ± 14.3%; PDFVE:69.32 ± 8.8 mmHg; PDVE:31.45 ± 11.26%), glyburide (AI: 27.37± 7.0%; PDFVE: 68.41± 8.30 %mmHg; PDVE: 32.32± 9.09%)and 5HD(AI: 28.32± 6.31%; PDFVE: 71.26± 8.55mmHg; PDVE: 23.02± 9.5%), p < 0.05 vs <3kDa. Conclusion: PCI and the transfer of coronary effluent or its fraction with a molecular weight <3kDa induce cardioprotection against ischemia/reperfusion injuries. Cardioprotection induced by the <3kDa fraction involves the activation of adenosine and opioid A1 receptors, and sarcolemmal and mitochondrial ATP-sensitive potassium channels. Support: FAPERJ, CNPq and CAPES. Protocol: 01200.001568/2013-87</p>

Title	Cardioprotection by transfer of human plasma after remote ischemic preconditioning: identification of cardioprotective humor factors through omics techniques.
Authors	RODRIGO VERAS DA SILVA MIRANDA, FÁBIO C S NOGUEIRA, ANTONIO CARLOS CAMPOS DE CARVALHO, GILBERTO DOMONT, GUSTAVO MONNERAT, ALBERTO GRIMALDI, JOSE HAMILTON, DAHIENNE DE OLIVEIRA, AINA EIRAS DOMINGUES, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Fisiologia, IBCCF
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Remote ischemic preconditioning (RIPC) provides myocardial resistance against ischemia/reperfusion (I/R) injury. It is suggested that the protective mechanism of RIPC is mediated by humoral factors. However, the identity of these humoral factors remains enigmatic. Objective: The objective is to characterize and identify the humoral factors responsible for cardioprotection induced by RIPC. Methods: For this study, a total of 74 male rats, Wistar variety, with body weights between 300-350 g were used. The animals were purchased at the CCS Central Animal Facility. The experimental protocol was approved by the Committee on Ethics in the Use of Animals (CEUA) in Scientific Experimentation, CCS/UFRJ (protocol 154/21). All volunteers were provided with an informed consent form to participate in the study. The study is submitted to the Ethics Committee of the National Institute of Cardiology. This project is registered under Ethics Committee in Research in Human Beings CEP 28998819.9.0000.5272. Human volunteers signed a consent form and completed a health survey. The volunteers were submitted to the RIPC protocol (3 cycles of 5 minutes of ischemia alternated with 5 minutes of reperfusion in the arms). Venous blood was collected before (Placebo plasma) and after RIPC (RIPC plasma). Human plasmas were fractionated into different molecular weight ranges and cardioprotection was evaluated in isolated rat hearts submitted to 30 minutes of ischemia and 120 minutes of reperfusion in an isolated heart apparatus. Mass spectrometry (MS) was performed on placebo plasma and RIPC plasma. Groups: Ischemia and reperfusion (I/R); Placebo plasma < 10 kDa; Preconditioned plasma (RIPC) < 10 kDa; Total preconditioned plasma (RIPC); Preconditioned plasma (RIPC) > 10 kDa. Results: The fraction of less than 10kDa of RIPC plasma reduced infarct size by 50% and induced hemodynamic recovery compared to I/R group. The fraction less than 10kDa of placebo plasma did not induce protection. Hearts perfused with a fraction greater than 10kDa or total RIPC plasma also did not show cardioprotection. MS showed differences in protein content, including higher adenosine and kininogen content in quantitative analysis, and the presence of 15 putatively cardioprotective proteins in qualitative analysis in RIPC plasma compared to placebo. Conclusion: Cardioprotective humoral factors are in the fraction less than 10kDa of RIPC plasma. Furthermore, cardioprotection by RIPC can be transferred between different species. Adenosine, kininogen and 15 other proteins may be responsible for the cardioprotection generated by RIPC. Support: CNPq, PIBIC, FAPERJ Protocol: 28998819.9.0000.5272</p>

Title	THE IMPACT OF AGING IN CARDIAC ELECTROPHYSIOLOGY AND VASCULAR REACTIVITY IN MICE
Authors	GABRIEL SOUZA DE JESUS, YGOR SCHLEIER FRANCISCO DAS CHAGAS, THAIS BARENCO-MARINS, ISLAINE SILVA DE MENEZES, FREDERICO LUIS LIMA ROSA, CLEBER FARIAS VIEIRA, DIANA MAYRA DO CARMO COSTA, ANA CAROLINA PEREIRA DA SILVA, KARINE TAVARES DE JESUS, MARCELLO GONÇALVES PEREIRA, AINÁ EIRAS DOMINGOS, ANTONIO CARLOS CAMPOS DE CARVALHO, FERNANDO DE AZEVEDO CRUZ SEARA
Affiliations	Centro de pesquisa em medicina de precisão (CPMP), Universidade Federal do Rio de Janeiro (UFRJ)
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Aging is a natural biological process that affects almost all living beings and is characterized by the deterioration of the physiological mechanisms that regulate the milieu interieur. The resulting allostatic overload leads to systemic dysfunctions, especially notably a decline in the cardiovascular homeostasis. In Aged hearts, exhibit myocardial stiffening, increased interstitial fibrosis due to collagen deposition, and cardiomyocyte hypertrophy are commonly observed. These factors together collectively result in loss of compliance and lower reduced conductance of electrical current conductance through the cardiac tissue. Similarly, Aged aged vasculature also exhibits shows progressive collagen deposition, stiffening, and calcification. Additionally, there is an increase in oxidative stress and endothelial dysfunction, characterized by the inability to release nitric oxide (NO), resulting in loss of vessel compliance. Objective: To evaluate the impact of aging on vascular reactivity and cardiac electrophysiological properties Methods: All procedures were submitted to the Animal Use Ethics Committee of the Federal University of Rio de Janeiro under protocol number 030/21. For the present study, C57BL/6 mice aged 4 to 24 months were used. These being segmented into adult (4-6 months) and old (22-24 months) groups. Animals were submitted to electrocardiogram (ECG) recording in D1 derivation. After that, they were submitted to the arrhythmia susceptibility test, a model in which it is A score was conferred according to the arrhythmic event presented (0: absence of events; 1: premature ventricular beats or extrasystoles; 2: bigeminy; 3: ventricular tachycardia; 4: ventricular fibrillation), through the application of dobutamine (50µg/ kg) intravenously and caffeine (120mg/kg) intraperitoneally. At the end of these experiments, euthanasia was performed and the aorta artery, from the thoracic portion, was removed to analyze the vascular reactivity. For the statistical analysis of the ECG and the arrhythmia score outside the unpaired T test was used, while for vascular reactivity one way anova with Bonferroni's post hoc. Results: The results, regarding the electrical activity of the cardiac tissue, demonstrate that the aged animals presented a longer duration of the R-R interval ($p < 0.05$), PR ($p < 0.001$) and of the P wave ($p < 0.01$), however, no significant difference was demonstrated in the QRS, QT or QTc intervals compared to the adult animal ($p > 0.05$), as well as during the arrhythmia susceptibility test it was not possible to observe a statistical difference ($p > 0.05$). In the vascular reactivity test, no difference was shown in the contractile capacity of the vessels during the application of sodium nitropussiate (SNP, $p > 0.05$). However, in the presence of acetylcholine (ACH), the adult animal showed a greater capacity for relaxation, unlike the elderly that still developed vasoconstrictor action ($p < 0.05$) Conclusion: Based on the results acquired during the analyses, this study demonstrated that aging is capable of delaying electrical propagation through cardiac tissue, but without altering the susceptibility to arrhythmias. In addition, it was possible to observe a loss in vascular relaxation capacity with advancing age Support: FAPERJ; CAPES; CNPq Protocol: 122/23</p>

Title	The Cerebral Dopamine Neurotrophic Factor promotes cardioprotection via activation of the PI3K/AKT pathway and plasma membrane KDEL receptor
Authors	JULIANA ALMEIDA FERREIRA, DAHIENNE OLIVEIRA, DEBORA FOGUEL, LEONARDO MACIEL
Affiliations	Fisiologia Cardiovascular, UFRJ, Biologia Estrutural, UFRJ
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ischemic heart disease is the biggest cause of death in the world. Recently, the Cerebral Dopamine Neurotrophic Factor (CDNF) has been described as neuroprotector. However, the function of CDNF in the cardiac context is not well understood. Objective: Evaluate the effects of CDNF under conditions of endoplasmic reticulum (ER) stress induced by ischemia and reperfusion (I/R), identifying the possible receptor for CDNF and the signaling pathway that leads to cardioprotection. Methods: (CEUA154-21 and 119-21). Human cardiomyocytes were derived from induced pluripotent stem cells (hiPSC-dCM) CEP (27044614.3.0000.5272) and from neonatal CD-1 mice (1-3 days) or H9C2 cardiomyocytes. To investigate CDNF secretion and cardioprotection mechanisms, cells were induced to ER stress with TG (1 µmol/L) for 20 h or 3 h. For I/R, the isolated hearts from male Wistar rats (9-12 weeks) weighing 300 to 400g were submitted to the I/R protocol in the presence of 1 µmol/L of CDNF before or after I/R. To evaluate the signaling pathways involved, PI3K/AKT (wortmannin), PKC (Chelerytrine and Rotenone) and JAK-STAT3 (AG490) inhibitors were used before or after I/R. To identify the cellular CDNF receptor, heptapeptides from the C-terminal domain of CDNF were used, or a version of CDNF with deletion of the last four amino acids, or even the anti-CDNF antibody. The presence of the KDEL receptor on the membrane and its interaction with CDNF was monitored in H9C2 cells by immunocytochemistry. Results: CDNF is secreted under ER stress caused in cardiomyocytes and in isolated hearts under I/R. Recombinant CDNF (exoCDNF) protected human and mouse cardiomyocytes against ER stress. In isolated hearts undergoing I/R, exoCDNF protected against I/R damage. This protection was inhibited by the PI3K/AKT antagonist (wortmannin). Regarding the CDNF receptor, our results point to the plasma membrane KDEL receptor as a possible CDNF receptor, since heptapeptides containing the KTEL sequence inhibited the protection by exoCDNF and the construct of CDNF without KDEL signal, did not show protection. Furthermore, we observed that exoCDNF labeled with fluorescein binds to the KDEL receptor on the membrane of H9C2 cardiomyocytes under ER stress. Besides, only the C terminal domain from CDNF showed an effect like those described for the full-length CDNF. Conclusion: CDNF shows cardioprotective activity, especially in the C-terminal domain, mediated by the KDEL receptor present in the cell membrane, and this protection is dependent on the activation of the PI3K/AKT pathway. Thus, this work proposes CDNF as a new cardioprotective cardiomyokine. Support: Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: 154-21/01200001568/2013-87 an</p>

Title	EVALUATION OF THE INTERACTION BETWEEN CEREBRAL DOPAMINE NEUROTROPHIC FACTOR (CDNF) AND KDEL RECEPTOR AT THE CELL MEMBRANE
Authors	DÉBORA FOGUEL, MARCELO SANTIAGO, FERNANDO PALHANO, DAHIENNE OLIVEIRA, ANA PAULA OLIVEIRA CAVALCANTE, LEONARDO MACIEL
Affiliations	Departamento de Fisiologia Cardiovascular, UFRJ, Departamento de Biologia Estrutural, UFRJ
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: CDNF (Cerebral Dopamine Neurotrophic Factor) is a neurotrophic factor that has been newly identified. The function of CDNF in the cardiac environment is not well understood. Our research team was the first to classify CDNF as a cardiomyokine, and we have demonstrated its role in promoting cardioprotection. This is achieved through its interaction with the KDEL receptor (KDEL-R) and the subsequent activation of the PI3K/AKT signaling pathway. Additionally, there is currently no evidence to suggest the translocation of the KDEL-R, which typically resides in the endoplasmic reticulum (ER), to the plasma membrane (PM) during ER stress, nor its association with exogenous CDNF (exoCDNF). Furthermore, the mechanism by which this complex is internalized by cells remains to be elucidated. Objective: Investigate whether ER stress caused by thapsigargin (TG) induces KDEL-R exposure at the PM leading to its binding to CDNF and CDNF isolated domains. Methods: H9C2 cells were plated in plaques in 24-well plates, treated with TG for 3 hours and, during the last 15 minutes the cells were treated with fluorescein isothiocyanate (FITC) (1μM) for confocal microscopy images. For the evaluation, H9C2 cardiomyocytes were treated with TG during 3 hours for time-lapse experiments. CDNF or its isolated domains were applied after the first reading. Results: Our data show that fluorescein-labeled exoCDNF binds to the KDEL-R at the membrane of the H9C2 cardiomyocytes treated with TG. Regarding the time-lapse experiment, we observed that CDNF is internalized within approximately 5 to 15 minutes. Our data show cardioprotective activity of CDNF, which binds to the KDEL receptor at the cell membrane of cardiomyocytes, and its internalization leading to ER stress reduction. Conclusion: This study suggests that CDNF interacts with KDELR1 leading to the complex internalization, although the downstream mechanism remains uncertain. Support: Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES); Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: 154/21</p>

Title	CARDIAC AUTONOMIC CONTROL UNDER ACUTE HYPOXIA IN ASYMPTOMATIC POST-COVID-19 SUBJECTS
Authors	ELISSA SILVA DE FARIAS MELLO, ANDRÉ LUIZ MUSMANNO BRANCO OLIVEIRA, THAIS DILLINGER CONWAY SANTANNA, PEDRO PAULO DA SILVA SOARES, GABRIEL DIAS RODRIGUES
Affiliations	Department of Physiology and Pharmacology, UFF, Department of Clinical Sciences and Community Health, UNIMI
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Patients affected by COVID-19 may have manifested severe dyspnea and silent hypoxia to mild or no symptoms in an acute phase. The coronavirus invades cells through ACE-2 receptors systemically throughout the body, such as those in the carotid bodies (CB). These chemosensitivity cells are primarily responsible for cardiac and respiratory autonomic responses to hypoxia, and it is unclear whether the coronavirus changes or inactivates the normal operation of the CB after the acute phase of infection. Also, it is unknown if asymptomatic post-covid subjects (COVID) have preserved cardiac and respiratory autonomic responses to hypoxia. Objective: We aimed to investigate cardiac autonomic modulation and respiratory response in asymptomatic post-covid subjects exposed to acute hypoxia. We hypothesized that COVID group presents blunted autonomic responses to hypoxia, as a possible consequence of the previous disturbance of the CB. Methods: The procedures in this study were previously approved by the ethics committee of the Federal Fluminense University (CAAE:49273321.4.0000.5243). The COVID group (27 ± 5 ys; 74 ± 12 Kg; 1.69 ± 0,1 m) was compared to a group evaluated before the coronavirus pandemic (CTRL) (i.e., no contact with coronavirus) (27 ± 4 ys; 74 ± 9 kg; 1.72 ± 0,1 m). Twenty-six (sex- and age-matched) participants, 13 for each group (5 men and 6 women) at rest were evaluated breathing 10 min of a normoxic mixture (FiO₂: 21%) and 10 min under acute normobaric hypoxia (FiO₂: 11.5%). During the experiments, cardiorespiratory variables were continuously recorded, as follows: breathing rate (BR), tidal volume (VT), ventilation (VE), oxygen saturation (SpO₂), and heart rate (HR) by electrocardiogram. Cardiac autonomic response to hypoxia was analyzed through spectral analysis of R–R intervals, providing frequency-domain bands with physiological meaning as follows: low-frequency component (LF: 0.04–0.15 Hz, sympathetic and vagal) and high-frequency component (HF: 0.15–0.40 Hz, vagal and respiratory), and sympathovagal balance (LF/HF). The physiological responses to hypoxia were assessed by the delta (Δ = hypoxia, normoxia) of all variables. Results: Both groups responded similarly to ΔSpO₂ (COVID: -4.5 ± 2.6 vs CTRL: $-6.8 \pm 3.7\%$; $p=0.10$), ΔBR (COVID: -0.8 ± 2.9 vs CTRL: 0.9 ± 1.6 cycles/min; $p=0.08$), ΔVT (COVID: $0.32 \pm 1,0$ vs CTRL: 0.03 ± 0.1 L; $p=0.31$), ΔVE (COVID: 0.7 ± 3.1 vs CTRL: 1.3 ± 1.9 L/min; $p=0.61$). Regarding cardiac responses, heart rate (ΔHR: COVID: 2.1 ± 3.4 vs CTRL: 3.6 ± 2.9 bpm; $p=0.23$), ΔLF (COVID: -121.9 ± 450.7 vs CTRL: -714.4 ± 1303.5 ms²; $p=0,76$), and ΔLF/HF (COVID: 0.15 ± 0.83 vs CTRL: 0.9 ± 2.3, $p=0.33$) were not different between groups. However, the COVID group showed a lower ΔHF when compared to the CTRL (COVID: -381.2 ± 582.4 vs CTRL: -970.3 ± 1294.4 ms², $p=0.04$). Conclusion: Asymptomatic post-COVID-19 young subjects have a blunted cardiac vagal response to hypoxia compared to age-matched controls. Support: FAPERJ, CNPq, CAPES. Protocol: CAAE:49273321.4.0000.5243</p>



Title	Efeito do Material Particulado Encontrado no Ar Atmosférico de Região Industrializada sobre o Sistema Cardiovascular de Ratos Wistar
Authors	ENES FRANCISCO BERALDO DE QUEIROZ, LUCIANO DO SANTOS AGGUM CAPETTINI
Affiliations	Patologia Geral, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A quantidade de material particulado (PM) encontrado no ar atmosférico aumentou significativamente nas últimas décadas devido a processos naturais e antrópicos. Vários estudos têm mostrado que o PM está envolvido com a ocorrência de doenças respiratórias como asma, bronquite e com o aparecimento ou agravamento de doenças cardiovasculares (DCV) como aterosclerose, hipertensão, arritmia cardíaca e infarto do miocárdio. Objective: O presente estudo visa verificar o efeito do PM encontrado no ar atmosférico de região industrializada sobre o sistema cardiovascular de ratos Wistar previamente expostos a esse material. Methods: Filtros coletores expostos ao ar em região industrializada foram diluídos em solução salina para extrair o PM. O extrato obtido foi administrado por via intraperitoneal (IP) ou por instilação nasal (IN), durante 8 semanas em ratos Wistar. Ao final desse período, os ratos foram eutanasiados, para coleta do coração e segmento da artéria aorta torácica. O segmento foi dividido em anéis, uma parte foi submetida a banho de órgãos para análise de contração vascular, a outra parte e os corações foram submetidos a estudo histopatológico, para investigação de alterações morfofuncionais. Results: Os dados encontrados indicam que o PM foi eficaz na promoção da disfunção endotelial (DE). Ambos os tratamentos reduziram a resposta contrátil induzida pela fenilefrina (CT:9,02±0,2; IN:2,78±0,2; IP:1,26±0,06; p<0,0001). A inibição da produção de óxido nítrico (NO) com L-NAME restaurou a contração no grupo IN (CT:9,41±0,10; IN:8,49±0,1; p<0,0001) via aumento da biodisponibilidade de NO. A contração no grupo IP não foi alterada pelo L-NAME (CT:9,41±0,10; IP:1,26±0,06;). Estudos histopatológicos mostraram aumento do infiltrado inflamatório mononuclear na artéria e no coração. Na maioria dos casos, as alterações observadas foram mais expressivas nos ratos tratados pela via IP. Conclusion: O tratamento IN com PM resultou em redução da contratilidade e aumento do infiltrado mononuclear na aorta. A redução da contração esteve relacionada ao aumento do NO. O tratamento IP reduziu a contratilidade, mas não foi relacionado ao aumento de NO. Este tratamento aumentou o infiltrado inflamatório no coração dos animais, mas não nas aortas. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) Protocol: CEUA:249/2022</p>

Title	Blunted arterial pressure response to sympathoexcitation evoked by Valsalva maneuver but not handgrip exercise in patients with Long COVID and Chronic Fatigue Syndrome: Evidence of an arterial baroreflex dysfunction
Authors	JOAO P. F. FONSECA, MONICA V. MORAES, GUILHERME H. M. SOUZA, ELOARA V. M. FERREIRA, RUDOLF K. F. OLIVEIRA, BRUNO M. SILVA
Affiliations	Setor de Função Pulmonar e Fisiologia Clínica do Exercício (SEFICE), Unifesp
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Millions of people were infected by the SARS-CoV-2 virus acquiring the COVID-19 disease. Most fully recovered after the infection, whereas a portion developed debilitating fatiguing symptoms compatible with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS). Orthostatic intolerance has been reported in these patients, suggesting a cardiovascular autonomic dysfunction, perhaps because the SarCov-2 virus entered the arterial baroreflex circuitry, impairing the baroreflex control of the sympathetic nervous system. Objective: Investigate whether an arterial baroreflex dysfunction occurs in patients with Long COVID and ME/CFS. Methods: So far, 14 patients have been assessed (mean \pm SD: 46 \pm 10 years, 10 female). The Compass-31 questionnaire assessed overall autonomic dysfunction symptoms. Patients expired against a closed circuit (i.e., Valsalva maneuver) while seated, maintaining the expiratory pressure close to 40 mmHg for 15 seconds to evoke arterial baroreflex-induced sympathoexcitation. Static handgrip exercise performed at 30% of the maximal voluntary contraction for 2 minutes, followed by post-exercise circulatory occlusion, evoked sympathoexcitation via alternative mechanisms to the arterial baroreflex. Still, the arterial baroreflex should modulate the sympathoexcitation. Electrocardiogram and photoplethysmographic volume clamp continuously recorded beat-by-beat heart rate and arterial pressure. In a subset, microneurography recorded muscle sympathetic nerve activity (MSNA) in the fibular nerve by (n = 6). Results: All patients scored over 20 points in the COMPASS-31 questionnaire, suggesting a systemic autonomic dysfunction. During the Valsalva maneuver, seven patients showed arterial pressure data compatible with a blunted sympathetic baroreflex response [e.g., mean arterial pressure (MAP) recovery during late phase II: altered Valsalva (n = 7): 3 \pm 11 vs. normal Valsalva (n = 7): 24 \pm 8 mmHg from rest, P = 0.002]. Patients with altered Valsalva indexes had similar MAP response to static handgrip exercise than those with normal Valsalva indexes [altered Valsalva (n = 7): Δ = 13 \pm 4 vs. normal Valsalva (n = 7): Δ = 11 \pm 5 mmHg from rest; P = 0.520), but their MAP response to post-exercise circulatory occlusion was enhanced [altered Valsalva (n = 7): Δ = 9 \pm 3 vs. normal Valsalva (n = 7): Δ = 5 \pm 2 mmHg from rest, P = 0.021], indicating a preserved or even enhanced exercise-induced sympathoexcitatory response. Direct analysis of sympathetic activity suggested that total MSNA increased more during Valsalva's phase II in the group with altered Valsalva indexes [altered Valsalva (n = 3): Δ = 518 \pm 326 vs. normal Valsalva (n = 3): Δ = 446 \pm 336 % of rest], via a greater increase in burst frequency [altered Valsalva (n = 3): Δ = 607 \pm 269 vs. normal Valsalva (n = 3): Δ = 388 \pm 294 % of rest] that overcame a smaller increase in burst amplitude [altered Valsalva (n = 3): Δ = 84 \pm 15 vs. normal Valsalva (n = 3): Δ = 109 \pm 29 % of rest]. Conclusion: Collectively, these preliminary findings suggest that patients with Long COVID and ME/CFS have abnormal baroreflex function. During Valsalva, the baroreflex did not sufficiently counteract the arterial pressure decay, whereas, during PECO, it did not avoid an excessive arterial pressure increase. Additionally, a blunted sympathetic transduction might contribute to the insufficient baroreflex response during the Valsalva maneuver. Support: CAPES and CNPq Protocol: CAAE: 69858623.3.0000.5505</p>

Title	Sodium appetite during the 2-kidney-1-clip hypertension development in male Wistar rats
Authors	MAXWEL SAMPAIO PEREIRA, CAMILA FERREIRA RONCARI, RICHARD BOARATO DAVID
Affiliations	Departamento de Fisiologia e Farmacologia, UFC
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The renin-angiotensin-aldosterone system (RAAS) modulates Na⁺ intake. Hypertensive 2-kidney-1-clip (2K1C) rats show chronic RAAS activation and high NaCl intake induced by central angiotensin II injection. Thus, hypovolemic 2K1C rats may show higher NaCl intake. Objective: The aim was to evaluate the Na⁺ appetite in distinct phases of 2K1C hypertension. Methods: Male Wistar rats (~150 g) had unilateral renal artery stenosis or sham surgery. They were housed in collective cages with chow and water ad libitum. In the 3rd post-surgical week (PSW), for 6 days, rats were housed in individual cages with ad libitum regular chow, cornmeal (low-Na⁺), water, and 0.23 M NaCl solution. On the 7th day, the diuretic furosemide was injected (10 mg/rat, subcutaneous) to induce hypovolemia, water and cornmeal remained available. After 24 h (8th day, 4th PSW), food was removed, water and 0.23 M NaCl were offered in graduated bottles and fluid intake was recorded for 3 h in the Na⁺ appetite test (SAT). Then, rats were returned to collective cages and the protocol was repeated twice: SATs performed on 8th and 12th PSWs. After the last SAT, mean arterial pressure (MAP) was recorded and 3 groups were formed: H-2K1C (MAP > 129 mmHg), N-2K1C (MAP ≤ 129 mmHg) and SHAM. Results: Averaged daily 0.23 M NaCl intake (ml/100 g bw ± SEM) by H-2K1C (3rd PSW: 16 ± 2, 7th PSW: 6 ± 2, 11th PSW: 7 ± 2; n = 8) was higher than N-2K1C (3rd PSW: 6 ± 2, 7th PSW: 4 ± 1, 11th PSW: 7 ± 1; n = 8) and SHAM (3rd PSW: 4 ± 1, 7th PSW: 4 ± 1, 11th PSW: 3 ± 1; n = 6; p < 0.05) only in the 3rd PSW. In all SATs, 0.23 M NaCl intake by H-2K1C (1st: 7.2 ± 0.4, 2nd: 7.3 ± 0.9, 3rd: 7.0 ± 0.8; n = 8) was higher than N-2K1C (1st: 5.0 ± 0.3, 2nd: 5.2 ± 0.5, 3rd: 4.4 ± 0.4; n = 8) and SHAM (1st: 3.8 ± 0.4, 2nd: 4.2 ± 0.5, 3rd: 3.4 ± 0.4; n = 6; p < 0.05). Water intake was similar between groups in daily intake and SATs. Conclusion: The results showed long-last enhancement of Na⁺ appetite in the hypertensive 2K1C rats. Support: CAPES, CNPq & FUNCAP. Protocol: N.A.</p>

Title	Effect of single administration of interference current on the cardiovascular autonomic nervous system of healthy wistar rats
Authors	ANDRÉ LUIZ SILVA SANTOS, ANNANDA OLIVEIRA SANTOS, IVANA MARIA BARBOZA DOS SANTOS, VITOR ULISSES DE MELO, VALTER JOVINIANO DE SANTANA FILHO, JOSIMARI MELO DESANTANA
Affiliations	Departamento de Ciências Fisiológicas, UFS
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Interferential current (IFC) is a type of transcutaneous electrical nerve stimulation classified as a medium-frequency alternating current, composed of sequences of alternating current pulses. IFC is a non-pharmacological, non-invasive, and low-cost treatment method for pain relief. Studies suggest that IFC may improve cardiac autonomic modulation when administered in a long-term. However, the effect of a single session has not been previously tested, and the mechanism of action of IFC on the cardiovascular autonomic nervous system remains unclear. Objective: To evaluate the effect of IFC on cardiovascular autonomic modulation after a single application with motor and sensory intensities administered on the chest of healthy rats. Methods: This study was approved by the Animal Research Ethics Committee of the Federal University of Sergipe (CEPA/UFS no. 51/2018). Thirty-six male Wistar rats weighing between 250 to 350 g and aged two months were used. The rats were divided into two experimental series: series 1 (evaluation of cutaneous response), subdivided into motor IFC group, sensory IFC group, and inactive IFC group; and series 2 (evaluation of heart rate variability, HRV), subdivided into motor IFC group, sensory IFC group, and inactive IFC group. In series 1, the animals' chests were stimulated for 20 minutes, and thermographic recordings of the region were taken every 5 minutes. One hour after IFC treatment, the cutaneous response was reassessed. In series 2, animals underwent surgery for implantation of a catheter in the left femoral artery. After 24 hours, IFC was applied to the animals' chests for 20 minutes. Beat-to-beat arterial blood pressure recordings were made before and 30 minutes after treatment. Statistical analyses were performed using GraphPad Prism® 7.0 software. Mean ± standard error of the mean was calculated, and values were considered significant when $p < 0.05$. Normality was assessed using the Shapiro-Wilk test. ANOVA and Bonferroni post hoc tests were conducted. Z-score test was used for outlier detection. Results: There was no significant increase in thoracic cutaneous temperature after interferential current application in the sensory and motor IFC groups compared to baseline, as well as between experimental groups ($p > 0.05$). The control group also showed no temperature change when compared before and after treatment ($p > 0.05$). Regarding heart rate variability, no significant difference was observed between the IFC-stimulated groups with motor or sensory intensity and the control group, as well as before and after treatment ($p > 0.05$). Conclusion: These findings suggest that a single application of interferential current is not sufficient to modulate the cardiovascular autonomic nervous system, even when applied to the thoracic region. However, interferential current appears not to induce adverse reactions in the cardiovascular system. Support: Coordination for the Improvement of Higher Education Personnel (CAPES); National Council for Scientific and Technological Development (CNPq). Protocol: CEPA/UFS no. 51/2018</p>

Title	REACTIVE OXYGEN SPECIES DRIVE THE PREGANGLIONIC SYMPATHETIC ACTIVITY IN EXPERIMENTAL RENOVASCULAR HYPERTENSION.
Authors	FERNANDA MANO TAGLIAPIETRA DA SILVA, ANA CAROLINE MARREIROS, RAFAEL SANTOS CARVALHAL, CASSIA MARTA DE TOLEDO BERGAMASCHI, MAYCON IGOR DE OLIVEIRA MILANEZ, RUY RIBEIRO DE CAMPOS JÚNIOR
Affiliations	Fisiologia Cardiovascular e Respiratória, Universidade Federal de São Paulo, UNIFESP
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Arterial hypertension is a widely prevalent disease with a multifactorial and polygenic origin; among other factors, oxidative stress is an important mechanism in hypertension, particularly acting in the brain nuclei involved in cardiovascular control. The regulation of sympathetic vasomotor activity relies on a complex system involving brain areas that project directly to the intermediolateral column (IML), which contains a significant concentration of sympathetic preganglionic neurons. We previously reported that in Goldblatt's experimental model of renovascular hypertension (2 kidneys, 1 clip; 2K1C), there is an overexpression of spinal angiotensin II (Ang II) type I (AT1) receptors. Objective: Considering that Ang II drives oxidative stress, the present study aims to clarify the role of reactive oxygen species and the renin-angiotensin system in the spinal cord in controlling the activity of sympathetic preganglionic neurons in the 2K1C rats. Data were expressed as mean \pm standard error of the mean – SEM; Two-way ANOVA followed by Fisher's post-test, and unpaired Student's t-test. (*$p \leq 0.05$), GraphPad Prism 7®. Methods: Male Wistar rats were divided into control (8 weeks: 350 – 400g, n=29) and 2K1C (5 weeks: 150 – 180g, n=26) groups. Renovascular hypertension was induced by inserting a silver clip around the left renal artery (gap of 0.2 mm) 6 weeks before carrying out the experimental protocols. Femoral vessels were catheterized 24 hours before the experiments under anesthesia with Ketamine (80 mg/kg) and Xylazine (10 mg/kg) to record mean arterial pressure (MAP), heart rate (HR), and for intravenous injections. Intrathecal (it) administrations of Tempol (5 nmol in 2 μL) and Apocynin (1 nmol in 2 μL) were given through a PE-10 catheter inserted into the subarachnoid space under urethane anesthesia (1.2 mg/kg, i.v.). The splanchnic and renal nerves were assessed through a retroperitoneal incision to record their activity (sSNA and rSNA, respectively) before and after the administration of Tempol and Apocynin. In a series of independent experiments, spinal segments were evaluated for gene expression analysis of enzymes that participate in oxidative balance, components that participate in the renin-angiotensin system (RAS), and inflammatory processes (NADPH oxidase, Nox2, and p47 subunits, SOD, catalase enzymes, aminopeptidase A, prorenin receptor, ADAM17 metalloproteinase, and TNF-α inflammatory mediator). Results: Tempol administration did not trigger significant variations on MAP, and HR in both groups. However, there was a significant reduction in rSNA only in the 2K-1C group at 30 and 40 minutes after Tempol administration compared to normotensive rats (Control vs 2K-1C: 7 ± 9 vs -15 ± 7 Δspikes/seconds). On the other hand, a significant increase in eSNA 50' and 60' (14 ± 5 Δspikes/seconds) was found after Tempol injection in both groups. The administration of Apocynin triggered hypotensive effects in both groups (100': -20 ± 5; 120': -23 ± 4 ΔmmHg). An overexpression of NADPH oxidase 2 (Nox2) in the lumbar section and of the ADAM17 was found in the IML only in 2K1C animals. Conclusion: The results suggest that oxidative stress in sympathetic preganglionic neurons drives sympathoexcitation and hypertension in renovascular hypertension. The origin of Ang II is still undetermined, that is, circulating, locally generated, or both. Support: Support: FAPESP (19/25295-0) and Capes (finance, code 001) Protocol: 8757070223/2023</p>

Title	MYOCARDIAL INFARCTION: HUMORAL FACTORS ARISING FROM REMOTE PRECONDITIONING AND THE INFLUENCE OF COMORBIDITIES ON CARDIOPROTECTION
Authors	ALBERTO BARRETO GRIMALDI, DAHIENNE FERREIRA DE OLIVEIRA, MARIA EDUARDA MACIEL FERNANDES PAVARINO, ANTÔNIO CARLOS CAMPOS DE CARVALHO, LEONARDO MACIEL-
Affiliations	CPMP, UFRJ
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Acute myocardial infarction, an ischemic heart disease, is responsible for about a third of all deaths worldwide. The remote ischemic preconditioning maneuver (RIPC), which consists of ischemia and reperfusion (I/R) cycles in a distant organ from the heart, is related to release endogenous cardioprotective factors. However, PCIR is not satisfactory in clinical studies with patients. Objective: Thus, the present study aims to understand how comorbidities could affect cardioprotection by RIPC. Methods: The 55 plasmas from healthy volunteers and 21 patients with comorbidities (CAAE 28998819.9.0000.5272), were previous ultrafiltered in a molecular weight fraction lower than 10 kDa (< 10 kDa) and followed perfused in isolated hearts in Langendorf model. (CEUA 154.21). The plasma were collected before RIPC (placebo) and after RIPC (conditioned). The animal experimental groups was composed of a group control (health rats), a hypertense group with SHR Wistar Kyoto rats, a group of diabetics rats induced by streptozotocin and a group of rats with high levels of sodio consumption. The Perfused isolated rat hearts were submitted to an ischemia and reperfusion (I/R) protocol, consisting of 30 min. of ischemia followed by 120 min. of reperfusion. The ultrafiltrated plasma placebo or conditioned of each donor were diluted in Krebs Solution (1:10) and perfused before I/R. Results: The < 10kDa conditioned plasma from health volunteers were capable to induce cardioprotection by the infarct area reduction and increase in hemodynamics parameters in heart under I/R. However, the < 10kDa plasma placebo, or the < 10kDa conditioned plasma and < 10kDa placebo plasma from patients with comorbidities did not show cardioprotection. Furthermore, in the animals with comorbidities (Hypertension, diabetes and High sodium) the cardioprotection was abolished or reduced. Total conditioned plasma and > 10kDa conditioned plasma did not induce protection in heart under I/R. Conclusion: Therefore, we conclude that despite the positive cardioprotective response from the administration of plasma from healthy volunteers to healthy animals, it was observed that comorbidities affect the humoral factors actions in cardiac tissue, abolishing the cardioprotection that could be provided by PCIR. Support: FAPERJ, PIBIC e CNPQ Protocol: CAAE 28998819.9.0000.5272 /</p>

Title	ACUTE EXPOSURE EFFECTS OF TRIVALENT SODIUM ANTIMONIATE AND PENTAVALENT SODIUM ANTIMONIATE ON ISOLATED MITOCHONDRIA FROM HEART OF MICE
Authors	BRENDA EMANOELE RODRIGUES, ITANNA ISIS ARAUJO DE SOUZA, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Departamento de Ciências da Saúde, UFRJ
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Pentavalent sodium antimoniate (Sb(V)) has been one of the main drugs used in the treatment of leishmaniasis for over 50 years. Sb(V) is a prodrug that needs to be activated by converting it to the trivalent form (trivalent antimoniate, Sb(III)). Sb(V) is metabolically converted in the intramacrophagic medium to Sb(III) showing leishmanicidal function. After its conversion, Sb(III) interferes in the process of beta-oxidation of fatty acids and glycolysis, impairing the energy metabolism of the parasite. However, the effect of antimoniates on host mitochondria is unknown. Objective: Therefore, the main objective of this work was to examine the effects of Sb(V) and Sb(III) on isolated mitochondria from mouse hearts. Methods: For this study, a total of 7 animals were involved, protocol CEUA number 119/21, 4-week-old male C57BL/6 mice, with 25-30 grams, were euthanized by cervical dislocation. Hearts were quickly removed and mitochondria were isolated by a differential centrifugation method. Immediately after isolation, mitochondrial function was evaluated by measurement of O₂ consumption in different respiratory states, ATP production, ROS production, and transmembrane potential. Isolated mitochondria were exposed to 1ng/ml, 1ug/ml, and 1 mg/ml of Sb(V) and Sb(III). Results: The results of the present study are presented as the mean ± standard error of the mean (SEM), for the analysis, the One-way ANOVA test was applied for comparison between all groups. When a significant difference was detected, the ANOVA test was followed by Bonferroni post-tests, $p < 0.05$ was considered statistically significant. This study shows that the oxygen consumption of isolated mitochondria in respiratory states 2 and 3 of complex I showed a reduction from 1ug/ml and 1ng/ml of Sb(V), respectively, compared to the control. The Sb(III) levels showed no difference in complex I state 2 respiration compared to the control. However, the respiration of state III, complex I was reduced from 1ng/ml, compared to the control. No significant differences were observed in the production of ROS between the experimental groups. ATP production was reduced after exposure to 1ng/ml and 1ug/ml of Sb(V). The Sb(III) group was able to reduce ATP production from 1ng/ml. The transmembrane potential was not significantly different in the dosages of 1ng/ml, 1ug/ml, and 1 mg/ml of Sb(V) or Sb(III). Conclusion: The results presented here suggest a direct action of Sb(V) and Sb(III) antimonials on isolated mitochondria from mice. They were impairing mitochondrial functions and reducing ATP production. Support: CNPQ, CAPES, FAPERJ Protocol: 1.20E+15</p>

Title	Lack of estrogen impairs cardiac recovery during Takotsubo-like cardiomyopathy through fibroblast activation
Authors	BRUNO DE LIMA SANCHES, FERNANDA TUPINI, KIANY MIRANDA, VICTOR MOURA VIDAL, GABRIEL MATOS, FERNANDO SOUZA-NETO, MARCOS ELIEZECK, SÉRGIO SCALZO, AMANDA DE SÁ MARTINS BESSA, CARLOS HENRIQUE DE CASTRO, RAPHAEL SKAWZA, JOP VAN BERLO, SILVIA GUATIMOSIM
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Departamento de Ciências Fisiológicas, UFG, Dept of Integrative Biology, University of Minnesota
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Takotsubo cardiomyopathy (TC) has been the subject of increasing interest due to its multifactorial origin and symptomatology that mimics myocardial infarction. This disease occurs mainly in postmenopausal women where the cardioprotective effects of estrogen are lost, leading to hypertrophy and inflammation, events that can result in cardiac dysfunction and death. Despite the critical role of estrogen in preventing and ameliorating the effects of the disease, the mechanisms involved in its cardioprotection are poorly understood. Objective: To study the cellular and molecular basis of cardiac dysfunction in an ovariectomized mouse model of TC. Methods: Female C57BL/6J mice, 8 weeks old and weighing 20-25g, were divided into four groups: Sham/CTR (sham-operated mice treated with saline); Sham/ISO (treated with a single intraperitoneal dose of 200 mg/Kg of isoproterenol, an acute inflammation model); OVX/CTR (mice subjected to bilateral ovariectomy) and OVX/ISO. Thirty days after OVX, mice were treated with ISO and euthanized ten days later. Western blot and immunofluorescence were performed in cardiac tissue and isolated cardiac fibroblasts. Results: Ten days post-ISO, Sham cardiomyocytes showed no signs of hypertrophy indicating that those hearts recovered from the ISO-induced injury, on the contrary, OVX/ISO mice showed pronounced cardiomyocyte hypertrophy (OVX/ISO: $272.47 \pm 3.13 \mu\text{m}^2$ vs Sham/ISO $204.7 \pm 2.26 \mu\text{m}^2$, $n=500$ cells) and marked GRK5 staining (OVX/ISO: $26.80 \pm 2.32 \text{a.u.}$ vs Sham/ISO: $12.49 \pm 0.94 \text{a.u.}$) in the heart. These changes were prevented by 17β-estradiol ($1 \mu\text{g/day}$) replacement therapy. Interestingly, we found that total collagen deposition was elevated in OVX/ISO group (OVX/ISO: $10.45 \pm 1.41\%$ vs Sham/ISO: $3.97 \pm 0.44\%$) by picosirius red staining, which was confirmed by western-blot analysis showing the increase in α-SMA (OVX/ISO: $7.34 \pm 1.35 \text{a.u.}$ vs Sham/ISO: $2.87 \pm 0.44 \text{a.u.}$) and TGF-$\beta$ (OVX/ISO: $1.38 \pm 0.53 \text{a.u.}$ vs Sham/ISO: $0.35 \pm 0.05 \text{a.u.}$) in this group. Importantly, in the OVX/ISO heart we found marked GRK5 staining in α-SMA-positive cells, an important indicator of fibroblast activation. To assess whether lack of estrogen induces a persistent fibroblast activation in the heart from ISO mice, we isolated cardiac fibroblasts from each experimental group and measured reactive oxygen species production and GRK5 staining. Consistent with our previous findings, fibroblasts obtained from OVX/ISO hearts showed marked GRK5 nuclear translocation and augmented ROS (OVX/ISO: $13.64 \pm 0.26 \text{a.u.}$ vs Sham/ISO: $10.83 \pm 0.25 \text{a.u.}$, $n=160$ cells). These findings strongly indicate that lack of estrogen leads to sustained fibroblast activation under adrenergic overload, which could explain the persistent hypertrophic phenotype observed in OVX/ISO mice. To critically test this idea, we incubated neonatal cardiomyocytes for 48 hours with conditioned media from cardiac fibroblasts isolated from each experimental group. Strikingly, only the conditioned media from OVX/ISO fibroblasts induced cardiomyocyte hypertrophy (OVX/ISO: $85.99 \pm 4.82 \mu\text{m}^2$ vs Sham/ISO: $50.95 \pm 2.95 \mu\text{m}^2$, $n=200$ cells), confirming our hypothesis. Conclusion: Our results provide evidence that estrogen deficiency leads to sustained fibroblast activation under adrenergic overload, demonstrating the critical role of this hormone in the cardiac repair that occurs during TC. These findings open the door for novel experimental and clinical approaches directed at menopausal women affected by TC. Support: CNPq, FAPEMIG, CAPES. Protocol: CEUA: 175/2021</p>

Title	Looking into Reperfusion After Post-Occlusive Reactive Hyperemia with Sub-systolic Pressure
Authors	SERGIO FALLONE DE ANDRADE, JOANA CAETANO, MARISA NICOLAI, LUIS ANTONIO MONTEIRO RODRIGUES
Affiliations	ECTS, ULHT
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Post-occlusive reactive hyperemia (PORH) has been used to investigate human microcirculatory response in vivo. The transitory occlusion of a major artery, such as the brachial artery, by a pressure cuff evokes a reperfusion period thought to be due to a local vasodilation induced by ischemia. Recent findings suggested that similar responses to PORH can be seen with other maneuvers capable of modifying the local perfusion homeostasis by reducing perfusion pressure and flow. These finding indicate that the mechanism involved might be better explained by a centrally mediated reflex. Objective: This study was designed to quantitate the detectable POHR response in both forearms when the brachial artery is occluded with sub-systolic pressure in one arm. Methods: Ten participants (female, 21.6 ± 2.4 years old) were enrolled. PORH was performed in one randomly chosen arm using a pressure cuff. Perfusion was measured by Laser Doppler flowmetry (LDF) in both hands during the procedure. Other hemodynamical variables were measured with the CNAP® technology (non-invasive, continuous blood pressure, advanced hemodynamics and dynamic parameters monitoring) by the Task Force platform. All procedures followed principles of Good Clinical Practice, being previously approved by the institutional Ethics Committee (approval number 10/21). Measurements were taken before measurements for baseline (Phase 1), during occlusion kept 20 mmHg below systolic pressure for 2 minutes (Phase 2), and during recovery (Phase 3). Results: LDF revealed that the profile of post-occlusive reactive hyperemia (PORH) with sub-systolic pressure matched the classical profile obtained with a suprasystolic occlusion. The response was observed in both limbs, although more pronounced in the ipsilateral side. A significant reduction of perfusion in both hands was followed by an intense reperfusion, also in both limbs. No other hemodynamical changes were detected during PORH. Conclusion: This data clearly demonstrates that ischemia cannot be in the origin of the reperfusion since the occlusion was short (2 minutes) and only partial, away from a zero perfusion. Therefore, the rapid reperfusion following PORH can only be explained by hypoxia and hypovolemia, which triggered a global cardiovascular adaptive response observable in the contralateral limb. These results indicated that PORH induces a reflex meant to restore the acutely modified local perfusion. We also conclude that reactive hyperemia must be redefined to better use this concept to explore human cardiovascular physiology. Support: Foundation for Science and Technology, I.P. (Portugal) (DOIs 10.54499/UIDP/04567/2020 and 10.54499/UIDB/04567/2020), Cooperativa De Formação e Animação Cultural CRL/Instituto Lusófono de Investigação e Desenvolvimento (COFAC/ILIND/CBIOS/2/2021) Protocol: CE.ECTS/P10.21</p>



Title	Avaliação do Potencial Efeito Cardioprotetor da Angiotensina-(1-7) em Modelo Experimental da Cardiomiopatia de Takotsubo
Authors	MARIA LUIZA DIAS PINTO, BRUNO DE LIMA SANCHES, SILVIA GUATIMOSIM, THIAGO VERANO-BRAGA
Affiliations	Fisiologia, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A cardiomiopatia de Takotsubo (CT) é uma condição cardiovascular com alta prevalência em mulheres, desencadeada por eventos estressantes que aumentam os níveis de catecolaminas, como a norepinefrina, levando à estimulação suprafisiológica do tecido cardíaco, culminando no desenvolvimento de alterações cardíacas, como a hipertrofia ventricular esquerda e inflamação. Nesse cenário, pesquisas buscam terapias para reduzir a ocorrência da CT ou minimizar os seus efeitos deletérios. A Angiotensina-(1-7) [Ang-(1-7)] é um componente do sistema renina-angiotensina (SRA) que induz cardioproteção, regulando a liberação de norepinefrina e reduzindo a remodelação cardíaca, além disso, atua como um agente anti-inflamatório. Contudo, o potencial efeito terapêutico da Ang-(1-7) ainda não foi avaliado em modelo experimental de CT. Objective: Estabelecer um modelo experimental de CT em camundongos para avaliar o potencial efeito terapêutico da Ang-(1-7). Methods: Foram utilizados camundongos da linhagem C57Bl6/J, fêmeas, com idade entre 8 e 12 semanas de vida e pesando 20-22 g. Primeiramente, visando caracterizar o modelo experimental de CT, os animais foram tratados com dose única de ISO (300 mg/Kg via IP) ou salina (NaCl 0,9% via IP). Posteriormente, os animais dos grupos Controle (NaCl 0,9% via IP) e ISO (ISO 300 mg/Kg via IP) foram tratados com uma formulação oral de Ang-(1-7) incluída em ciclodextrina (CD) com uma dose diária de 105 µg/Kg (Ang-(1-7) = 45 µg/Kg + CD = 60 µg/Kg) ou apenas com CD (60 µg/Kg/dia) por 4 dias. Results: Foi possível implementar o modelo experimental de CT, representado pelo aumento do peso normalizado do coração [controle = $5,7 \pm 0,72$ vs. CT = $6,5 \pm 0,68$; $P = 0,04$; $n = 8$] e do aumento de infiltrado inflamatório [controle = $0 \pm 0,0$ vs. CT = $0,85 \pm 0,68$; $P < 0,0001$; $n = 8$]. O tratamento com a Ang-(1-7) diminuiu significativamente a hipertrofia cardíaca [ISO + CD = $6,4 \pm 0,63$ vs. ISO + Ang-(1-7)-CD = $5,7 \pm 0,36$; $P = 0,015$; $n = 12$] e a área transversal dos cardiomiócitos [ISO + CD = $246,4 \pm 61,44 \mu\text{m}^2$ vs. ISO + Ang-(1-7)-CD = $201,2 \pm 48,27 \mu\text{m}^2$; $P < 0,0001$; $n = 6$]. Conclusion: Os resultados apoiam a hipótese de que a Ang-(1-7) possui um efeito cardioprotetor no modelo de CT, abrindo novas possibilidades para o seu uso na clínica. Os próximos passos deste projeto visam elucidar os mecanismos de ação da Ang-(1-7) na patologia da CT. Support: CNPq, CAPES, FAPEMIG, INCT Nanobiofarmacêutica Protocol: 223-2023</p>

Title	Angiotensin II, blood-brain barrier permeability and microglia interplay during the transition from pre- to hypertensive phase in SHR
Authors	MARIANA MAKUCH-MARTINS, CAMILLA G. VIEIRA DE MORAIS, SANY MARTINS PÉREGO, LISETE COMPAGNO MICHELINI
Affiliations	Departamento de Fisiologia e Biofísica, USP
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chronic hypertension is characterized by upregulation of the renin-angiotensin system, increased blood-brain barrier permeability (BBBp), microglia (MG) activation within autonomic nuclei and sympathoexcitation. There is no information on the interplay of these events during the development of neurogenic hypertension. Objective: We sought now to identify the interaction and time-course changes of Ang II availability, BBBp, MG activation and autonomic control during the transition from pre- to hypertensive phase in SHR. Methods: Hemodynamic/autonomic parameters (n=12 animals/group), BBBp (high+low molecular weight dyes injected intra-arterially; n=3 animals/group), MG and Ang II expression (IBA-1 and Ang II immunofluorescence, n=5 animals/group) and MG structural changes (Neurphology), a plug-in to ImageJ) were evaluated within the paraventricular hypothalamic nucleus, nucleus of solitary tract and rostral ventrolateral medulla in SHR aged 4, 5, 6, 8 and 12 weeks. Age-matched Wistar rats were used as controls. Values are presented as means \pm SEM and compared by 2-way factorial ANOVA. Results: At the 4th week SHR exhibited MAP (80\pm7 mmHg), BBBp (0.42\pm0.04 %area), MG density (1306\pm93 A.U.) and Ang II expression (1718\pm85 A.U.) values and sympathetic activity (LF-SAP=5\pm1 mmHg²) similar to those of normotensive controls. Within the 3 nuclei augmented Ang II density (on average +48%) was the first observed change at the 5th week followed by incipient BBB leakage (4%) and MG activation (+11%) at the 6th week. From 6 to 12 weeks BBBp increased continuously in SHR adding leaked plasma to locally synthesized Ang II, the augmented peptide content strongly activated MG thus driving the blood pressure elevation and autonomic responses (increased sympathetic vasomotor activity and pressure variability) that occurred from the 8th week on. At the 12th week SHR reached the chronic phase of hypertension (152\pm4 mmHg) showing high values of Ang II expression (6931\pm84 A.U.), BBBp (15.85\pm0.51% area), MG density (4312\pm292 A.U.) and robust sympathoexcitation (LF-SAP=15\pm2 mmHg²). Augmented local Ang II availability was able to colocalize with the microglial cells and alter their morphologic phenotype from highly ramified cells at the 4th-5th weeks, indicative of a basal surveillant condition to short process arbors, fewer ramifications and enlarged soma size in the chronic phase, suggestive of the secretory phenotype. These responses were not specific for autonomic nuclei also occurring, but with smaller magnitude in the somatosensory cortex and hypoglossal nucleus, indicating the predominance of hypertension-induced effects on autonomic areas. No changes were observed in age-matched controls where Ang II density did not change. Conclusion: Our data indicated that brain-synthesized Ang II is the initial stimulus to drive coordinated BBB permeability changes and MG activation. BBB leakage activates a vicious cycle in which augmented brain Ang II availability further potentiates barrier permeability, MG activation, autonomic imbalance and pressure elevation during the establishment of hypertension. Support: FAPESP; CNPq; CAPES Protocol: 3112251119; 6194060324</p>

Title	Afferent renal nerves promote differential cardiovascular and sympathetic nervous responses in response to furosemide in normotensive and hypertensive rats
Authors	RAFAEL SANTOS CARVALHAL, ANA CAROLINE MARREIROS, FERNANDA MANO TAGLIAPIETRA DA SILVA, MARK KNUEPFER, CASSIA MARTA DE TOLEDO BERGAMASCHI, CRISTIANE DAMAS GIL, ERIKA EMY NISHI, MAYCON IGOR DE OLIVEIRA MILANEZ, RUY RIBEIRO DE CAMPOS JUNIOR
Affiliations	Fisiologia cardiovascular, UNIFESP EPM, Pharmacological and Physiological Science, Saint Louis University (SLU) – School of Medicine – USA, SLU, Morfologia e Genética, UNIFESP EPM
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Based on previous studies, we hypothesized that renal sympathetic nerve activity would increase in response to furosemide (subtherapeutic) infusion. The role of capsaicin-sensitive afferent renal nerves was evaluated in control rats. Furthermore, sympathetic nervous activity in hypertensive rats subjected to furosemide. Objective: To investigate whether furosemide modulates sympathetic nerve activity by activating renal afferents. Methods: All experimental procedures used in the present study were according to the guidelines recommended by the CEUA (Comissão de Ética de Uso de Animais – Brazilian Government) and were approved by the Ethics in Research Committee of the Paulista School of Medicine – Federal University of São Paulo (process No. 9214060819). Male Wistar rats (6 à 8 weeks, 150-300 g) were housed in group cages, given access to rat chow and water ad libitum, and maintained in a temperature-controlled environment (23 °C) with a 12/12-hour light/dark cycle. Four independent series of experiments were performed. In the first, furosemide (FURO, N=9), second, animals deafferented (DEAF+FURO, N=6) with capsaicin (Galena®, 33mM) and third, renovascular hypertensive rats (2K1C+FURO, n=6) series of experiments, cardiovascular, mean arterial pressure, heart rate (MAP and HR), renal sympathetic nerve activity (rSNA), and splanchnic sympathetic nerve activity (sSNA) were recorded (20 k, 100- 1000 Hz, Neurolog System – Digitimer UK), before and after intravenous infusion of a subtherapeutic dose of furosemide (SANOFI®, i.v, 1 mg/kg/h). The fourth series of experiments (SHAM) was performed without furosemide infusion under thiopental anesthesia (Cristalia®, i.v, 10mg/kg/h, 1ml/h). Statistical analysis, the GraphPad Prism 7® program was used. Data are expressed as mean ± standard error of the mean (SEM). Analyzed by the one-way or two-way ANOVA analysis of variance followed by Fisher's post-test. Only values of p<0.05* were considered statistically significant. Results: Furosemide induced a greater reduction in MAP in the DEAF+FURO group when compared to control rats (maximal decrease of -10 ± 7 vs -23 ± 3 ΔmmHg at 120 min, *P<0,05), however, no statistically significant differences in the HR responses between groups was found. A significant reduction in rSNA (spikes/s) was found in DEAF+FURO compared to FURO group (maximal decrease of 10 ± 10 vs -21 ± 7 Δspikes/s at 120 min, *P<0,05). A larger reduction in MAP was found in 2K1C+FURO compared to FURO (FURO vs 2K1C+FURO: 110 min: -7 ± 7 vs -21 ± 7 mmHg*) as well as in HR (FURO vs 2K1C+FURO: 120 min: -19 ± 9 vs -72 ± 13 bpm*). In addition, a reduction in rSNA was found in 2K1C rats (FURO vs 2K1C+FURO: 110 min: 5 ± 9 vs -34 ± 13 spikes/sec*), FURO vs 2K1C+FURO: 90 min: 0.06 ± 0.08 vs, 0.18 ± 0.08 AU*). Conclusion: From the results we conclude that in normotensive rats, TRPV1-positive renal sensory fibers participate in renal sympathetic activation induced by acute infusion of furosemide at a subtherapeutic dose. In Goldblatt rats, however, renal afferents trigger sympathoinhibition in response to furosemide. Support: Supported by FAPESP (19/25295-0), CAPES (finance code 001), and CNPq. RRC and CTB were recipients of the CNPq fellowship. Protocol: N.A.</p>

Title	Characterization of cardioprotective humoral factors released during ischemic preconditioning
Authors	CÉSAR FRANCISCO MARICATO DA ROSA, DAHIENNE FERREIRA DE OLIVEIRA, JOSE HAMILTON MATHEUS NASCIMENTO, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Departamento de Ciências da Saúde, UFRJ
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Brief periods of ischemia and reperfusion in the heart induce resistance to a sustained ischemia. This phenomenon was termed ischemic preconditioning (IPC). The IPC can be induced by regional ischemia in the heart or “at distance” in non-cardiac tissues, suggesting the release of an unknown humoral activator. Objective: The aim of this study is evaluating the protein content of humoral factors released during IPC by mass spectrometry techniques. Methods: Perfused isolated rat hearts were submitted to an ischemia and reperfusion (I/R) protocol, consisting of 30 min. of ischemia followed by 60 min. of reperfusion. IPC consisted of 3 cycles of 5 min. of ischemia and 5 min. of reperfusion applied before I/R. The coronary effluent was collected during the IPC and fractionated in different molecular weight ranges by ultrafiltration. Total (Efl-ipc) or fractionated (<3kDa; 3-5 kDa; 5-10 kDa; 10-30 kDa; 30-50 kDa>50 kDa) coronary effluent were perfused before I/R. 5-10 kDa fraction was also tested in the presence of blockers for sarcolemmal ATP-sensitive K⁺ channels (KATP) gliburide (10 μM) and for mitochondrial KATP 5HD (100 μM), or JAK-STAT (10 μM AG490), or PKC (10 μM chelerythrine) pathway inhibitors. The humoral factors were analyzed by LC-MS/MS, using a ESI-Q-ToF mass spectrometer. Results: Efl-ipc and IPC hearts had lower infarct area (IA), lower end diastolic pressure (LVEDP) and better recovery of left ventricular developed pressure (LVDP), compared to the control group (only I/R; p <0.001). Only the fractions 5-10 kDa and <3 kDa were able to reduce the IA and improve the postischemic recovery of LVDP and LVEDP (p<0.001 vs. control). The cardioprotection induced by 5-10 kDa fraction was inhibited by glibenclamide and 5HD (p<0.05 vs. control) and attenuated by chelerythrine and AG490 (p <0.05 vs. Control and 5-10 kDa fraction). The mass spectrometry analysis revealed the presence of proteins involved with cardioprotection in the fraction 5-10 kDa. Conclusion: The cardioprotection exerted by 5-10 kDa fraction is sensitive to K ATP channel blockers, and inhibitors of JAK-STAT and PKC pathways, suggesting the involvement of these pathways in the cardioprotection mechanism. Support: CNPQ, CAPES, FAPERJ. Protocol: 01200.001568/2013-87</p>

Title	VENOUS FUNCTION AT REST AND DURING SYMPATHOEXCITATION IN PATIENTS WITH LONG COVID AND MYALGIC ENCEPHALOMYELITIS/CHRONIC FATIGUE SYNDROME
Authors	GUILHERME HENRIQUE MARTINS DE SOUZA, MONICA VASCONCELOS DE MORAES, JOÃO PAULO FINOTTI FONSECA, ELOARA VIEIRA MACHADO FERREIRA ÁLVARES DA SILVA CAMPOS, RUDOLF KRAWCZENKO FEITOZA DE OLIVEIRA, BRUNO MOREIRA DA SILVA
Affiliations	Setor de Função Pulmonar e Fisiologia Clínica do Exercício, UNIFESP
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Some people infected by the SARS-CoV-2 virus developed long-term signs and symptoms of Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), including orthostatic intolerance. The underlying mechanisms of such dysfunction remain unclear, but one possibility is that the infection compromised the baseline venous function and venous responsiveness to sympathoexcitation. Objective: Investigate the venous function at rest and under sympathoexcitation in patients with Long COVID and ME/CFS. Methods: Fourteen patients have been evaluated. A tight cuff placed on the dominant limb was inflated at 60 mmHg for 5 minutes, inducing venous congestion. This protocol phase allowed analysis of venous capacity (i.e., total venous volume at standard pressure). Then, the cuff was deflated at a rate of 1 mmHg/s to estimate venous capacitance (i.e., venous volume at a transmural pressure of 0 mmHg – unstressed volume) and venous compliance (i.e., change in venous volume per change in venous pressure) combining quadratic and linear regressions. A Near Infrared Spectroscopy (NIRS) probe measured the microvascular concentration of total hemoglobin (THb) in the dominant limb calf. The venous congestion and decongestion protocol was performed at rest and during a 2-minute static handgrip exercise at 30% of the maximal voluntary contraction, followed by a 2-minute post-exercise circulatory occlusion (PECO). The handgrip exercise and PECO started in the 3rd and 5th minutes of the venous congestion protocol. Microneurography of the fibular nerve measured muscle sympathetic nerve activity in a subgroup (n = 6). Results: Eight patients had alterations in the Valsalva maneuver compatible with an increased risk for orthostatic hypotension, whereas six patients had a normal response to the Valsalva maneuver. THb increase from rest to the 5th minute of venous congestion was enhanced in patients with altered than normal Valsalva response during rest [ΔTHb (mean \pm SD): altered Valsalva (n = 8) = 77 ± 15 vs. normal Valsalva (n = 6) = 113 ± 29 μM, P = 0.030] and sympathoexcitation [ΔTHb: altered Valsalva (n = 8) = 71 ± 18 vs. normal Valsalva (n = 6) = 109 ± 45 μM, P = 0.024], indicating an increase in venous capacity. Sympathoexcitation attenuated the venous congestion-induced THb increase from the 3rd to the 5th minute of venous congestion only in the group with normal Valsalva response (P < 0.050). Venous capacitance and compliance were similar between groups at rest and during sympathoexcitation (P > 0.050). MSNA increase during exercise [Δburst frequency: altered Valsalva (n = 3) = 133 ± 58 vs. normal Valsalva (n = 3) = 132 ± 82 % of rest; Δtotal MSNA: altered Valsalva (n = 3) = 143 ± 141 vs. normal Valsalva (n = 3) = 180 ± 87 % of rest] and PECO [Δburst frequency: altered Valsalva (n = 3) = 116 ± 75 vs. normal Valsalva (n = 3) = 105 ± 62 % of rest; Δtotal MSNA: altered Valsalva (n = 3) = 115 ± 78 vs. normal Valsalva (n = 3) = 117 ± 79 % of rest] appeared similar between groups. Conclusion: These preliminary results suggest that patients with long COVID and ME/CFS at increased risk for orthostatic hypotension have increased venous capacity and blunted sympathetically induced microvascular venous constriction during venous congestion. Support: CAPES CNPq Protocol: 69858623.3.0000.5505</p>

Title	VASCULAR PROTECTIVE EFFECTS OF RED QUINOA HYDROLYZATE AGAINST CADMIUM EXPOSURE IN RATS
Authors	SAMIA HASSAN HUSEIN KANAAN, PAOLA ZAMBELLI MORAES, NATHALIA SILVA DE OLIVEIRA SILVA, JOSÉ EUDES GOMES PINHEIRO JR, FRANCK MACIEL PEÇANHA, DALTON VALENTIM VASSALLO, MARTA MIGUEL-CASTRO, GIULIA ALESSANDRA WIGGERS
Affiliations	Grupo de Pesquisa em Fisiologia Cardiovascular, Universidade Federal do Pampa, UNIPAMPA, Laboratório de Eletrofisiologia e Reatividade Vascular, UFES, Instituto de Investigación en Ciencias de la Alimentación, CSIC
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cadmium (Cd) exposure promotes vascular damage in the aorta, leading to vascular dysfunction and increased vasoconstriction mediated by redox imbalance generated by increased oxidative stress, reduced nitric oxide bioavailability, and increased expression of inflammatory markers, mainly COX-2. Natural therapeutic alternatives, especially those derived from diet, should be encouraged to treat the damage caused by this metal, as conventional strategies could have side effects. A Red Quinoa Hydrolyzate (RQH) obtained by hydrolysis with Alcalase demonstrated antihypertensive and antioxidant proprieties in spontaneously hypertensive rats and may help deal with Cd damage to vessels, considering that the metal has high oxidative characteristics. Objective: To investigate whether RQH protects the aorta from damage induced by exposure to high concentrations of Cd. Methods: Male Wistar rats (12 weeks, \pm 350g) were treated for 14 days and divided into four groups (N=10 each): Control (Ct): intraperitoneal (i.p.) injections of distilled water and tap water by gavage; Cadmium (Cd): 1mg/kg/day i.p and tap water by gavage; RQH, 1g/kg/day by gavage and distilled water i.p; CdRQH, Hydrolysate plus Cadmium. (CEUA/Unipampa, protocol number: 010/2023). At the end of treatment, the animals were euthanized. The aorta reactivity was performed in an isolated organ bath, and concentration-response curves to acetylcholine, sodium nitroprusside, and phenylephrine were conducted in the presence and absence of endothelium, nitric oxide synthase inhibitor (L-NAME), selective COX-2 inhibitor (NS398), scavenger of superoxide anion (Tiron) and superoxide dismutase (SOD) were analyzed. Also, aorta immunofluorescence was analyzed for NOX-1 and COX-2. Data are expressed as mean \pm SEM, compared by two-way ANOVA considering $p < 0,05$. Results: Treatment with RQH: a) reduced the increase in the contractile response to Phe promoted by Cd (Rmax: Ct: 63.4 ± 1.6; RQH: 61.8 ± 2.7; Cd: $84.0 \pm 2.3^*$; CdRQH: $62.1 \pm 3.2\%$, % KCl, * vs Ct and # vs Cd); b) prevented endothelial dysfunction caused by Cd and also restored the bioavailability of nitric oxide in the aorta; c) reduced the participation of the COX-2 pathway in the aortic contractile response; d) prevented the increase in ROS/superoxide anion promoted by Cd exposure; f) corroborating the functional data, it reduced the fluorescence intensity of NOX-1 and COX-2 in the aorta, increased by exposure to Cd, demonstrating antioxidant and anti-inflammatory action (NOX-1, Ct: 0.74 ± 0.05; RQH: 0.83 ± 0.11; Cd: $3.95 \pm 0.35^*$; CdRQH: $1.14 \pm 0.13\#$/ COX-2, Ct: 0.94 ± 0.14; RQH: 0.85 ± 0.14; Cd: $3.70 \pm 0.43^*$; CdRQH: $0.98 \pm 0.09\#$, FU). Conclusion: RQH presents itself as a potential therapeutic alternative, with antioxidant and anti-inflammatory properties in the damage caused by Cd in the aorta. Support: CAPES-CNPq, FAPERGS, FAPES, Spanish Government. Protocol: CEUA/Unipampa, Protocol numbe</p>

Title	Anti-Hypertensive and Vasoprotective Effects of Red Quinoa Hydrolysate on Resistance Arteries in Rats Exposed to Cadmium
Authors	PAOLA ZAMBELLI MORAES, SAMIA HASSAN HUSEIN KANAAN, KATYE YASMIN DE SOUZA DE OLIVEIRA, JOSÉ EUDES GOMES PINHEIRO JUNIOR, FRANCK MACIEL PEÇANHA, DALTON VALENTIM VASSALLO, MARTA MIGUEL-CASTRO, GIULIA ALESSANDRA WIGGERS
Affiliations	Programa de Pós Graduação Multicentrico em Ciências Fisiológicas, Universidade Federal do Pampa, Physiological Sciences, Universidade Federal do Espírito Santo, Instituto de Investigación en Ciencias de la Alimentación, CIAL/CSIC
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Red Quinoa Hydrolysate (RQH) is a functional food of plant origin with antioxidant and antihypertensive properties that may be useful in reversing or mitigating the effects of toxic metals on the cardiovascular system. Knowing that exposure to cadmium (Cd) through consumption of drinking water, food, and cigarette smoke causes adverse effects on the cardiovascular system and these effects are related to the increase in oxidative stress and the inflammatory process, research into natural alternatives to combat these effects is essential. Objective: Investigated the effects of RQH supplementation on cardiovascular damage induced by exposure to cadmium chloride (CdCl₂) in rats. Methods: For that, three-month-old male Wistar rats were divided and treated for 14 days (N=10 each): Control (Ct): intraperitoneal (i.p.) injections of distilled water and tap water by gavage; Cadmium (Cd): 1mg/kg/day i.p and tap water by gavage; RQH, 1g/kg/day by gavage and distilled water i.p; CdRQH, Hydrolysate plus cadmium. (CEUA/Unipampa, protocol number: 010/2023). Systolic blood pressure was measured weekly by noninvasive tail plethysmography. At the end of treatment, rats were euthanized, and vascular reactivity was performed in the third branch of mesenteric resistance arteries (MRA) using a wire myograph. Vasoconstrictor response to norepinephrine in the presence of endothelium and NOS inhibitor, superoxide dismutase, and selective COX-2 inhibitor were analyzed. Biochemical parameters of vascular reactive oxygen species and antioxidant capacity were measured in MRA. Results were expressed as mean ± SEM, compared by ANOVA followed by Bonferroni test (P<0.05). Ethics Approval 010/2023, Unipampa. Results: RQH prevented: a) the increased SBP after Cd exposure (Ct: 124.10 ± 1.08; RQH: 123.82 ± 1.56; Cd: 140.81 ± 2.68; CdRQH: 122.97 ± 2.24, mmHg); b) the increased vasoconstrictor response to NE; c) restored the endothelium vasoconstrictor modulation and nitric oxide bioavailability; c) prevented the contractile prostanoids from COX-2; inhibited the increased mesentery ROS production (Ct: 85.32 ± 3.51; RQH: 83.98 ± 4,62; Cd: 136.21 ± 14.70; CdRQH: 87.92 ± 6.88, FU) as well as the imbalance in antioxidant capacity after Cd exposure (Ct: 73.80 ± 10.91; RQH: 44.56 ± 7.71; Cd: 160.81 ± 13.97; CdRQH: 59.95 ± 9.25, nM Trolox equivalents). Conclusion: RQH counteracts the vascular toxic effects after Cd exposure, highlighting a novel therapeutic agent based on functional vegetable food against environmental contaminants. Support: Cnpq; Capes; Fapergs; Fapes; Spanish Government Protocol: 010/2023</p>

Title	AVALIAÇÃO DA REATIVIDADE CARDIOVASCULAR AO ESTRESSE AGUDO APÓS ADMINISTRAÇÃO SISTÊMICA DE DIAZEPAM E GABA
Authors	ANA CLARA ROCHA VIANA, ANA FLÁVIA PALMIERI BORGES, CARINA CUNHA SILVA, ERICK BRYAN DE SOUZA LIMA, MARCO ANTÔNIO PELIKY FONTES
Affiliations	Fisiologia, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Evidências indicam que há uma associação positiva entre ansiedade comórbida e hipertensão. A ativação simpática é uma característica marcante da ansiedade e do estresse emocional levando ao aumento do débito cardíaco e da resistência periférica. O ácido γ-aminobutírico (GABA) é o principal neurotransmissor do SNC de mamíferos e está envolvido no controle cardiovascular. Além de suas ações centrais o GABA e seus receptores também são detectados no sistema periférico. Benzodiazepínicos (BDZ) são uma classe de medicamentos usados para tratar doenças como ansiedade e insônia modulando os efeitos do GABA. Os efeitos do GABA bem como dos BDZs administrados por via sistêmica na resposta cardiovascular ao estresse não são totalmente conhecidos. Objective: Avaliar os efeitos da injeção sistêmica do BDZ diazepam e do GABA na resposta cardiovascular ao estresse agudo. Methods: Ratos Wistar, machos (300 e 350g), foram anestesiados com 0,8mg/Kg de ketamina e 0,1mg/Kg de xilazina, i.p., para a canulação da artéria e da veia femoral. Após 24 horas, inicialmente foram registrados os valores basais de pressão arterial média (PAM) e frequência cardíaca (FC) por vinte e cinco min. Dez min antes do estresse por mudança de ambiente (CSS) grupos separados receberam: Diazepam: 1mg/Kg (n=7) e 10mg/Kg (n=5); GABA 1 mg/Kg (n=5) e 10 mg/Kg (n=5); grupo controle, salina 0,1ml/100g (n=4). Results: Em animais do grupo controle, a exposição ao CSS produziu taquicardia ($\Delta 85 \pm 55$ bpm) e aumento moderado de PAM ($\Delta 9 \pm 2$ mmHg). A administração sistêmica de diazepam reduziu em aproximadamente 28% (1mg/Kg; $P < 0.03$) e 68% (10mg/Kg; $P < 0.05$) a taquicardia produzida pelo CSS. Diazepam não resultou em alterações significativas na reatividade pressórica ao estresse (Diazepam 1mg/Kg, $\Delta 26 \pm 19$; Diazepam 10mg/Kg, $\Delta 24 \pm 19$ mmHg). A administração do GABA não produziu alterações significativas nem na resposta taquicárdica, nem na resposta pressora ao estresse agudo quando comparado ao grupo controle. Conclusion: Os resultados obtidos indicam eficácia do diazepam em atenuar a taquicardia produzida pelo estresse emocional agudo, o que não foi observado para o GABA administrado isoladamente. Support: CNPq: MAPF 308923/2021-9, ACVG 165774/2021-5; MAPF FAPEMIG: APQ-01128-21. Protocol: CEUA UFMG nº248/18</p>

Title	Cardiovascular and neuromuscular responses to orthostatic stress under a heated environment
Authors	FELIPE CASTRO FERREIRA, MICHELLE CRISTINA SALABERT VAZ PADILHA, JOÃO VICTOR VELTRI XAVIER, GUIDO ROBBS MOREIRA, JÚLIO ALVES CRUZ, PEDRO PAULO DA SILVA SOARES, MARCO ANTONIO ARAUJO LEITE, GABRIEL DIAS RODRIGUES
Affiliations	Department of Physiology and Pharmacology, UFF, Clinical Research Unit in Neurology and Neurosciences, UFF
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The orthostatic position depends on the circulatory adjustments, which require an integrated control of cerebral blood flow and blood pressure (BP) mechanisms and the coordinated activity of postural muscles. At the onset of orthostatic position (ORT onset), greater postural instability is associated with a deep fall in BP. Due to thermoregulatory mechanisms of skin vasodilation, heat stress (HOT) provokes an additive effect on cardiovascular control by challenging BP regulation during ORT. However, the effects of HOT on BP and postural control responses during ORT onset remain unclear. Objective: to investigate whether postural control is affected by the hemodynamic changes provoked by HOT during ORT onset.</p> <p>Methods: 14 healthy individuals aged 25 ± 3 years (eight women) participated in this study, each one performing two orthostatic tests: first under thermal comfort (TC, 24 °C) and subsequently under HOT (38 °C). Systolic blood pressure (SBP) and R-R intervals for heart rate (HR) were continuously recorded for 30 min in supine (SUP) and during the initial orthostasis (ORT onset) after the supine-to-stand challenge. Supine-to-stand variations ($\Delta\%$) were calculated. Sublingual temperature (Tsl) was measured after 30 min in SUP. Postural control was assessed by evaluating center-of-pressure (COP) distance oscillations and through electromyography (EMG) activity of the calf muscles (medial gastrocnemius and tibialis anterior) during ORT onset (15 seconds of ORT), in the same period from hemodynamic analysis. Paired t-test was used. Results: Tsl increased in HOT compared to TC (TC 36.5 ± 0.3 vs. HOT 36.7 ± 0.3 °C; $p < 0.01$). At SUP, SBP (TC 119.5 ± 11.44 vs. HOT 106.8 ± 18.81 mmHg; $p = 0.05$) decreased, while HR increased (TC 62 ± 8 vs. HOT 68 ± 7 bpm; $p < 0.01$) under HOT comparing to TC condition. Regarding supine-to-stand variations, SBP showed a greater fall in HOT compared to TC condition ($\Delta\%TC -24.5 \pm 13.2$ vs. $\Delta\%HOT -33.2 \pm 20.2\%$; $p = 0.01$). No difference was found between thermal conditions for HR ($\Delta\%TC 58.4 \pm 14.1$ vs. $\Delta\%HOT 52.7 \pm 15.1\%$; $p = 0.12$). COP distance was greater in HOT compared to TC condition (TC 596.6 ± 242.4 vs. HOT 680.2 ± 249.1 mm; $p < 0.01$). EMG activity of the gastrocnemius decreased in HOT compared to TC condition (TC 95.5 ± 19.8 vs. HOT $78.4 \pm 22.8\%$ mV; $p = 0.02$), while EMG of tibialis did not change between thermal conditions (TC 83.5 ± 42.9 vs. HOT $66.1 \pm 31.9\%$ mV; $p = 0.29$). Conclusion: Heat stress causes a greater fall in blood pressure and a reduction in musculoskeletal pump activity during orthostatic onset. These effects could be potential mechanisms that underlie augmented postural instability under a heated environment. Support: CAPES, FAPERJ, CNPq. Protocol: CAAE 28151519.0.0000.5243</p>

Title	The short-term estrogen deprivation increases the vulnerability of cardiomyocytes to Gq-induced remodeling
Authors	TAMIRES AMORIM MARINHO, MÁRIO DE MORAIS E SILVA, MARCOS ELIEZECK DOS SANTOS INÁCIO, KIANY MIRANDA, NAOMI ALVES REZENDE, VITORIA ESTANISLAU GANDRA, SILVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	DFIB, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The existence of sexual dimorphism in cardiovascular disease predisposition, as well as differences between reproductive-aged and postmenopausal women, underscores the importance of studying the influence of estrogen on pathophysiological processes. G-protein coupled receptors (GPCRs) are highly expressed in cardiomyocytes (CMs), with Gq-coupled GPCRs playing a pivotal role in the cardiac response to a multitude of biologically hormones. Hyperactivation of these receptors has been demonstrated to stimulate hypertrophic and pro-fibrotic responses, endothelial dysfunction, inflammation, and rhythm disturbances associated with pathological remodeling. Objective: The objective of this study is to examine the impact of Gq activation in CMs of intact and short-term ovariectomized (OVX) female mice in order to elucidate the mechanisms of estrogen mediated protection. Methods: The study employed transgenic mice expressing DREADD-hM3Dq receptors, which are modified GPCRs that specifically couple to Gαq proteins. Upon clozapine-N-oxide (CNO) these receptors induce classical Gαq signaling responses. In this model, the CRE recombinase enzyme removes a stop codon in the DREADD construct, thereby enabling DREADD expression. Two methods achieved CRE expression: crossing with Myh6-CRE mice for CM-specific DREADD-hM3Dq expression or using AAV9 as a vector for TnT-CRE, allowing control over the percentage of CMs expressing the DREADD receptor based on viral particle delivery. Female mice expressing hM3Dq-CRE and hM3Dq-AAV9-CRE, along with CRE-negative controls, were divided into SHAM and OVX groups. Seven days post-ovariectomy, the females were treated with CNO for three days via intraperitoneal injection, followed by heart harvesting for analysis of weight, CM area and calcium transient. Results: The activation of Gq by CNO had no effect on heart weight between the groups. However, at the CM level, Gq activation resulted in a statistically significant increase in CM area only in the OVX group (hM3Dq-CRE/OVX/CNO: 273µm² ± 5.1, n=291 cells vs hM3Dq-CRE/SHAM/CNO: 240µm² ± 4.2, n=302 cells p= 0.0001). Short-term OVX effects on CM area were also significant (hM3Dq-WT/OVX 255µm² ± 4.8, n=223 cells vs. hM3Dq-WT/SHAM 230.8µm² ± 5.7, n=183 cells, p=0.006). These data suggest that estrogen deprivation, even at short-term, renders CMs more susceptible to the effects of Gq activation. In the hM3Dq-CRE model, all CMs express the DREADD receptor, allowing Gq activation in all cells. To determine whether the number of cells with Gq activation influences the hypertrophic response in short-term OVX CMs, mice were infected with AAV9-TnT-CRE at dose that resulted in 25% of CMs expressing the DREADD receptor. The AAV9-TnT-CRE mice, along with CRE-negative controls were divided into two groups: a SHAM and an OVX group, treated with CNO. Interestingly, under this new condition Gq+ activation had no effect on CM hypertrophy of OVX mice, indicating that the number of cells with Gq activation influences the level of hypertrophic growth. Despite the aforementioned lack of effect, Gq+ cells from OVX hearts exhibited reduced calcium release compared to OVX CRE-negative controls cells (cells with no Gq activation). Conclusion: These findings underscore the notion that even brief estrogen deprivation renders CMs more susceptible to stressors, thereby corroborating the protective role of estrogen in the heart. Future experiments will endeavor to elucidate the underlying mechanisms responsible for these effects. Support: CNPq, CAPES, FAPEMIG, PRPq e INCT NanoBioFar. Protocol: 68/2022</p>

Title	Probiotic treatment reduces metabolic and cardiovascular responses to chronic stress in a preclinical model
Authors	LÍVIA BRUNI DE SOUZA, ANA BEATRIZ BRANDÃO, FABIANA FERREIRA GOMES, VINICIUS GUZZONI, RAQUEL ALBUQUERQUE, DULCE ELENA CASARINI, NÁDIA BERTONCELLO, FLAVIO AIMBIRE, RITA DE CÁSSIA MARQUETI, KARINA RABELLO CASALI, TATIANA SOUSA CUNHA
Affiliations	Department of Medicine, UNIFESP, Medpace Core Laboratories, Medpace Core Laboratories, Physiotherapy Division, UnB, Institute of Science and Technology, UNIFESP
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chronic stress negatively affects the cardiovascular system, causing pathological changes in the left ventricle. Objective: Investigate whether probiotics can alleviate stress-induced cardiovascular disturbances. Methods: Male Wistar rats were randomly assigned to four groups: Control (C), Stress (S), Control+Probiotic (CP), and Stres+Probiotic (SP) (8-12 rats/ group). Probiotics (Lacticaseibacillus rhamnosus and Limosilactobacillus reuteri, 1 billion colony-forming units per probiotic, Terapêutica Farmácia de Manipulação, Brazil) were administered for 8 weeks. Chronic mild unpredictable stress (CMUS) was applied during weeks 3, 4, and 5 (protocol #6533240621). The rats were euthanized 15 days after CMUS, and blood and left ventricle samples were collected. Corticosterone, total creatine kinase (CK), metalloproteinases (MMP), cytokines (TNF-α, IL-1β and IL-10) and lipid peroxidation were evaluated. Results: Stress increased corticosterone (S: 188\pm11 vs. C: 60\pm5 and SP: 65\pm31 ng/mL) and total CK (S: 17018\pm6591 vs. C: 7290\pm3275 and SP: 9875\pm1996 U/L). In heart tissue, the stressed group showed an increase in intermediate MMP-2 (S: 350991\pm52031 vs. C: 243421\pm21150 AU, p<0.01) and active MMP-2 (S: 19686\pm8438 vs. C: 10927\pm2376 AU, p<0.01). On the other hand, probiotics mitigated the expression of pro MMP-2 (SP: 43811\pm21071 vs. S: 75111\pm9441 AU, p<0.01), intermediate MMP-2 (SP: 284009\pm63207 vs. S: 350991\pm52031 AU, p<0.05), and active MMP-2 (SP: 10359\pm894 vs. S: 19686\pm8438 AU, p<0.01). Stress increased cardiac TNF-α (S: 5.8\pm2.18 vs. C: 1.1\pm0.2 pg/mg, p<0.0001), IL-1β (S: 5.1\pm0.9 vs. C: 1.1\pm0.1 pg/mg, p<0.0001), and the anti-inflammatory cytokine IL-10 (S: 19.9\pm14 vs. C: 6.1\pm1.4 pg/mg, p<0.05). Probiotics reduced IL-1β even under chronic stress (SP: 3\pm0.5 vs. S: 5.1\pm0.9 pg/mg, p<0.0001). We did not observe statistical differences in lipid peroxidation. Conclusion: These findings support the potential of probiotics in alleviating stress-induced cardiovascular disturbances. Support: The authors thank Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) [grant number 2021/05331-1 and 2017/17027-0] for financial support. Protocol: CEUA nº 6533240621</p>

Title	Temporal Influence on Cardiac Responses during Takotsubo-like Cardiomyopathy
Authors	GABRIEL MATOS NOGUEIRA, BRUNO SANCHES DE LIMA, FERNANDO SOUZA-NETO, SÉRGIO RICARDO ALUOTTO SCALZO JÚNIOR, JOP VAN BERLO, CIBELE ROCHA-RESENDE, MARCOS ELIEZECK DOS SANTOS INÁCIO, SILVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Department of Integrative Biology and Physiology, University of Minnesota
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Takotsubo cardiomyopathy (TC) is a detrimental cardiac event primarily affecting women. In this condition, stressful events such as the loss of loved ones or grieving lead to intense catecholamine release, which induces pathological changes in the heart including hypertrophy, cell death, inflammation, and fibrosis. Previous data from our group have shown that immune response in a pharmacological model of TC using an overdose of isoproterenol (ISO) is more robust when animals are challenged at night. However, the impact of the time of the day on cardiac hypertrophy and functional parameters following ISO overload remains unclear. Objective: To investigate the temporal influence on cardiac function and hypertrophy during TC. Methods: We used 8-week-old female mice weighing 20-25g, divided into 4 experimental groups: CTRL ZT0 (animals treated with a sterile saline solution when the animal facility room lights are on); ISO ZT0 (animals treated with a single dose of ISO, 300 mg/Kg, intraperitoneally); CTRL ZT12 (animals treated with saline when the animal facility room lights are off); and ISO ZT12. One hour post-treatment, animals were anesthetized with isoflurane, and M-mode echocardiography was performed. Three days post-treatment, animals were sacrificed at their respective ZTs, and hearts were collected for cardiomyocyte isolation. Each experimental group comprised 5 animals. Results: ISO increased ejection fraction (CTRL ZT0: 47.7±4.0%; ISO ZT0: 64.9±6.1% vs CTRL ZT12: 76.1±3.3%; ISO ZT12: 76.7±6.2%) and fractional shortening (CTRL ZT0: 23.4±2.4%; ISO ZT0: 35.1±4.4% vs CTRL ZT12: 43.6±2.8%; ISO ZT12: 45.4±6.2%) of the heart only at ZT0, compared to the control groups. Consistently, functional assessment of cardiomyocytes showed increased contractility only in cells isolated from ISO-treated animals at ZT0 (CTRL ZT0: 528.6±28.4µm² vs ISO ZT0: 687.5±30.2µm², n=130 cells), indicating a functional impairment in cardiomyocytes treated at ZT12. This idea was supported by calcium transient analysis, where ISO increased calcium transient amplitude only in ZT0-treated cells (CTRL ZT0: 3.09±0.12A.U. vs ISO ZT0: 3.78 ± 0.16A.U. n=120 cells) and decreased the calcium transient amplitude at ZT12 (CTRL ZT12: 3.81±0.17 vs ISO ZT12: 2.93±0.09 n=120 cells). We further assessed cardiomyocyte hypertrophy, as increased cell size would indicate the occurrence of pathological remodeling resulting in cellular function impairment. Surprisingly, ISO induced greater cardiomyocyte area (CTRL ZT0: 2127±63.49µm²; ISO ZT0: 2503±57.9µm² vs CTRL ZT12: 2211±60.9µm²; ISO ZT12: 2725 ± 59.05µm², n=150 cells) and width (CTRL ZT0: 22.79±0.55µm; ISO ZT0: 25.59±0.47µm vs CTRL ZT12: 22.31±0.60µm; ISO ZT12: 26.58±0.52µm, n=150 cells) at ZT12. Conclusion: Our data indicate that the time of the day strongly affects the cardiomyocyte remodeling and functional responses that occur following ISO overload. This finding underscores the need to consider temporal factors in therapeutic and experimental approaches involving acute and pathological cardiac events during TC. Support: CNPq, FAPEMIG, CAPES Protocol: 175/2021</p>

Title	PAPÉL DA HIPERATIVIDADE SIMPÁTICA NA MANUTENÇÃO DA HIPERTENSÃO ARTERIAL (HA) EM RATOS ESPONTANEAMENTE HIPERTENSOS (SHR)
Authors	STEPHANIE FURTADO GEROLIN, GUSTAVO DOS REIS MARTINS, VINICIUS CAVALCANTE DINIZ, ALEXANDRE SIMÃO BIQUIZA, CRISTIANE DAMAS GIL, RUY RIBEIRO CAMPOS JUNIOR, CASSIA M DE TOLEDO BERGAMASCHI
Affiliations	Fisiologia Cardiovascular, Unifesp, Morfologia e Biologia Estrutural, Unifesp
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Diversos estudos têm sugerido a interação entre a ativação do sistema nervoso autônomo e consequente elevação da pressão arterial. No entanto, quando e como ocorre esta influência ainda não é totalmente compreendido. Objective: Buscamos estabelecer a cronologia da progressão da HA e sua correlação com neuroinflamação e atividade vasomotora simpática renal (ANSr) e esplênica (ANSe) em ratos espontaneamente hipertensos (SHRs). Methods: Utilizamos SHRs adultos (10 a 15 semanas – 210 a 320g), jovens (5 a 7 semanas – 90 a 150g) e wistar controle (12 semanas – 350 a 400g) para registros direto de pressão arterial, frequência cardíaca e ANSr e ANSe. Foram coletadas amostras de sangue e tecido esplênico e encefálico para análises de citocinas séricas e teciduais de regiões específicas envolvidas no controle cardiovascular, sendo elas RVLM e PVN. Também foi analisada a presença de citocinas na região de córtex como controle. Results: O valor basal de pressão arterial média (PAM) foi de 109 ± 7 mmHg para os SHRs jovens e de 163 ± 9 mmHg para adultos, como esperado. Em relação à ANS, os níveis basais de ANSr dos animais jovens foram de $126,6 \pm 27,6$ spikes/seg e dos adultos de $138,5 \pm 32,7$ spikes/seg. A ANSe basal do SHR jovens foi de $144,0 \pm 30,3$ spikes/seg e do SHR adultos foi de $130,7 \pm 26,3$ spikes/seg. No grupo controle de ratos Wistar adultos (CTRL, 12 semanas), os valores de ANSr foram de $87,2 \pm 5$ spikes/seg e $102,8 \pm 18,1$ spikes/seg para ANSe. Observamos aumento da IL-1beta no baço dos SHR Adultos (89.5 ± 26.47 pg/mg) em relação aos SHR jovens (56.92 ± 14.8 pg/mg) e diminuição em relação Wistar CTRL (144.9 ± 17.05 pg/mg) e também diminuição do TNF-alfa (SHR Adulto 0.7 ± 1.6 pg/mg, SHR Jovem 0.63 ± 0.63 pg/mg e Wistar CTRL 0.98 ± 0.19 pg/mg. Na RVLM observamos aumento do TNF-alfa no grupo SHR adulto (0.28 ± 0.05 pg/mg) em comparação tanto com SHR Jovem (0.17 ± 0.47 pg.mg) quanto Wistar CTRL (0.18 ± 0.02 pg.mg). Conclusion: Os resultados obtidos até o momento demonstram, que apesar da diferença de pressão arterial entre os grupos de SHR jovens e adultos, não foi observado diferença de ANSr e ANSe. Entretanto, em comparação com animais Wistar adultos, observamos aumento na ANSr e ANSe tanto para animais jovens quanto adultos, indicando que a hiperatividade simpática precede o desenvolvimento da HAS em SHRs. Quanto à análise histológica e imuno-histoquímica do tecido cerebral para avaliar o nível de neuroinflamação entre os grupos, foi possível observar aumento de citocinas na RVLM. Ademais, observamos também diminuição de citocinas teciduais do parênquima esplênico e circulantes. Conclui-se assim que a neuroinflamação pode ser um parâmetro ainda mais evidente na HAS que a própria inflamação periférica. Support: CAPES, FAPESP e CNPq Protocol: CEUA-Unifesp nº 835908322</p>

Title	Cardiomiócitos regulam a proliferação de macrófagos cardíacos?
Authors	GIOVANE LUCAS DO CARMO PIRES, HENRIQUE ABRAMO, MÁRIO MORAIS, SILVIA GUATIMOSIM, CIBELE ROCHA-RESENDE
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A ativação da via da proteína Gq no coração é um dos fatores envolvidos no remodelamento cardíaco em várias doenças. Dados prévios do nosso grupo demonstram que a composição das subpopulações de macrófagos residentes no coração está alterada em camundongos DREADD-Gq, um modelo murino que permite a ativação específica da via da proteína Gq apenas nos cardiomiócitos. Sabe-se que os macrófagos residentes do coração se mantêm principalmente por proliferação in situ, porém o mecanismo que regula este fenômeno ainda não é bem compreendido. Nossa hipótese é que exista um cross-talk cardiomiócito/macrófago e que seja o cardiomiócito um dos reguladores da população de macrófagos residentes cardíacos. Objective: Investigar se a ativação da via Gq no cardiomiócito leva a um aumento na proliferação de macrófagos cardíacos. Methods: Para induzir a ativação da via Gq exclusivamente em cardiomiócitos, tratamos camundongos DREADD-GqCre⁺ (com 4 semanas de idade e aproximadamente 15 gramas) com clozapina (CNO 0,5 mg/Kg, IP), agonista dos receptores DREADD, por 7 dias. Animais DREADD-GqCre⁻ foram utilizados como grupo controle. Após o período de tratamento, os animais foram eutanasiados e os corações foram coletados para análise. Para avaliar as alterações no potencial proliferativo dos macrófagos cardíacos no modelo DREADD-Gq, nós utilizamos as técnicas de imunofluorescência e citometria de fluxo e avaliamos a expressão do marcador Ki-67 e a incorporação de BrdU, ambos marcadores de proliferação. Results: Inicialmente, nós confirmamos o aumento no número de macrófagos CD68⁺ no coração dos animais DREADD por imunofluorescência (DREADD-GqCre⁻: 7.7+/-0.7 vs DREADD-GqCre⁺: 11.53+/-0.7). Interessantemente, o número de células CD68+Ki-67⁺ está aumentado no coração dos animais com ativação da via Gq no cardiomiócito (DREADD-GqCre⁻: 2.0+/-0.2 vs DREADD-GqCre⁺: 3.3+/-0.3), sugerindo que estas células apresentam uma taxa de proliferação aumentada. Para confirmar estes achados, nós avaliamos a incorporação de BrdU pelos macrófagos cardíacos através da técnica de citometria de fluxo. Nossos dados mostram que a incorporação de BrdU também está aumentada nos macrófagos cardíacos dos animais DREADD-GqCre⁺ (1.0+/-0.1) em comparação aos animais DREADD-GqCre⁻ (6.6+/-0.7). Conclusion: Nossos dados indicam, por duas metodologias complementares, que a proliferação de macrófagos residentes está aumentada após a estimulação da via Gq no cardiomiócito. Em conjunto, estes dados apontam para um nível de regulação destas células dependente da interação com os cardiomiócitos. Nosso próximo passo é avaliar a proliferação destes macrófagos quando mantidos em cultura e incubados com cardiomiócitos de animais DREADD ativados com CNO. Support: FAPEMIG Universal (APQ-01154-23), Instituto Serapilheira (Chamada 06/2022, 8192 #2211-42259), FAPEMIG (APQ-05838-23), Recém-contratados UFMG (Chamada FUNDEP 01-2022), PROBIC/FAPEMIG. Protocol: CEUA 331/2023</p>

Title	Cardiomyocyte Gq signaling activation through DREADD-Gq/CRE-lox system induces an irreversible loss-of-function cardiac remodeling
Authors	VITORIA ESTANISLAU GANDRA, MÁRIO MORAIS, ANDERSON KENEDY, ANDRÉ MONTEIRO, ITAMAR COUTO, SÉRGIO SCALZO, VICTOR MOURA, SILVIA GUATIMOSIM
Affiliations	Fisiologia e Biofísica, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Pathological cardiac remodeling is an important clinical burden encompassing molecular, cellular, and interstitial changes associated with size and function alterations. In this stressful environment, cardiomyocytes (CMs) respond with hypertrophy and increased contractility due to their limited turnover capacity. CM loss-of-function associated with fibrosis caused by fibroblasts (FB) impairs cardiac function, leading to heart failure. Despite the advancements in managing these alterations, many patients still exhibit resistance to treatments, and reverse remodeling is not easily achieved. To investigate the aspects of cardiac remodeling caused by CMs and the intrinsic recovery capacity of the myocardium, we used the DREADD/CRE-lox platform to express hM3Dq receptors exclusively in CMs. hM3Dq is a modified GPCR for Gq-selective signaling responses that can induce cardiac remodeling when activated by clozapine N-oxide (CNO). Objective: To characterize cardiac remodeling induced by DREADD-Gq activation exclusively in CMs and the occurrence of spontaneously reverse remodeling. Methods: By crossing DREADD and CRE mice, we produced animals expressing the hM3Dq receptor in CMs, as CRE enzyme is necessary for DREADD expression. The male mice (6 weeks old, 20g) received CNO (0.5 mg/kg) for 7 days in a control group (Dq) without DREADD and also in the Dq/CRE group to activate Gq via in CMs. To investigate the capacity of the myocardium to achieve reverse remodeling, mice injected with CNO for 7 days were allowed to rest for 14 (Dq/CRE-R14) or 28 (Dq/CRE-R28) days without CNO (CEUA: 243/2021). To analyze cardiac remodeling, slices of frozen cardiac tissue were stained with WGA fluorescent probe and antibodies (α-SMA, collagen III and TGF-β) in western blot or immunofluorescence assays. Cardiac function was assessed through echocardiography (long axis). Data are presented as MEAN \pm SEM. Statistical analysis was performed using one-way ANOVA with Tukey's post hoc test. Results: CNO treatment for 7 days induced hypertrophy (μm²): Dq 315,4 \pm 9,88 (n=7) versus Dq/CRE 460,0 \pm 10,87 (n=8) and an increase in collagen III deposition (A.U.): Dq 2,30 \pm 0,22 (n=3) versus Dq/CRE 4,24 \pm 0,23 (n=3). After the 14 days resting period neither hypertrophy (μm²): Dq/CRE-R14 428,3 \pm 12,83 (n=4) or collagen III normalized (A.U.): Dq/CRE-R14 4,17 \pm 0,9 (n=3). FB activation was evaluated through α-SMA and CNO treatment increased its expression (A.U.): Dq 0,46 \pm 0,13 (n=6) versus Dq/CRE 1,01 \pm 0,26 (n=5), which remained activated after resting period (A.U.): Dq/CRE-R14 1,04 \pm 0,51 (n=7). Interestingly echocardiogram showed a loss of function in Dq/CRE-R14 group compared to the others groups with a reduction in ejection fraction (%) Dq 65,70 \pm 4,22 (n=7) versus Dq/CRE 63,65 \pm 6,46 (n=8) versus Dq/CRE-R14 55,73 \pm 4,76 (n=8). To access if reverse remodeling could be achieved, we increase the rest period to 28 days after 7 days of CNO treatment, but once again hypertrophy (μm²) Dq 306,0 \pm 30,10 (n=4) versus Dq/CRE 407,8 \pm 32,75 (n=4) versus Dq/CRE-R28 416,5 \pm 20,96 (n=4) and collagen III deposition (A.U.) Dq 1,16 \pm 0,21 (n=3) versus Dq/CRE 6,01 \pm 1,08 (n=3) versus Dq/CRE-R28 4,6 \pm 0,28 (n=3) remained elevated. Conclusion: These data show that DREADD-Gq activation for 7 days can cause a broad spectrum of irreversible pathological alterations in the heart. In this context, we presented new evidence indicating that cardiac unloading by the removal of initial Gq activation results in a deterioration of heart function. Support: CNPq, CAPES, FAPEMIG Protocol: 243/2021</p>



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Title	O impacto da disbiose intestinal induzida por antibioticoterapia no efeito cardiovascular de peptídeos do sistema renina-angiotensina
Authors	YASMIN KOLZ BROZEGHINI, CRISTIANE AMORIM DE PAULA, ADELSON HERIC ALVES MONTEIRO, GABRIELA DE CASTRO MAGALHÃES, NÍCIA PEDREIRA SOARES, KAMYLLE SILVA FERRAZ, THIAGO VERANO-BRAGA
Affiliations	Fisiologia, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Um dos maiores problemas de saúde pública no Brasil é a hipertensão arterial, causada, dentre outros fatores, pelos hábitos de vida adotados pela população, incluindo uma alimentação pobre em fibras e predominantemente ultra-processada. Além disso, o uso inadequado de antibióticos tem se mostrado outro fator de risco. Paralelamente, o sistema renina-angiotensina (SRA) é fundamental para a regulação do sistema cardiovascular, mas esse sistema é inefetivo na ausência de microbiota. Sendo assim, se faz necessário estudar a correlação entre a microbiota intestinal e o SRA. Objective: Analisar a influência da disbiose intestinal na modulação cardiovascular exercida pelo SRA. Methods: Ratos Wistar (normotensos), 3 meses e pesando 400g foram divididos em dois grupos: normobiose e disbiose, que foi induzida pelo tratamento com ampicilina 1 g/L na água de beber por 2 semanas e uma dose única de 200 mg de estreptomicina por gavagem no sétimo dia do tratamento. Animais do grupo normobiose receberam apenas o veículo (NaCl 0,9%). Ao término do tratamento, os animais foram submetidos à cirurgia de canulação (artéria e veia femoral). No dia seguinte, iniciou-se o registro dos parâmetros cardiovasculares: pressão arterial média (PAM) e frequência cardíaca (FC). Foi administrado (i.v.) doses crescentes de angiotensina II (ang II): 7,5 nmol/kg (dose 1), 15 nmol/kg (dose 2) e 30 nmol/kg (dose 3). Results: Foi possível observar uma tendência de valores maiores de PAM e FC nos ratos Wistar com disbiose: PAM (normobiose vs. disbiose) = $118 \pm 4,6$ mmHg vs. $122 \pm 3,5$ mmHg ($P > 0,05$; $n = 3$); FC (normobiose vs. disbiose) = $337 \pm$ bpm vs. $371 \pm 37,5$ bpm ($P > 0,05$; $n = 3$). Essa tendência também foi observada após a administração (i.v.) de ang II: DOSE 1: PAM (normobiose vs. disbiose) = $123 \pm 5,3$ mmHg vs. $127 \pm 12,0$ mmHg ($P > 0,05$; $n = 3$); FC (normobiose vs. disbiose) = $301 \pm 70,5$ bpm vs. $334 \pm 18,4$ bpm ($P > 0,05$; $n = 3$); DOSE 2: PAM (normobiose vs. disbiose) = $135 \pm 9,6$ mmHg vs. $149 \pm 17,6$ mmHg ($P > 0,05$; $n = 3$); FC (normobiose vs. disbiose) = $311 \pm 14,3$ bpm vs. $301 \pm 8,6$ bpm ($P > 0,05$; $n = 3$); DOSE 3: PAM (normobiose vs. disbiose) = $146 \pm 8,3$ mmHg vs. $157 \pm 11,6$ mmHg ($P > 0,05$; $n = 3$); FC (normobiose vs. disbiose) = $291 \pm 20,8$ bpm vs. $287 \pm 21,5$ bpm ($P > 0,05$; $n = 3$). Após converter os valores (PAM e FC) para área sob a curva (ASC), foi possível detectar, apenas para a PAM, um valor significativamente maior para os animais com disbiose: ASC (PAM x dose normobiose vs. disbiose) = $265 \pm 7,1$ mmHg x nmol/kg vs. $285 \pm 12,2$ mmHg x nmol/kg ($P = 0,04$; teste t unilateral; $n = 3$); ASC (FC x dose normobiose vs. disbiose) = $926 \pm 51,9$ bpm x nmol/kg vs. $964 \pm 25,9$ bpm x nmol/kg ($P > 0,05$; $n = 3$). Conclusion: Apesar de preliminar, este estudo parece promissor, pois a PAM dos animais Wistar com disbiose parece alterar de forma mais pronunciada à ang II. Contudo, será necessário realizar mais experimentos para se elaborar uma conclusão mais assertiva sobre o impacto da disbiose nos efeitos cardiovasculares do SRA. Support: INCT-Nanobiofar, CNPq, Fapemig, Capes. Protocol: 156/2024</p>



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Title	The co-chaperone STI1 functions as a novel regulator of the NRF2 oxidative stress response in cardiomyocytes
Authors	VICTOR MOURA VIDAL COSTA, FERNANDO ARAUJO ESPANHOL, IAGO NASCIMENTO PINHEIRO, ANDERSON KENEDY SANTOS, FERNANDO PEDRO NETO, IARA PASTOR NOGUEIRA, ITAMAR COLTO GUEDES DE JESUS, SERGIO SCALZO, DIANA GÓMEZ MENDOZA, THIAGO VERANO BRAGA,- SILVIA GUATIMOSIM
Affiliations	fisiologia e biofísica, Universidade Federal de Minas Gerais
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Stress-induced protein 1 (STI1) is a co-chaperone widely studied in neurons, where it plays a role in cytoprotection. In the heart, our group was the first to investigate the role of STI1. By employing a knockdown model of STI1 expression (STI1+/-), we demonstrated that their hearts are more susceptible to isoproterenol (ISO)-induced injury. Conversely, hearts with elevated STI expression (STI1-TGA) demonstrated enhanced protection against ISO-induced damage. In a clinical context, we demonstrated that the STI1 protein is reduced in cardiac samples from patients with heart failure. Viewed together these data provide evidence that STI1 plays a role in cardioprotection. However, the mechanism by which this occurs remains unclear. Objective: To investigate the signaling pathways activated by STI1 in response to chronic adrenergic activity and hypoxia, with the aim of elucidating the mechanisms underlying STI1-induced cardioprotection. Methods: STI1+/-, STI1-TGA and their littermates were treated with ISO (25mg/kg) for 7 days. Cardiac samples were subjected to proteomic analysis and immunofluorescence. In an in vitro model, STI1 was silenced in a neonatal rat cardiomyocyte culture (NRCMs) and the cells treated with CoCl₂ (500µM). In addition, we conducted experiments with neonatal mouse cardiomyocytes (NMCMS) isolated from WT and STI1+/- mice. Results: Proteomic predictions indicated the presence of cell death and fibrosis in the STI1+/-/ISO heart compared to the WT/ISO. This phenotype was validated by performing picosirius red staining and quantifying caspase 3 activation, which were both elevated in the STI1+/-/ISO heart compared to WT/ISO. Among the dysregulated signaling pathways identified by proteomics in the STI1+/-/ISO heart, the inhibition of NRF2 signaling was observed. The immunofluorescence data obtained using anti-NRF2 staining, confirmed a reduction in the STI1+/-/ISO heart relative to WT/ISO heart (Intensity/area: WT 4±2; WT/ISO 27.2±8; STI1+/- 6.8±1.5; STI1+/-/ISO 4.1±1.7; N=3 hearts). An upregulation of NRF2 was observed in the STI1-TGA mice treated with ISO, a finding that opposes the NRF2 reduction observed in the STI1+/-/ISO heart. To gain further insight into this relationship, we transfected NRCMs with siRNA directed to STI1. Cardiomyocytes transfected with STI1-siRNA exhibited an 80% reduction in STI1 mRNA, and an increase in ROS relative to MOCK transfected cells (Intensity/area: MOCK 336±16.6; siRNA 779±80; N=44 cells/3 cultures). Similar findings were observed in NMCMS isolated from STI1+/- mice. In light of these observations, we sought to determine whether STI1-deficiency would enhance the susceptibility of NMCMS to ROS-induced cell death. To address this question, we treated STI1+/- and WT cardiomyocytes with the hypoxia-mimetic agent CoCl₂ for 12h. STI1+/- cardiomyocytes exhibited a greater degree of cell death in response to CoCl₂ relative to WT (%Dead cells: WT 3±1.3; WT/CoCl₂ 22.4±1.7; STI1+/- 3.2±1.3; STI1+/-/CoCl₂ 32.6±2.9; N=3). NRCMs transfected with STI1-siRNA exhibited a comparable elevation in cell death in comparison to MOCK group. Supporting the proteomic data, NRCMs transfected with STI1-siRNA do not exhibit an increase in NRF2 levels in response to CoCl₂. Conclusion: Our findings underscore the pivotal role of STI1 in the regulation of NRF2 levels and survival under stress conditions within cardiomyocytes. These findings highlight the potential therapeutic value of this co-chaperone in the context of cardiovascular disease. Support: CAPES, FAPEMIG, CNPq, Pró-reitoria de Pesquisa-UFGM Protocol: 97/2022</p>

Title	CARDIAC INFLAMMATION DURING TAKOTSUBO-LIKE CARDIOMYPATHY IS WORSE AT NIGHT PHASE IN FEMALE MICE
Authors	FERNANDA TUPINI DAS DORES, BRUNO SANCHES LIMA, FERNANDO P SOUZA-NETO, ANDERSON KENEDY SANTOS, MARCOS ELIEZECK, SÉRGIO A SCALZO, CIBELE ROCHA RESENDE, SILVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	Fisiologia e Farmacologia, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS, Pediatrics, Yale, Dept of Integrative Biology and Physiology, University of Minnesota
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Takotsubo cardiomyopathy (TC) is an acute cardiac event in which physical and emotional stressors induce the release of high levels of catecholamines. It primarily affects women leading to detrimental cardiac changes such as cell death and inflammation. It has been demonstrated that myocardial inflammation plays a pivotal role in the pathogenesis of TC. Given that the immune response exhibits a diurnal rhythm, it is of major importance to study the implications of the time of the day for the TC.</p> <p>Objective: To investigate the impact of the time of day on the morphological and inflammatory outcomes of TC. Methods: A single intraperitoneal dose (300mg/kg) of isoproterenol (ISO) was used to induce the TC in mice. Female C57BL/6 mice, aged 10-12 weeks, weighting 20-25g, were divided in 4 experimental groups: CTRL ZT0 (treated with saline at 7 am) and ISO ZT0; CTRL ZT12 (treated with saline at 7 pm) and ISO ZT12. The experimental design consisted of 6-8 animals per group. After 72 hours of ISO-treatment, the animals were sacrificed, and the hearts were processed for histology and flow cytometry analysis. We used 2-way ANOVA following the appropriate post-hoc test for statistical analysis, and null hypothesis was rejected when $p < 0.05$. Results: ISO induced greater cardiac hypertrophy at ZT12 compared to ZT0, which was accompanied by cellular hypertrophy (ZT12: $433.8\mu\text{m}^2 \pm 7.0$ vs ZT0: $383\mu\text{m}^2 \pm 7.0$). Immunofluorescence for NFAT, a pro-hypertrophic transcription factor, indicated a higher increase in its fluorescence at ZT12 (ZT12: $6.5\text{A.U.} \pm 0.4$ vs ZT0: $3.9\text{A.U.} \pm 0.1$). Although the Evans Blue assay showed that ISO induced similar cell death at both ZT0 and ZT12, flow cytometry analysis revealed a greater elevation in the number of leukocytes (CD45+ cells) (ZT12: $529.1 \text{ cells/mg} \pm 93.3$ vs ZT0: $241.2 \text{ cells/mg} \pm 28.3$), macrophages (CD45+Ly6G-Ly6CintCD64high cells) (ZT12: $402.1 \text{ cells/mg} \pm 75.9$ vs ZT0: $146 \text{ cells/mg} \pm 28.2$), and monocytes (CD45+Ly6G-Ly6ChighCD64int cells) (ZT12: $376.5 \text{ cells/mg} \pm 67$ vs ZT0: $131.5 \text{ cells/mg} \pm 27.8$) in response to ISO at ZT12 compared to ZT0. The increase in CCR2+MHC-IIhigh cells was observed in ISO treated-mice at both ZTs (ZT12 = $84.2 \text{ cells/mg} \pm 18$ vs ZT0 = $65.0 \text{ cells/mg} \pm 14.4$), while the increase in CCR2+MHC-IIlow monocytes was restricted to mice treated at ZT12 (ZT12: $139 \text{ cells/mg} \pm 27$ vs ZT0: $31 \text{ cells/mg} \pm 6$). Immunofluorescence for CD68 confirmed the higher presence of macrophages in the heart of mice treated with ISO at ZT12 (ZT12: $4.3\text{A.U.} \pm 0.3$ vs ZT0: $2.5\text{A.U.} \pm 0.26$). Conclusion: ISO overload is influenced by time of the day in female mice, resulting in more severe inflammation and subsequently worst cardiac phenotype at ZT12. These findings represent an important step towards a better understanding of the pathogenesis of TC and can contribute for the improvement of current therapeutic approach. We demonstrate for the first time that the cardiac immune response following ches. Support: CNPq, CAPES, FAPEMIG Protocol: CEUA: 175/2021</p>

Title	Using the new DREADD-hM3Dq/Cre-lox model of Gq Signaling in Cardiomyocytes to gain insights into Reverse Remodeling
Authors	MÁRIO DE MORAIS E SILVA- SÉRGIO SCALZO, ANDRÉ MONTEIRO, ITAMAR COUTO, VICTOR MOURA, VITORIA GANDRA, SILVIA GUATIMOSIM
Affiliations	Fisiologia e Biofísica, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cardiac remodeling is a marker of heart disease severity. Under stress conditions, cardiomyocytes (CMs) suffer hypertrophy and increase calcium transient as a form to maintain cardiac function. Normalization of these parameters has been described in different conditions, although it does not occur frequently in clinical observations. To investigate mechanisms involved in reverse remodeling we used the DREADD technology along with the CRE-lox system to produce mice that express the DREADD-hM3Dq receptor exclusively in CMs. hM3Dq is a mutated receptor that couples to the Gq signaling when activated by clozapine N-oxide (CNO) to produce classical effects of this pathway. Gq is a common via shared by different molecules that are clinically relevant. Objective: To characterize the occurrence of reverse remodeling in the DREADD-hM3Dq model of Gq activation. Methods: We used male mice (8 weeks-old 20g) in which CMs expressed the hM3Dq by crossing DREADD and CRE animals (hM3Dq/CRE). To assess whether the percentage of CMs with hM3Dq activation influences the occurrence of reverse remodeling, we developed a new model using an adeno-associated virus type 9 to delivery CRE, and titrated the virus in order to promoted a mosaic hM3Dq expression in 25% of CMs (CEUA:243/2021; 68/2022). Mice received CNO (0.5mg/Kg) for 3 or 7 days. To assess the occurrence of reverse remodeling, following the CNO treatment mice were let at rest for 14 days without CNO (R14). To analyze hypertrophy and Ca²⁺ transient, CMs were isolated and loaded with the Ca²⁺ dye Rhod-2AM. Data are presented as MEAN ± SEM. one-way/Tukey. Results: CNO treatment for 3 and 7 days induced CM hypertrophy (µm²): hM3Dq (control): 2258±87 (n=5) versus hM3Dq/CRE (CNO3) 3092±64 (n=4) versus hM3Dq/CRE (CNO7) 2993±79 (n=3). After the resting period, hypertrophy reversion was observed only in the hM3Dq/CRE (CNO3-R14) (µm²): 2618±51 (n=4), since hypertrophy was still seen in the (CNO7-R14) 2895,0±95 (n=3). Consistently, 3 days of CNO treatment induced an increase in Ca²⁺ transient fluorescence, which was reversed after 14 days of rest (F/F0): hM3Dq (control) 2,20±0,43 (n=5) versus hM3Dq/CRE (CNO3) 2,64±0,40 (n= 4) versus hM3Dq/CRE (CNO3-R14) 2,13 ± 0,34 (n= 4). Once again, the reversal of the Ca²⁺ increase was not observed in the group hM3Dq/CRE (CNO7-R14) 3,02±0,05 (n=3). Strikingly, in the mosaic model with only 25% of CMs expressing the hM3Dq, when subjected to CNO treatment for 7-days, we observed CM hypertrophy, which was reversed following 14-days of rest. Comparison in the mosaic was performed between CMs expressing hM3Dq (Gq+) or not (Gq-) from the same heart. Likewise, Ca²⁺ transient increased in response to 7-day CNO (F/F0): (Gq-) 2,54 ± 0,41 versus (Gq+) 3,08 ± 0,49, and it reversed following the rest period. Conclusion: From these data we can draw important conclusions: Pathological remodeling is maintained in the heart even in the absence of the initial stimuli, as seen in the CNO7-R14 group. The occurrence of reverse remodeling is influenced by the duration of the pathological stimuli (3 or 7 days) and the number of CMs affected by stimulus (25% or 100%). Support: CNPq, CAPES, FAPEMIG. Protocol: 243/2021 and 68/2022</p>

Title	EFEITO AGUDO DO FERULATO DE ETILA SOBRE PARÂMETROS HEMODINÂMICOS DE RATOS SHR E WISTAR
Authors	LEONARDO GUEDES RODRIGUES, JOSÉ GUILHERME VERAS DE ASSUNÇÃO, SAMUEL DE SOUSA PEREIRA ARAÚJO, JOÃO PAULO JACOB SABINO
Affiliations	Biofísica e Fisiologia, UFPI
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A Hipertensão Arterial Sistêmica (HAS) é uma condição clínica multifatorial caracterizada pela elevação sustentada dos níveis pressóricos acima de 140 mmHg (pressão arterial sistólica, PAS) e/ou 90 mmHg (pressão arterial diastólica – PAD). O rato espontaneamente hipertenso (SHR) é considerado um dos melhores modelos de HAS, por mimetizar as alterações funcionais observadas em humanos, como hiperatividade simpática e redução do tônus vagal, e, em alguns casos, respondem aos tratamentos de forma semelhante aos humanos. O Ferulato de etila (FE), um fenilpropanóide presente em plantas, especialmente em grãos como arroz e milho, podem exercer efeitos terapêuticos, apresentando uma ação anti-inflamatória, antioxidante, neuroprotetora e cardioprotetora. No entanto, não existem relatos da ação do FE sobre o sistema cardiovascular de ratos SHR e Wistar. Objective: Avaliar o efeito agudo do FE nos parâmetros hemodinâmicos de ratos SHR e Wistar Methods: Os experimentos foram realizados em ratos Wistar (250g a 300g) e SHR (200g a 250g), machos e organizados em 8 grupos com 7 amostras: Wistar veículo, Wistar FE 7,5 mg/kg, Wistar FE 15 mg/kg, Wistar FE 30 mg/kg, SHR veículo, SHR FE 7,5 mg/kg, SHR FE 15 mg/kg, e SHR FE 30 mg/kg. Os ratos foram anestesiados com cetamina (80 mg/kg) e xilazina (20 mg/kg) e submetidos à canulação da artéria e veia femoral para o registro da pressão arterial pulsátil (PAP) e administração intravenosa de drogas, respectivamente. Após 48 horas da cirurgia, os animais receberam salina heparinizada na cânula arterial para prevenir coágulos e foram conectados ao transdutor de pressão para registro da pressão arterial pulsátil (PAP) a 2000 Hz. Durante 60 minutos de aclimação, os parâmetros hemodinâmicos foram estabilizados. Após um registro basal de 30 minutos, os efeitos do composto ou veículo foram avaliados por 60 minutos, com intervalos entre as doses de 20 minutos. A partir da PAP, foram obtidas a pressão arterial sistólica (PAS), diastólica (PAD), média (PAM) e a frequência cardíaca (FC) durante o monitoramento. A cânula venosa foi conectada a uma extensão de tubo para facilitar a administração de drogas. Results: Os resultados mostraram que as doses de 7,5; 15 e 30 mg/kg, administradas por via endovenosa, promoveram, em Wistar, reduções significativas da PAS ($\Delta=-21\pm3$; -27 ± 6; -29 ± 6 vs 7 ± 6 mmHg), PAD ($\Delta=-23\pm6$; -33 ± 6; -42 ± 6 vs 0 ± 2 mmHg), PAM ($\Delta=-22\pm5$; -31 ± 6; -38 ± 6 vs 2 ± 3 mmHg) e FC ($\Delta=-166\pm48$; -272 ± 43; -291 ± 44 vs -12 ± 9 bpm), em comparação ao grupo Wistar veículo. Já nos SHR, as doses de 7,5; 15 e 30 mg/kg também promoveram reduções significativas na PAS ($\Delta=-24\pm7$; -36 ± 7; -47 ± 5 vs 1 ± 2 mmHg), PAD ($\Delta=-21\pm5$; -31 ± 6; -54 ± 6 vs -1 ± 1 mmHg) e PAM ($\Delta=-22\pm6$; -32 ± 4; -52 ± 5 vs 0 ± 2 mmHg), no entanto, na FC apenas as doses de 15 e 30 mg/kg obtiveram reduções significativas ($\Delta=-187\pm44$; -243 ± 32 vs -8 ± 3 bpm), quando comparado ao grupo controle SHR. Conclusion: Com base nos resultados observados, podemos concluir que o FE promoveu uma redução significativa nos valores pressóricos, advindo, pelo menos em parte, de uma intensa bradicardia em ratos Wistar e SHR. Esses efeitos sugerem um potencial efeito anti-hipertensivo da substância em estudo, necessitando, ainda, caracterizar o mecanismo de ação sobre o sistema cardiovascular. Support: Bolsa de Doutorado FAPEPI Protocol: 804/2023</p>

Title	Short-term Mitoquinone treatment on Cardiac Performance After Myocardial Infarction
Authors	LAIS DE OLIVEIRA TRACHEL, GEORGIA AZEVEDO DE OLIVEIRA TRACHEL, SARA BIANCA OLIVEIRA MENDES, KATYANA KALINE SILVA FERREIRA, ANNA KAROLINA NASCIMENTO COSTA, THIAGO BARBOSA SPALENZA, EDUARDO HERTEL RIBEIRO, AURÉLIA ARAÚJO FERNANDES, IVANITA STEFANON
Affiliations	Programa de Pós graduação em Bioquímica, UFES, Programa de Pós graduação em Ciências Fisiologia, UFES
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Mitochondrial dysfunction has been identified as a key perturbation underlying numerous pathologies, including myocardial ischemia-reperfusion injury, which leads to impaired left ventricular systolic function and compensatory cardiac hypertrophy. Mitoquinone (MitoQ) has been studied as a protective agent against oxidative damage and mitochondrial dysfunction caused by these heart injuries.</p> <p>Objective: To evaluate the effects of Mitoquinone treatment on cardiac performance 7 days after acute myocardial infarction (MI) induced by the permanent occlusion of a branch of the left coronary artery.</p> <p>Methods: Wistar male rats, 10-12 weeks old, after MI surgery by ligation of the left anterior descending coronary artery or sham surgery, were divided into groups: Sham, MI, Sham+MitoQ, and MI+MitoQ. MitoQ (4,36mg/Kg/day) was administered in drinking water during 7 days after MI. Echocardiography studies were performed using Vivid T9, Philips Medical Systems, GE Healthcare. The performance of the left ventricle (LV) was assessed using parasternal long and short-axis. The parameters analysed were: LV end-diastolic diameter (LVEDD), LV end-systolic diameter (LVESD), LV end-diastolic volume (LVEDV), LV end-systolic volume LVESV, ejection fraction (EF), ejection fraction shortening (EFS). Ponderal parameters were analysed: lungs and heart were weighed, infarct area (IA) was measured. Data are expressed as mean±SEM. Two-way ANOVA and t-test were used; p<0.05 was considered significant; Fisher's or Tukey's post-tests were applied. Results: The IA did not differ between groups (MI %=50.15±4.5; MI+MitoQ %=49.45±1.8). Heart failure was confirmed using the parameters: EF less than 50%, pulmonary congestion or right ventricular hypertrophy. Infarcted animals had greater weight loss (Δ=Final body- Initial body) (ΔSham=6±3.8g; ΔSham+MitoQ=-5±5g; ΔMI=-22±18g*; ΔMI+MitoQ=-30±6g*#; p<0.05: *vs Sham; #vs Sham+MitoQ). Delta lung weight (wet lung weight - dry lung weight) in MI+MitoQ was decreased compared to MI (Sham=3.9±0.3g; Sham+MitoQ=3.5±0.2g; MI=8.1±0.6g*#; MI+MitoQ=5.7±0.4g*#&; p<0.05: *vs Sham; #vs Sham+MitoQ; &vs MI). Echocardiographic parameters showed differences due to infarction, but not in response to MitoQ treatment. LVEDD, LVESD, LVEDV, LVESV, EF, and EFS were not different between the MI groups, suggesting that the treatment was not able to change these parameters, at least in the short term (LVEDD: Sham=7.29±0.22mm; Sham+MitoQ=7.43±0.28cm; MI=8.78±0.68*; MI+MitoQ=8.97±0.16*#; LVESD: Sham=4.32±0.23; Sham+MitoQ=4.38±0.22; MI=7.1±0.55*; MI+MitoQ=6.94±0.23*#; EF: Sham=76.63±1.9%; Sham+MitoQ=77.1±1.8%; MI=45.3±3.3*%; MI+MitoQ=50.4±2.8*#; EFS: Sham = 40.8±1.8%; Sham+MitoQ = 41.3±1.7%; MI= 19.8±1.7*; MI+MitoQ = 22.73±1.7*#; p<0.05: *vs Sham; #vs Sham+MitoQ). LV free wall thickness was not different in MI treated with MitoQ (Sham=2.41±0.28cm; Sham+MitoQ=2.35±0.34cm; MI=1.33±0.38*; MI+MitoQ=1.38±0.66*#; p<0.05: *vs Sham; #vs Sham+MitoQ. Conclusion: Mitoquinone treatment attenuated pulmonary congestion in infarcted animals but did not alter left ventricular or right ventricular masses. Additionally, Mitoquinone treatment did not change cardiac function as evaluated by echocardiography in the early term after myocardial infarction. Support: FAPES, CAPES, CNPq, UFES Protocol: CEUA – UFES: 06 / 2023</p>

Title	Targeted Gi signaling activation exclusively in cardiomyocytes treats cardiac damage induced by adrenergic overload
Authors	MARCOS ELIEZECK DOS SANTOS INÁCIO, SÉRGIO RICARDO ALUOTTO SCALZO JÚNIOR, MATEUS CHAVES DA COSTA, VICTOR MOURA VIDAL COSTA, DAVI EMMANUEL LOPES, CIBELE ROCHA-RESENDE, THAIS MARQUES DA SILVA, HELIO CESAR SALGADO, SILVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	Fisiologia, UFMG, Fisiologia, USP
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: G-protein coupled receptors (GPCRs) play a pivotal role in the modulation of cardiac function. Hyperactivity of the Gs and Gq pathways is frequently associated with the development of cardiac disease. Conversely, activation of the Gi pathway via ACh binding to the muscarinic type 2 receptor is associated with cardioprotection. Objective: Here, we targeted Gi signaling activation exclusively in cardiomyocytes (CMs) and assessed its ability to treat cardiac damage induced by adrenergic overload. Methods: To selectively activate Gi in CMs, we crossed the R26-LSL-Gi-hMD4i model with Myh6-CRE to create Myh6-hM4Di mice, in which we can activate Gi upon CNO stimulation. 8 wks old male and female mice were subjected to the following procedures: Protocol 1: In vitro treatment of isolated CMs with isoproterenol (ISO, 50nM) and clozapine N-oxide (CNO, 100nM). Protocol 2 (prevention): In vivo treatment with ISO (25 mg/kg/day) with or without CNO (0.5 mg/kg/day) for 7 days. Protocol 3 (treatment): To implement this protocol, we identified when the ISO-induced lesion does not heal spontaneously. We found that 3 days of ISO injection induced hypertrophy, inflammation, and CM death. Then we applied protocol 3: in vivo treatment with ISO for 7 days followed by CNO for the last 4 days. Mice were sacrificed on day 8. Statistical analysis: Student's t-test or Tukey's One-Way ANOVA post hoc test. Results: To confirm activation of the Gi pathway in CMs, the cells were exposed to CNO or ACh (positive control for Gi activation), and the contraction was recorded. Myh6-hM4Di cells exhibited a diminished shortening area upon CNO stimulation (in μm^2: CTR 565 ± 34 vs CNO 342 ± 33 vs ACh 320 ± 30; n=40 cells per group), whereas no effect was observed in cells from Myh6-CRE or hM4Di mice. After confirming the functionality of the model, we next investigated whether CM-derived Gi activation would attenuate ISO-induced tissue injury (protocol 2). CNO treatment of Myh6-hM4Di mice prevented the ISO-induced pathological remodeling, including cardiac hypertrophy (HW/TL mg/cm: CTR 78 ± 3 vs ISO 95 ± 1 vs CNO+ISO 77 ± 3; n=9 mice) and CMs enlargement (in μm^2: CTR 2627 ± 47 vs ISO 3175 ± 40 vs CNO+ISO 2584 ± 54; n=220 cells). immunofluorescence analysis revealed that the CNO-treated group exhibited a reduction in ISO-induced cell death, a diminished recruitment of inflammatory cells, and a decreased activation of fibroblasts. Additionally, the upregulation of collagen I and III transcripts by ISO was prevented by CM-restricted Gi activation with CNO. In light of these protective effects, we evaluated whether late CNO treatment could reverse pre-existing cardiac injury. The results of protocol 3 demonstrated that late Gi activation in CMs effectively reversed the ISO-induced cardiac hypertrophy (HW/TL mg/cm: CTR 79 ± 2 vs ISO 97 ± 2 vs CNO+ISO 82 ± 2 n=17 mice) and CM hypertrophy (in μm^2: CTR 1987 ± 37 vs ISO 2641 ± 44 vs CNO+ISO 2116 ± 40; n=222 cells), inflammatory infiltrate and upregulation of transcripts for collagen I and III. Echocardiographic data demonstrated the efficacy of late CNO treatment in the prevention of ISO-induced injury (ejection fraction in %: CTR 54 ± 2 vs ISO 44 ± 1 vs CNO+ISO 51 ± 2; n= 9 mice). Conclusion: This is the first demonstration that targeted activation of Gi in CMs protects against cardiac injury induced by adrenergic overload. These intriguing data reveal the role of CM-Gi in orchestrating cardiac repair, possibly involving dynamic interactions between CMs, macrophages, and fibroblasts. Support: CNPq/CAPES/FAPEMIG. Protocol: 102/2022</p>

Title	Vascular Reactivity in Spontaneously Hypertensive Rats with Magnesium Supplementation
Authors	LIVIA SEIF EDDINE, LIVIA SUZANO DE PAULA DOS SANTOS, PAULA DOS SANTOS ATHAYDE, MICHELLE ROSSANA MARTINS HORTELAN, AURÉLIA ARAÚJO FERNANDES, IVANITA STEFANON
Affiliations	Ciências Fisiológicas, Universidade Federal do Espírito Santo
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Magnesium is a mineral that plays a crucial role in blood pressure regulation by modulating vascular reactivity. A diet rich in magnesium has been suggested to have antihypertensive effects. However, the impact of magnesium chloride (MgCl₂) supplementation on vascular tone and reactivity remains unclear.</p> <p>Objective: This study aimed to investigate the hypothesis that a diet rich in MgCl₂ reduces vasoconstrictor response. Methods: Thirty six-week-old male Spontaneously Hypertensive Rats (SHR), weighing between 90 and 120 grams, were divided into two groups. The SHR-Mg group received a daily dose of 50 mg/kg of MgCl₂ in their drinking water for two months, while the SHR-CT group received plain water. Following the treatment period, aortic vascular reactivity was assessed in response to increasing concentrations of phenylephrine (PHE, % KCl 75 mM). The evaluation was conducted in the presence of various inhibitors and antioxidants, including NS398 (a selective COX2 inhibitor), ML171 (a selective NOX inhibitor), Tiron (an antioxidant), MitoQ (a mitochondria-targeted antioxidant), Apocynin (a non-selective NADPH oxidase inhibitor), L-NAME (a nitric oxide synthase inhibitor), and Indomethacin (a cyclooxygenase inhibitor). These assessments were conducted both in the presence and absence of the endothelium (E-). Data were analysed using Student's t-test (Animal Ethics Committee at UFES: 16-2020). Results: The maximum response (R_{max}) to phenylephrine was significantly lower in the magnesium-treated group compared to the control group (SHR-Mg: 103.3±7.2, N= 8; SHR: 139.6±9.6, N=10, % KCl 75 mM, p<0.05). This difference disappeared when the endothelium was removed (E-) and NOS was inhibited (LNAME: SHR-Mg: 159.4±6.44, N=14; SHR: 145.5±7.31, N=8, % KCl 75 mM, p>0.05), (SHR-Mg E-: 172.1±15.27, N=11; SHR E-: 196.3±17.56, N=12, % KCl 75 mM, p>0.05). COX-2 inhibition also showed significant differences (SHR-Mg NS398: 92.52±7.87, N=8; SHR NS398: 117.2±13.57, N=8, % KCl 75 mM, p>0.05). The NOX inhibitor (ML171) reduced the R_{max} in both groups: SHR-Mg ML171: 68.24±11.34, N=7; SHR ML171: 89.16±9.91, N=10, % KCl 75 mM, p>0.05. However, in the presence of Tiron, MitoQ and APO, the R_{max} to PHE was normalized among groups (TIRON: SHR-Mg: 98.97±5.45, N=5; SHR: 110.9±5.02, N=6, % KCl 75 mM, p>0.05; MITOQ: SHR-Mg: 113.1±8.54, N=5; SHR: 120.1±3.56, N=3, % KCl 75 mM, p>0.05; APO: SHR-Mg: 91.45±10.83, N=5; SHR: 125.6±9.73, N=3, % KCl 75 mM, p>0.05). Conclusion: The findings of this study indicate that two-month supplementation with magnesium chloride decreases the vasoconstrictor response in aortic rings of SHR dependent on the oxidative stress pathways. Support: FAPES (Fundação de Apoio à Pesquisa do Espírito Santo) Protocol: UFES Animal Ethics Committee 1</p>

Title	Evolution of Blood Pressure Based on a Diet Rich in Magnesium Chloride in Spontaneously Hypertensive Rats (SHR)
Authors	LIVIA SUZANO DE PAULA DOS SANTOS, LIVIA SEIF EDDINE, PAULA DOS SANTOS ATHAYDE, MICHELLE ROSSANA MARTINS HORTELAN, AURÉLIA ARAUJO FERNANDES, IVANITA STEFANON
Affiliations	Departamento de Ciências Fisiológicas, UFES
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Arterial hypertension (AH) remains the leading cause of cardiovascular disease (CVD), affecting approximately 1 billion people worldwide. Epidemiological studies suggest that diet plays an important role in determining AH. Recently, it has been shown that magnesium supplementation can help control and even reduce blood pressure levels, but these studies are inconsistent. Objective: The present study aimed to investigate the hypothesis that a diet supplemented with MgCl₂ helps control and even modify blood pressure in hypertensive rats. Methods: Spontaneously hypertensive rats (SHR), male animals aged 6 weeks old (120-200 g), were divided into two groups: a treatment group that received a daily supplementation dose of 50 mg/kg of MgCl₂ (via drinking water for two months) (SHR-Mg), and control group that received no treatment (SHR). Blood pressure (BP) was measured weekly using the tail-cuff plethysmography method. The recorded arterial pulses were individually analyzed using a one-way ANOVA test with post hoc Tukey analysis (UFES Animal Ethics Committee 16-2020). Results: Systolic arterial pressure (SAP) at the beginning and at the end of 8 weeks-treatment period were comparable between the SHR-Mg group (Initial SAP SHR:156.9 ± 5.7 vs SHR-Mg:167 ± 5.8 mmHg, n=11; End SAP SHR: 164 ± 4.9 vs SHR Mg:175 ± 5 mmHg, n=9). Diastolic blood pressure was not affected by Mg²⁺ treatment. Initial and final heart rates (HR) did not show any significant differences between the groups (Initial HR SHR:360 ± 5 vs SHR-Mg:345 ± 8 bpm, n=11 and End HR SHR:336 ± 7 vs SHR-Mg:351 ± 5 bpm). Conclusion: In conclusion, the results of this study indicate that an eight-week supplementation with MgCl₂ at a dose of 50 mg/kg/day did not lead to any significant changes in blood pressure or heart rate in SHR animals. Support: FAPES (Fundação de Amparo à Pesquisa do Espírito Santo) e CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico) Protocol: UFES Animal Ethics Committee 1</p>



Title	A sinalização colinérgica e adrenérgica regulam a maturação do cardiomiócito.
Authors	MATEUS CHAVES DA COSTA, MARCOS ELIEZECK DOS SANTOS INACIO, VICTOR MOURA VIDAL COSTA, SERGIO ALUOTTO SCALZO JUNIOR, FERNANDO ARAUJO ESPANHOL, IAGO NASCIMENTO PINHEIRO, SILVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	Fisiologia e Biofísica, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS/ UP Universidade do Porto
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A maturação dos cardiomiócitos (CMs) envolve mudanças significativas na expressão gênica, no perfil metabólico e em sua estrutura. Os mecanismos moleculares que controlam essa maturação ainda não são completamente compreendidos. Recentemente, demonstramos que a sinalização adrenérgica desempenha um papel crucial na maturação dos CMs, com seus componentes se desenvolvendo principalmente até o 21º dia de vida pós-natal (Eliezeck e Jesus et al., 2024). Objective: Considerando a relação antagônica entre as sinalizações adrenérgica e colinérgica na manutenção da homeostase, este trabalho visa investigar o papel destas sinalizações no desenvolvimento cardíaco pós-natal. Methods: Utilizamos camundongos machos e fêmeas entre 1 e 21 dias, das linhagens C57BL6/J (WT) e Chat-ChR2, que apresentam aumento na atividade colinérgica sistêmica (ACh), além de ratos Wistar de 1 a 3 dias de idade para cultura de CMs. Executamos três protocolos distintos: Protocolo 1: Tratamento in vivo de camundongos WT com Propranolol (PRO) (5 mg/kg/dia) de P11 a P20 com eutanásia no P21. Protocolo 2: Eutanásia de animais Chat-ChR2 e seus littermates (CTR) no P8. Protocolo 3: Tratamento in vitro de cultura de CMs neonatais de ratos com ACh e o anticolinesterásico Piridostigmina (Pyr), 10 µM cada. Análise estatística: t-Student. Results: Inicialmente, observamos que os camundongos tratados com PRO apresentaram uma redução no peso do coração/comprimento da tíbia (HW/TL) em relação aos seus littermates tratados com salina (mg/mm: CTR 3.74±0.1 vs PRO 3.30±0.09 n=5 camundongos). Esse achado foi corroborado por uma redução na área da seção transversal dos cardiomiócitos (in µm²: CTR 171±3 vs PRO 152±2 n=241 células de 4 camundongos), posteriormente confirmada em miócitos ventriculares isolados (in µm²: CTR 1207±29 vs PRO 987±34 n=120 células de 5 camundongos). O tratamento com PRO não alterou a frequência de miócitos binucleados; no entanto, aumentou a proporção de células mononucleares em relação aos controles. Todos esses aspectos supracitados são considerados anti-maturacionais. Decidimos, portanto, avaliar outro importante aspecto maturacional, a janela proliferativa, que se encerra entre P7 e P10. Aplicamos o protocolo 2 e constatamos que animais Chat-ChR2 apresentaram um maior número de CMs em proliferação no P8 em comparação com seus littermates (número de células Ki67+ por campo: CTR 9,0±1,1 vs Chat-ChR2 18,4±1,3; n=5 corações). Utilizando o protocolo 3 para mimetizar um ambiente hipercolinérgico em cultura de CMs neonatais, tratando-os com ACh e Pyr, observamos que o aumento da disponibilidade de ACh em cultura reduzia a área dos CMs (CTR 803,9±31,8 vs ACh+Pyr 666,4±19,3; n=4 culturas). Esses achados sugerem que a hiperativação colinérgica durante a janela maturacional interfere negativamente na maturação dos CMs, prolongando sua janela proliferativa e atenuando seu crescimento fisiológico. Conclusion: Nossos achados mostram que o aumento da sinalização colinérgica pode atrasar o desenvolvimento normal dos CMs, prolongando a janela proliferativa, prejudicando a hipertrofia fisiológica do coração e dos CMs, além de aumentar a proporção de células mononucleadas. Support: CAPES, CNPq, FAPEMIG Protocol: 29/2021</p>

Title	Modulação Seletiva da Via Gi em Cardiomiócitos: Impacto na Cardiomiopatia e Resposta Inflamatória em um Modelo Mosaico de 30% de expressão
Authors	NAOMI ALVES REZENDE, MARCOS ELIEZECK DOS SANTOS INÁCIO, MATEUS CHAVES DA COSTA, TAMIRES AMORIM MARINHO, CIBELE ROCHA RESENDE, SILVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	DFIB, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Os GPCRs são importantes moduladores da função cardíaca. Estudos demonstram que em casos de eventos cardioestressores, os níveis de catecolaminas intersticiais aumentam drasticamente (100 a 1000 vezes), especialmente a noradrenalina, que passa a estimular a via Gs de forma crônica. Como a via Gi se opõe funcionalmente à via Gs, ela tem sido investigada como um importante via cardioprotetora.</p> <p>Objective: Nosso objetivo foi investigar o impacto da sinalização Gi restrita a 30% dos cardiomiócitos em resposta à cardiomiopatia induzida pelo Isoproterenol (ISO). Para isso, utilizamos a tecnologia DREADD em combinação com o vírus AAV9. Methods: Injetamos o AAV9 em camundongos machos e fêmeas da linhagem hM4Di com 1 dia de vida e aguardamos até 8 semanas para iniciarmos os experimentos. A expressão do receptor mutante foi induzida pela enzima CRE, carregada pelo vírus AAV9, sob controle do promotor da troponina-T, específico dos cardiomiócitos (CMs). Esse processo resulta em um coração em mosaico, com cardiomiócitos infectados expressando o receptor (hM4Di+) e não infectados (hM4Di-). A via Gi é ativada em células hM4Di+ pelo ligante N-Oxido-Clozapina (CNO). Submetemos esses animais a um protocolo de ISO (25 mg/kg/dia por 7 dias) e tratamos concomitantemente com CNO (0,5 mg/kg/dia), 30min antes de cada dose de ISO. No oitavo dia, realizamos a eutanásia. A taxa viral utilizada, denominada como baixa, infecta aproximadamente 30% dos miócitos. Análise estatística: t-Student e One-Way ANOVA-post hoc de Turkey. Results: Primeiramente, confirmamos que a carga viral utilizada levava a infecção de 30% dos cardiomiócitos (CMs). Em seguida, investigamos o impacto da ativação Gi em 30% dos CMs na progressão da fisiopatologia cardíaca. De forma interessante, nós observamos que a ativação Gi em 30% dos CMs era suficiente para prevenir o desenvolvimento da hipertrofia cardíaca induzida pelo ISO (Peso do coração normalizado pela tibia, mg/cm: CTR 86.5±1.7 vs ISO 96.7±3.3 vs CNO+ISO 86.2±1.1; n=4 corações por grupo). Em seguida, isolamos esses CMs e analisamos a área das células positivas (Gi+) e negativas (Gi-) em cada grupo com ou sem tratamento com CNO. Não observamos diferença na área dos cardiomiócitos em condições basais (CTR não tratado: Gi+ 1639±41 vs Gi-: 1593±51; n=70 células por grupo de 4 corações, p=0.5) nem em resposta ao estímulo hipertrófico (ISO: Gi+: 1858±68 vs G-: 1820±66; n=45 células por grupo de 4 corações, p=0.7). No entanto, no grupo em que os animais infectados foram tratados com CNO+ISO, a hipertrofia das células Gi+ foi mitigada, enquanto CMs Gi- hipertrofiaram normalmente (CNO+ISO: Gi+: 1946±55 vs Gi-: 1604±65; n=45 células de 4 corações, p=0.0001). Além disso, realizamos imunofluorescência em fatias do tecido cardíaco para células inflamatórias (células CD68+) e constatamos que em corações de animais tratados com CNO+ISO, as células inflamatórias se localizavam mais distantes de CMs Gi+ e mais próximas de CMs Gi-, sugerindo que os CMs Gi+ podem estar protegidos da lesão cardíaca. Conclusion: Nossos resultados indicam que a ativação da via Gi em 30% dos cardiomiócitos é eficaz para mitigar a cardiomiopatia induzida por ISO. Esses dados suportam um potencial papel citoprotetor da via Gi no CM. Support: CNPq/CAPES/FAPEMIG. Protocol: 102/2022</p>

Title	Gq protein activation in cardiomyocytes modulates the population of resident macrophages
Authors	HENRIQUE ABRAMO MENDES, GIOVANE PIRES, MARIO MORAIS SILVA, SILVIA GUATIMOSIM, CIBELE ROCHA RESENDE
Affiliations	Fisiologia e Biofísica, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Recent studies have shown the cardioprotective role of resident macrophages in the progression of cardiac diseases. Data from our group have demonstrated that activation of Gq protein in the cardiomyocyte leads to an increase in the number of cardiac macrophages. Objective: The aim of this study is to characterize dynamic changes in macrophage subsets in the heart of DREADD-Gq mice. Methods: To activate the Gq protein signaling pathway in cardiomyocytes, we treated 5-week-old male and female DREADD-Gq mice and littermate controls (CTR) with clozapine N-oxide (CNO; IP, 0,5mg/kg) for 7 days. To get further insight into the identity/ontogeny of cardiac macrophages, we performed a combination of immunofluorescence and flow cytometry. Results: Flow cytometry experiments have shown that the number of CD64+ macrophages has increased in the heart of DREADD-Gq (147.9+/-12.9) mice in comparison to littermate controls (105.2+/-10.87). In order to understand the participation of each subset in this increased population we performed a gating strategy focusing on CCR2- resident macrophages, in which we observed a significantly higher number of CCR2- cells in DREADD-Gq (116.0+/-8.1) hearts when compared to the control group(89.6+/-7.9). To further explore these findings, we sought to investigate whether there was a difference in the pool of CCR2- embryonic macrophages. Our data show that the number of Tim4+ embryonic cells is increased in the hearts with Gq protein activation (66.8+/-4.8) in comparison to control (48.4+/-5.4). Next, we performed an immunofluorescence assay to quantify the number of CD68+/Lyve 1+ embryonic macrophages. Corroborating our findings, there was an increase in the number of embryonic derived resident macrophages CCR2-Tim4+ in DREADD-Gq hearts (CTR: 4.4+/-0.4 vs DREADD-Gq: 10.1+/-1.1) . Conclusion: In conclusion, this study shows that activation of the Gq protein signaling in the cardiomyocyte leads to changes in cardiac macrophage subpopulations. Furthermore, there is a significant difference in the resident, embryonic-derived, macrophage subset, which is a known pro-reparative type. These data suggest that cardiomyocytes might modulate the population of cardiac macrophages upon some pathophysiological conditions. Further studies will be necessary in order to investigate whether depletion of this specific subset impairs cardiac function. Support: FAPEMIG Universal (APQ-01154-23), Instituto Serapilheira (Chamada 06/2022, 8192 #2211-42259), FAPEMIG (APQ-05838-23), Recém-contratados UFMG (Chamada FUNDEP 01-2022). Protocol: CEUA 331/2023</p>

Title	Distinguishing right ventricular contractility post-myocardial infarction in rats with and without heart failure signs
Authors	KATYANA KALINE SILVA FERREIRA, GUILHERME PEIXOTO TINOCO ARÊAS, SARA BIANCA OLIVEIRA MENDES, EDUARDO HERTEL RIBEIRO, AURÉLIA ARAÚJO FERNANDES, IVANITA STEFANON
Affiliations	Departamento de Ciências Fisiológicas, UFES
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Previous results from our laboratory have demonstrated a different ventricular performance in rats with same scar size (SS) depending on the presence of signs of heart failure (HF) at 30 and 60 days after myocardial infarction (MI) (Fernandes, et al. 2015). Objective: The aim of this study was to investigate the right ventricle (RV) contractility during the early phase (7 days) following myocardial infarction (MI) in rats with equivalent scar sizes (SS), distinguishing between those exhibiting signs of heart failure (HF) and those without HF. Methods: Male Wistar rats weighing 200 to 230g were categorized into: control (SHAM; n=10), infarct (INF; n=10), and infarct with HF (HF; n=6). Hemodynamic assessments were conducted seven days post-MI, and Langendorff perfusion was utilized for isolated heart analysis. RV contractility was evaluated through RV pressures and the first temporal derivative of pressure (dP/dt) in the presence of isoproterenol (10-5 M) and Ca²⁺ 0.62 to 3.5 mM. Statistical analysis involved mean ± SEM, Two-way ANOVA, and Bonferroni post-hoc test, *p<0.05. Results: The INF and HF groups exhibited identical SS (INF=31.6±1.6; HF=30.8±0.8%). RV systolic pressure (RVSP,mmHg) and RV end-diastolic pressure (RVEDP,mmHg) were elevated in the HF group while remaining unchanged in the INF group (RVSP: SHAM=29±2.2; INF=28±2.2; HF=40±2.3*#mmHg; RVEDP: SHAM=1.1±0.2; INF=1.33±0.3; HF=2.2±1.2*#mmHg; dP/dt+RV:SHAM=971±191; IC=1915±210*mmHg/s). Langendorff-perfused hearts from the HF group exhibited reduced RV isovolumic systolic pressure (RVISP,mmHg), +dP/dt, and -dP/dt in response to increased Ca²⁺ concentration and isoproterenol, while these parameters remained preserved in the INF group. Conclusion: Our study demonstrates that following MI, rats with equivalent scar sizes may either develop HF or remain HF-free, and the reduction in RV contractility is specifically observed in infarcted animals exhibiting signs of HF. These findings shed light on the complex dynamics of RV function in the context of post-MI outcomes. Support: Fundação de Amparo à Pesquisa e Inovação do Espírito Santo (Fapes), UFES, CNPq. Protocol: 18/2021</p>

Title	CARDIAC AUTONOMIC MODULATION AND VENTILATORY RESPONSES TO HYPOXIA: INSIGHTS FROM TWO DIFFERENT HYPOXIC EXPOSURE PROTOCOLS IN HUMANS
Authors	ANDRÉ LUIZ MUSMANNO BRANCO OLIVEIRA, GABRIEL DIAS RODRIGUES, PEDRO PAULO DA SILVA SOARES
Affiliations	Department of Physiology and Pharmacology, MFL, UFF, Department of Clinical Sciences and Community Health, UniMi
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Systemic hypoxia occurs in cardiopulmonary diseases or even in healthy subjects under hypobaric environments. Briefly, hypoxia evokes autonomic changes leading to an increased heart rate (HR) and ventilation (VE). However, these responses are highly variable among individuals, and whether they depend on oxygen saturation, or the hypoxic exposure time is unclear. We hypothesized that cardiac autonomic changes and ventilatory responses may depend on the time of the hypoxic exposure and target oxygen saturation. Objective: We aimed to investigate how hypoxia exposure duration and target oxygen saturation affect cardiac autonomic modulation and ventilatory responses. Methods: Ten participants (4 women; 25 ± 4 years; 72.7 ± 10.1 kg; 1.71 ± 0.08 m) visited the laboratory for two ‘isotime’ normobaric hypoxic protocols (CAAE: 28151519.0.0000.5243). In the first, the inspired oxygen fraction (FiO₂) was fixed at 11.5% for 40 minutes, and in the second, the oxygen saturation (SpO₂) was clamped (80–85%) for an equal period. Both visits were preceded by 10 minutes of normoxia (NOR). Participants were instrumented with an ECG for HR recordings, and with a pneumotachograph coupled to a facemask for recording breathing frequency (BF), tidal volume (VT), and ventilation (VE). The levels of SpO₂ were continuously recorded using a pulse oximeter. Spectral analysis (FFT) of the R–R intervals was used to obtain indexes in the frequency domain as the sympathetic-related ‘low-frequency component’ (LF: 0.04–0.15 Hz), the respiratory and vagally-related ‘high-frequency component’ (HF: 0.15–0.40 Hz), and the sympathovagal (LF/HF) balance. When differences over time were identified, the results were divided into segments and presented as follows: (NOR: 5–10; HYP: 15–20; 25–30; 35–40; 45–50 min). Results: Fixed FiO₂ reduced the SpO₂ levels from NOR (96 ± 1%) to HYP: (85 ± 6%), P<0.01. Clamped SpO₂ reduced the SpO₂ levels from NOR (96 ± 1%) to HYP (84 ± 2%) with a narrow dispersion, P<0.0001. Tachycardia and vagal withdrawal occurred similarly over time in both protocols as follows: Fixed FiO₂, HR (bpm): NOR: 73 ± 11 vs. HYP: 79 ± 11 (P<0.001) and HF_log (ms²) NOR: 7.4 ± 1.2 vs. HYP: 6.7 ± 1.2 (P<0.001). Clamped SpO₂, HR (bpm): NOR: 77 ± 12 vs. HYP: 83 ± 12 (P<0.001) and HF_log (ms²) NOR: 6.9 ± 0.9 vs. 6.2 ± 1.0 (P<0.001). Regarding ventilatory data, VE increased only in the protocol with clamped SpO₂ over time: VE_NOR: 15.1 ± 3 vs. VE_HYP10’: 16.5 ± 4; VE_HYP30’: 17.6 ± 4; VE_HYP40’: 17.9 ± 4 L/min; all increases were statistically significant compared to VE_NOR (P<0.05). Additionally, there was a significant difference between VE_HYP20’ and VE_HYP40’ (P<0.05). BF was unchanged (NOR: 18 ± 4 vs. HYP: 18 ± 3 cycles/min, P=0.87), thus the increment in VE followed tidal volume increases over time: VT (L) NOR: 0.888 ± 0.206; HYP_10’: 0.984 ± 0.248; HYP_20’: 0.959 ± 0.231; HYP_30’: 0.989 ± 0.237; HYP_40’: 1.046 ± 0.326; P<0.05 to all vs. NOR, and P<0.05 to HYP_20’ vs. HYP_30’. Conclusion: Vagally-mediated tachycardia remains constantly increased in both protocols, whereas only in clamped oxygen saturation does ventilation gradually increase over time. Support: FAPERJ, CAPES, CNPq. Protocol: 28151519.0.0000.5243</p>

Title	Assesing the impact of gut microbiota on metabolism and cardiac function of male mice
Authors	GABRIELA DE CASTRO MAGALHÃES, ANA CAROLINA LARA-RIBEIRO, NÍCIA PEDREIRA SOARES, MARCOS ELIEZECK, BRUNO SANCHES, SÉRGIO SCALZO, MARIA LUIZA DIAS-PINTO, YASMIN KOLZ BROZEGHINI, ADELSON HERIC ALVES MONTEIRO, PEDRO HENRIQUE MAYRINK, ROBSON AUGUSTO SOUZA SANTOS, THIAGO VERANO-BRAGA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Gut dysbiosis is a reduction in microorganisms diversity caused, for example, by poor fiber intake, chronic stress and sedentarism. Chronic treatment with antibiotics can also lead to dysbiosis and can lead to metabolic and cardiac disorders. Recent studies have shown that angiotensin-(1-7) [ang-(1-7)] induces a positive modulation of gut microbiota. This suggests that it may be a potential candidate in the treatment of gut dysbiosis and associated comorbidities. Objective: To investigate whether the depletion of gut microbiota by antibiotics can lead to metabolic and cardiac dysfunctions, and ang-(1-7) as a potential treatment. Methods: C57BL/6 male mice (8-10 weeks old) were treated (dysbiosis) or not (normobiosis) with antibiotics for 14 days. During this period, they were also subjected to constant administration of ang-(1-7) (0,15 mg/kg/day) or saline with osmotic minipumps. This study is, therefore, composed by the experimental groups: (i) normobiosis treated with saline (NS); (ii) normobiosis treated with ang-(1-7) (NA); (iii) gut dysbiosis treated with saline (DS); (iv) gut dysbiosis treated with ang-(1-7) (DA). Following treatments, oral glucose tolerance test (OGTT) and insulin tolerance test (ITT) were done. After euthanasia, cardiac tissues were collected and cardiomyocytes isolated for further experiments. The study was approved by the local ethical committee (CEUA: 99/2020). Results: Treatments [antibiotics ± ang-(1-7)] had no effects on glucose metabolism, observed as per OGTT and ITT assays. However, a deleterious effect in cardiac Ca²⁺ handling was observed in mice treated with antibiotics (DS), represented by increased Ca²⁺ decay time (50%) and decreased Ca²⁺ peak (F/F₀), and ang-(1-7) treatment induced a significant improvement of these parameters in DA-derived cardiomyocytes [50% decay time (in ms) = NS: 158.33 ± 41.79; NA: 164.02 ± 39.69; DS: 180.12 ± 48.45; DA: 152.53 ± 60.73] and [F/F₀ (in ms) = NS: 3.14 ± 0.83; NA: 3.29 ± 1.01; DS: 2.74 ± 0.77; DA: 3.53 ± 1.13]. We also observed an increase in the contraction-relaxation time (CRT), maximum contraction speed (MCS), relaxation speed (RS) and a decrease of cardiomyocytes' shortening area (SA) in cardiac myocytes derived from DS mice. Importantly, ang-(1-7) treatment (DA) restored these parameters to basal levels: CRT (in ms) [NS: 276.6 ± 51.09; NA: 325.97 ± 72.43; DS: 291.68 ± 60.75; DA: 250.93 ± 54.94], MCS (in μm/s) [NS: 65.24 ± 27.18; NA: 70.62 ± 33.50; DS: 49.40 ± 24.12; DA: 79.88 ± 33.82], RS (in μm/s) [NS: 52.36 ± 22.76; NA: 56.60 ± 34.55; DS: 36.78 ± 24.53; DA: 69.15 ± 34.69], and SA (in μm²) [NS: 525.75 ± 228.01; NA: 629.93 ± 261.18; DS: 398.90 ± 193.11; DA: 599.04 ± 251.43]. Conclusion: Neither antibiotics nor ang-(1-7) treatments significantly alter the studied metabolic parameters. However, antibiotic-induced gut dysbiosis negatively impacted cardiomyocyte contractility, but ang-(1-7) treatment restored to basal levels all assessed parameters. This study underscores the importance of proper management of cardiac patients undergoing antibiotic treatment. Support: INCT-Nanobiofar, CNPq, Fapemig, and Capes. Protocol: CEUA 99/2020</p>

Title	High-intensity interval training improves the contractile function of ventricular cardiomyocytes in obese rats
Authors	KIANY DE OLIVEIRA MIRANDA, MATHEUS CORTELETTI DOS SANTOS, DANIEL SESANA DA SILVA, ANA PAULA LIMA LEOPOLDO, ANDRÉ SOARES LEOPOLDO
Affiliations	Ciências Fisiológicas, UFES
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity is a multifactorial and complex condition characterized by the excessive accumulation of adipose tissue, which can lead to a decrease in quality and life expectancy, as well as cause various vascular and metabolic dysfunctions. Research has indicated that obesity is associated with dysfunction in myocardial contractility. Considering the exponential increase in the prevalence of obesity in the global population, numerous treatment strategies are documented in the literature, including physical exercise. In this context, physical exercise stands out as an important non-pharmacological intervention, with continuous aerobic exercise being the most frequently reported. Objective: This study aimed to investigate the effects of high-intensity interval training (HIIT) on the contractility of cardiomyocytes in obese rats induced by a diet high in saturated fat. Methods: Initially, 30-day-old Wistar rats were randomized into a standard diet control group (C) and a high-fat diet group, the obese group (OB). The experimental protocol consisted of 23 weeks, divided into obesity induction and maintenance (15 weeks) and HIIT (8 weeks), with the following groups: C; OB; CHIIT; OBHIIT. Performance was evaluated through the maximum oxygen consumption test (VO₂max). Contractility of isolated ventricular cardiomyocytes, and cardiac, adipose, and skeletal histology were analyzed. Results: Initially, we observed that from the third week, the OB group (272.3±7.493g, n=23) showed body weight gain compared to the C group (224.9±5.753g, n=24), characterizing obesity, which was maintained until the end of the protocol. Confirming its effectiveness, the training reduced the area of visceral adipose tissue in the CHIIT (1220±115.5µm², n=12) and OBHIIT (2970±164.3µm², n=10) groups compared to their respective controls C (2517±152.6µm², n=12) and OB (4087.3±119.5µm², n=13). Additionally, it promoted hypertrophy of the gastrocnemius muscle fibers in the CHIIT (43.9±0.74µm, n=12) and OBHIIT (36.4±0.27µm, n=10) animals compared to their respective controls C (29.6±0.79µm, n=12) and OB (25.4±0.43µm, n=13). The cardiorespiratory condition analyzed by the VO₂max test increased in the CHIIT group (52.45±8.219ml/min/kg^{0.75}; n=9) compared to the C group (42.48±2.44ml/min/kg^{0.75}; n=9) and OBHIIT (50.69±7.18ml/min/kg^{0.75}; n=9) compared to OB (39.64±3.19ml/min/kg^{0.75}; n=11). HIIT prevented the risk of insulin resistance in OB animals by reducing insulin levels in the OBHIIT group (1.67±0.094.64ng/mL, n=10) compared to the OB group (2.49±0.11ng/mL, n=13). Interestingly, the cardiomyocytes of OBHIIT animals exhibited an increase in shortening fraction (10.86±0.46%, n=70) compared to the OB group (7.14±0.33%, n=65), with a reduction in the maximum contraction rate in the OBHIIT group (-5.51±0.64µm/s, n=70) compared to the OB group (-3.14±0.17µm/s, n=65), and an increase in the maximum relaxation rate in the OBHIIT group (4.25±0.44µm/s, n=70) compared to the OB group (2.39±0.15µm/s, n=65), indicating improved contractility. Furthermore, morphological analysis showed that HIIT reduced interstitial fibrosis of the left ventricle in the OBHIIT group (38.88±2.30%, n=4) compared to the OB group (56.51±1.63%, n=5). Conclusion: HIIT improves the contractile parameters of ventricular cardiomyocytes in obese animals and reduces cardiac fibrosis. This approach also enhances cardiorespiratory and physical performance. Support: Espírito Santo Research and Innovation Support Foundation – FAPES. Protocol: N.A.</p>



Title	Testosterone and Aldosterone: Long-Term Modulation of Vascular Reactivity in Orchiectomized Wistar Rats Treated with Spironolactone.
Authors	ANNA KAROLINA NASCIMENTO COSTA, MICHELLE ROSSANA MARTINS HORTELAN, PAULA DOS SANTOS ATHAYDE, EDUARDO HERTEL RIBEIRO, AURÉLIA ARAÚJO FERNANDES, IVANITA STEFANON
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, UFES
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Testosterone, has been shown to exhibit endothelium-dependent vasodilation in acute scenarios. We test the hypothesis that testosterone plays a major role in the long-term modulation of vascular reactivity by an aldosterone-dependent pathway. Objective: We test the hypothesis that testosterone plays a major role in the long-term modulation of vascular reactivity by an aldosterone-dependent pathway. Methods: 12-week-old Wistar rats were segregated into Control (SHAM, N=8) and Orchiectomy (OQT, N=9) groups and treated for 3 months with spironolactone (SPI) (SHAM+SPI, N=10 and OQT+SPI, N=9, 80 mg/kg, gavage), aldosterone receptor antagonist. (CEUA-UFES 17/2020). Vascular reactivity was examined in isolated thoracic aorta rings during concentration-response curves to phenylephrine (Phe) (10⁻¹¹ to 10⁻³ M) in the presence and absence of L-NAME (LN) (NOS inhibitor, 100 μM), and with endothelium-denuded rings (E-). Results were expressed as mean±SEM. Results: After 3 months, the groups OQT show less body weight gain compared to the SHAM. This discrepancy was abolished with SPI treatment. (SHAM:231±11; OQT:158.4±13*; OQT+SPI:180.5±20.60*; SHAM+SPI: 215.3±26.1 g *p<0.05). There was no difference in the maximum response (Rmax) to Phe between the SHAM and OQT groups. However, OQT+SPI group demonstrated a decreased Rmax to Phe compared to the SHAM (SHAM:109.4±9.5%; OQT:120.5±10%; SHAM+SPI: 120.4±7.56 % N=10 vs OQT+SPI: 93.3±10.2 % N=10; *p<0.05). The reactivity to Phe increased in the presence of LN and in E-, with no difference between the groups. Conclusion: Our data suggest that testosterone has a role in angiotensin II-mediated NO production, since blocking NO production with LN resulted in a decrease in Rmax in the OQT group compared to its control. It highlights the potential of testosterone in the contractile response mediated by the angiotensin AT1 receptor. Support: FAPES-CAPEX edital 019/2022 Número: 2022-6C3F7 Protocol: CEUA 17/2020</p>

Title	ANALYSIS OF THE PREVALENCE OF HYPERTENSION IN THE CITY OF SÃO FÉLIX DO XINGU, PA, BRAZIL: A COMPARATIVE APPROACH OF LIFESTYLE AND HEALTH PARAMETERS
Authors	ELLEN THAÍS PEREIRA DE CASTRO, GEANE BORGES DOS SANTOS, RODRIGO DA SILVA SANTOS, ANGELA ADAMSKI DA SILVA REIS, ALINE ANDRADE MOURÃO
Affiliations	Grupo de Estudos e Pesquisas em Fisiologia e Saúde na Amazônia (GEPFSA), UNIFESSPA, Núcleo de Pesquisas em Neurogenética (NeuroGene), Departamento de Bioquímica e Biologia Molecular, UFG
Session	2- Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Arterial hypertension (AH) is a chronic and predominant health condition that significantly impacts both individual health and public health in several regions. Understanding the pathophysiology of AH and its associated factors is crucial, especially in areas lacking basic sanitation and investment in education, such as the Amazon region. Objective: The project aimed to analyze the prevalence of AH in the municipality of São Félix do Xingu, Pará-Brazil, and identify associated factors, comparing hypertensive and normotensive patients, through an observational case-control study. Methods: The study was approved by the Committee of Ethics in Human Research (CAAE:73126423.6.0000.0018). In the research's first phase, a comparative study was carried out with the hypertensive and normotensive population of the city, covering a total of 100 patients, aged between 18 and 90 years. Data were collected from users of four basic health units (UBS) and a Specialized Reference Unit (URE), using questionnaires to evaluate the sociodemographic profile, family history, clinical picture and lifestyle, during the months of October/2023 to June/2024. The factors age and quantity of food were expressed as mean \pm standard error of the mean. The remaining sociodemographic data were expressed as a percentage (%), considering the total number (n) of individuals in the case and control groups. All participants signed the Free and Informed Consent Form. Results: From the patients' clinical records, the prevalence of AH was observed in 47 of the 100 individuals tracked, constituting the case group (HYP). The 53 normotensive patients were considered in the study as the control group (CTR). The results indicated a predominance of women among study participants (71%), compared to the number of men (29%), in line with trends observed in previous studies. Furthermore, there was a correlation between the ethnicity/color variables and the incidence of AH, with a predominance among brown and black individuals. Aging was also a factor associated with the prevalence of AH, both in men (CTR:41\pm3.3y vs. HYP:68\pm2.0y; p<0.05) and in women (CTR:38\pm1.3y vs. HYP:56\pm1.7y; p<0.05). Other risk factors, such as obesity and family history of AH, were highlighted as relevant in this context, where the group assessed with AH had higher rates than the control group. Additionally, among those interviewed, the majority only had primary education (CTR: 42% and HYP: 57%) and, still considering the case group, 28% of patients did not have any level of education, highlighting the importance of education and early intervention to modify lifestyle habits and prevent complications related to AH. Conclusion: Taken together, the first findings of our study have the potential to guide effective strategies for preventing and controlling hypertension, adapted to the specific needs of this community, contributing to the promotion of local public health. The next steps of research include genetic susceptibility studies, aiming to identify variants in the genome of hypertensive individuals. The use of genotypic profile analysis can predict patients susceptible to AH, and these will benefit from personalized medicine, preventing the disease through the incorporation of biotechnologies and new guidelines, which can be incorporated into the Clinical Protocol and Therapeutic Guidelines defined by the Ministry of Health /SUS/Brazil. Support: GEPFSA; Unifesspa/PNAES; Secretária de Saúde de São Félix do Xingu-PA, Neurogene/UFG Protocol: 73126423.6.0000.0018</p>



Title	EFEITOS CARDÍACOS RESULTANTES DO ACIDENTE VASCULAR HEMORRÁGICO EXPERIMENTAL NO CÓRTEX INSULAR DE CAMUNDONGOS
Authors	ANA CAROLINE VENTRIS-GODOY, HENRIQUE ABRAMO, GIOVANE PIRES, CIBELE ROCHA RESENDE, MARCO ANTONIO PELIKY FONTES
Affiliations	Fisiologia e biofísica, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O córtex insular modula o controle autonômico cardiovascular. Em humanos, acidentes vasculares nesta área resultam em simpatooexcitação, taquicardia sustentada, lesão cardíaca e muitas vezes em morte prematura. O modelo de acidente vascular hemorrágico experimental no córtex insular em ratos, desenvolvido por nosso grupo, é capaz reproduzir alterações pós acidente vascular insular observadas em humanos. Camundongos, especialmente modelos knockout, são amplamente utilizados para o estudo de mecanismos de doenças. Objective: Desenvolver um modelo de acidente vascular hemorrágico experimental no córtex insular de camundongos e investigar possíveis alterações cardíacas. Methods: Camundongos C57BL/6J (CEUA UFMG 233/2023) (machos, entre 10 e 12 semanas de idade, n = 29) foram anestesiados com cetamina (80mg/Kg) e xilazina (10mg/Kg), submetidos a estereotaxia para a realização das injeções (veículo ou sangue autólogo) no córtex insular direito; grupos de um dia e três dias pós-AVC foram novamente anestesiados e submetidos ao eletrocardiograma (ECG) para avaliação da frequência cardíaca. Ao final desta primeira etapa, os animais foram eutanasiados e o tecido cardíaco coletado para avaliação por meio de imunofluorescência da área transversal dos cardiomiócitos (WGA) e infiltrado inflamatório (marcação de células CD68). Results: A hemorragia experimental no córtex insular provocou o aumento da frequência cardíaca (3 dias pós-AVC: sham 261±26 bpm vs AVC 308±58 bpm; P<0,01). As análises de imunofluorescência revelaram o aumento significativo da área da secção transversa dos cardiomiócitos (1 dia pós-AVC: sham 195±75µm², AVC 323±193µm²; 3 dias pós-AVC: sham 243±142µm², AVC 348±214µm²) e aumento de macrófagos CD68+ (1 dia pós-AVC: sham 18±3 células; AVC 43±21 células; 3 dias pós-AVC: sham 24±8 células; AVC 36±7 células) nos corações de camundongos com o AVC hemorrágico experimental. Conclusion: Nossos resultados mostraram que a hemorragia experimental no córtex insular de camundongos provocou o aumento da frequência cardíaca, hipertrofia do cardiomiócito e inflamação no no tecido cardíaco. Em conjunto estes dados sugerem que o AVC insular induzido resultou em hiperatividade simpática cardíaca. A caracterização deste modelo em camundongos representa um avanço importante da técnica para ampliar e otimizar os estudos de AVC hemorrágico. Support: CNPq: MAPF 308923/2021-9, ACVG 165774/2021-5; MAPF FAPEMIG: APQ-01128-21; CRR: FAPEMIG Universal (APQ-01154-23), Instituto Serapilheira (Chamada 06/2022, 8192 #2211-42259), FAPEMIG Acordo P, D & I (APQ-05838-23), Recém-contratados UFMG (Chamada FUNDEP 01-2022). Protocol: Protocolo CEUA UFMG: 233/2023</p>

Title	EFFECT OF ZINC ADMINISTRATION ON VASCULAR REACTIVITY IN THE AORTA OF RATS ACUTELY EXPOSED TO CADMIUM
Authors	CAMILLA LÓREN DA SILVA NASCIMENTO, LORRAINE CHRISTINY COSTA SEPULCHRO, RAKEL PASSOS SIMÕES, IVANITA STEFANON, ALESSANDRA SIMÃO PADILHA
Affiliations	Departamento de Ciências Fisiológicas, UFES
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cadmium (Cd) is a highly toxic metal that promotes metabolic and enzymatic changes. In the cardiovascular system, the endothelium and smooth muscle are the main targets, promoting oxidative stress and vascular dysfunction, contributing to cardiovascular disease development. Therefore, investigating substances to reverse or prevent this damage is crucial. Zinc (Zn), essential in several metabolic reactions, also acts as a potent antioxidant that can mitigate oxidative stress. Objective: The present study aims to evaluate the effects of Zn administration (50 μM) on vascular reactivity to phenylephrine in isolated rings from the thoracic aorta of rats acutely exposed to Cd (10 μM). Methods: Male Wistar rats (<i>Rattus norvegicus albinus</i>), 12 weeks old (320 g to 470 g) were used. During the experiment, they were divided into four in vitro exposures to metals, specifically: Ct, Cd, Zn and Cd+Zn. The experimental protocol was conducted on thoracic aorta rings which were cleaned of fat and connective tissue, in the presence (E+) and absence (E-) of endothelium to investigate the endothelium's participation. The effects of the following drugs were evaluated: L-NAME, Superoxide Dismutase (SOD), Apocynin (APO) and Catalase (CAT) to evaluate the involvement oxidative stress pathways. The Federal University of Espírito Santo Ethics Committee on the Use of Animals approved the experimental protocol (CEUA-UFES, nº 12/2022). The contractile responses were analyzed using two-way ANOVA followed by a Bonferroni test and expressed as the percentage of contraction induced by KCl. The effects of the drugs were analyzed as differences in the area under the concentration-response curves using the Student's t test (unpaired). $P < 0.05$ was considered significant. Results: The results revealed that acute exposure to Cd increased contractility to phenylephrine, while co-incubation with Zn allowed for the normalization of this response to control levels (Ct: 76,19\pm3,83%; Cd: 108,79\pm6,42%; Cd.Zn: 77,76\pm4,35%). The absence of endothelium caused higher vascular reactivity, indicating that the changes induced by Cd are endothelium-dependent (Ct.E+: 76,19\pm3,83%; Ct.E-: 134,15\pm8,35%; Cd. E+: 104,49\pm7,11%; Cd.E-: 93,60\pm7,68%). Incubation with L-NAME revealed that cadmium reduced NO bioavailability; with APO, it induced NADPH Oxidase participation; and with CAT, it stimulated hydrogen peroxide formation, favoring a major contractile response. In contrast, co-incubation with Zn enhanced NO bioavailability during the contractile response to phenylephrine, achieving values comparable to those of the control groups. Additionally, Zn demonstrated the ability to prevent ROS production by NADPH oxidase, associated with reduced hydrogen peroxide release (L-NAME: Ct: 135,53\pm9,50%; Cd: 111,63\pm12,70%; Cd.Zn: 144,34\pm9,56%. APO: Ct: 71,81\pm4,03%; Cd: 79,91\pm7,72%; Cd.Zn: 69,81\pm7,05%. CAT: Ct: 71,27\pm5,58%; Cd: 105,96\pm8,66%; Cd.Zn: 87,55\pm5,72%). Conclusion: Thus, Zn represents a promising non-pharmacological intervention for preventing damage to the cardiovascular system resulting from exposure to heavy metals. Support: This study was supported by grants from CNPq and FAPES. Protocol: (CEUA-UFES, nº 12/2022)</p>



Title	TIME-DEPENDENT MODULATION OF CARDIOMYOCYTE CONTRACTILITY BY ALAMANDINE IS IMPAIRED IN A MICE MODEL OF ADRENERGIC OVERLOAD
Authors	ANDRÉ LUIS LIMA MONTEIRO, ROBSON AUGUSTO SOUZA DO SANTOS, SILVIA GUATIMOSIM
Affiliations	Department of Physiology and Biophysics, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Alamandine (ALA), a renin-angiotensin-system (RAS) cardioprotective peptide has been described as a modulator of cardiomyocyte (CM) contractility in both wild type (WT) and hypertensive animal models. In CMs from WT mice, the modulation is susceptible to temporal variations, with ALA promoting positive modulation of contractility during the light phase, and negative modulation during the dark phase. Whether this cardiac temporal regulation is lost in a murine model of adrenergic overload is unknown.</p> <p>Objective: To determine the impact of β-adrenergic overstimulation on the day-night cycle of ALA-induced contractile effects in CMs. Methods: Mice between 10-14 weeks were treated intraperitoneally with either saline 0,9% (Sal) or Isoproterenol (β-adrenergic agonist, ISO) 25 mg/kg for 7 days. At the 8th day, CMs were isolated at two timepoints: ZT2 (light phase) and ZT14 (dark phase), considering ZT0 as the time in which lights are switched on and ZT12 as lights go off in the animal facility. For each timepoint, we evaluated CMs contractility parameters and nitric oxide (NO) production in response to acute ALA treatment (100 nmol/L) for 10-20min. Statistics: two-way and three-way Anova. Results: First, we observed that Sal CMs reproduced the physiological variation of basal function observed in cells from WT animals, with higher fractional shortening (FS) at ZT14 compared to ZT2 (ZT2 = $5.9 \pm 0.4\%$; ZT14 = $10.3 \pm 0.6\%$; $p < 0.05$). Strikingly, ISO CMs lost the circadian variation between both ZTs (ZT2 = $9.9 \pm 0.5\%$; ZT14 = $12.1 \pm 0.7\%$; $p = 0.07$). Considering Sal CMs treated with ALA, there was an increase in FS at ZT2 (CTR = $5.9 \pm 0.4\%$; ALA = $8.9 \pm 0.5\%$; $p < 0.05$). At ZT14, ALA promoted an opposite effect by reducing the FS of the CMs (CTR = $10.3 \pm 0.6\%$; ALA = $7.4 \pm 0.5\%$; $p < 0.05$). On the other hand, ISO CMs treated with ALA showed no changes in contraction at both ZTs 2 and 14 (ZT2: CTR = $9.9 \pm 0.5\%$; ALA = $8.6 \pm 0.4\%$; n.s. / ZT14: CTR = $12.1 \pm 0.7\%$; ALA = $10.9 \pm 0.5\%$; n.s.). Therefore, we demonstrate that the ALA temporal modulation of contractile function is lost in CMs from animals treated with ISO. Considering that NO is a key downstream molecule in the ALA pathway and crucial for contractility modulation, we preincubated CMs from both Sal and ISO groups at ZTs 2 and 14 with DAF-FM (NO probe, 5 μmol/L), and treated with ALA. First, a difference in peak basal NO levels was noted, with higher NO production observed in Sal CMs at ZT2 (ZT2 = 58.2 ± 1.7 a.u.; ZT14 = 43.4 ± 1.6 a.u.; $p < 0.05$), in contrast to ISO CMs which exhibited higher fluorescence at ZT14 (ZT2 = 49.3 ± 1.6 a.u.; ZT14 = 59.6 ± 1.3 a.u.; $p < 0.05$). Second, in Sal CMs, ALA induced an increased in NO at ZT2 (CTR = 58.2 ± 1.7 a.u.; ALA = 70.4 ± 2.1 a.u.; $p < 0.05$), whereas it failed to promote any changes at ZT14 (CTR = 43.4 ± 1.6 a.u.; ALA = 42.5 ± 1.5 a.u.; n.s.). In ISO CMs, as observed in the contractility evaluation, ALA did not promote changes in NO fluorescence at either ZT (ZT2: CTR = 49.3 ± 1.6 a.u.; ALA = 56.2 ± 1.1 a.u.; n.s. / ZT14: CTR = 59.6 ± 1.3 a.u.; ALA = 57.1 ± 1.4 a.u.; n.s.).</p> <p>Conclusion: This interesting data show that adrenergic overload impairs the modulatory effect of ALA on contractility of CMs through changes in NO physiology at ZT2. The impairment of ALA function at ZT14 remains to be elucidated. Our results confirm the importance of understanding how the modulation of ALA changes according to the time of the day, and how it is impacted by adrenergic overload. Support: Supported by INCT Nanobiofarmacêutica, FAPEMIG, CAPES, and CNPq Protocol: CEUA/UFMG: 236-2019</p>



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Title	The Antioxidante Mitoquinone, Mitigates Mitochondrial Damage and Promotes Energy Efficiency in Both Interfibrillar and Subsarcolemmal Subpopulations After Myocardial Infarction
Authors	GEÓRGIA AZEVEDO OLIVEIRA TRAICHEL, EDUARDO HERTEL RIBEIRO, LAIS DE OLIVEIRA TRAICHEL, SARA BIANCA OLIVEIRA MENDES, ANNA KAROLINA NASCIMENTO COSTA, CAMILLA LÓREN DA SILVA NASCIMENTO, MARCELLA PORTO TAVARES, THIAGO BARBOSA SPALENZA, KATYANA KALINE SILVA FERREIRA, IVANITA STEFANON, AURÉLIA ARAÚJO FERNANDES
Affiliations	Centro de Ciências da Saúde, UFES
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Mitoquinone (MitoQ) is an effective mitochondrial antioxidant. Objective: To investigate the effects of MitoQ on cardiac mitochondrial metabolism in rats, seven days after myocardial infarction (MI), in the interfibrillar (IFM) and subsarcolemmal (SSM) mitochondrial subpopulations. Methods: Male Wistar rats, 10-12 weeks old, after MI surgery by ligation of the left anterior descending coronary artery or sham surgery, were divided into groups Sham (n=9), Sham MitoQ (n=10), MI (n=5), and MI MitoQ (n=6) groups (CEUA 06/2023). The animals were treated with MitoQ (4,36 mg/Kg/day) or placebo for 7 days, in the drinking water. The mitochondrial subpopulations from the left ventricle (LV) were isolated to assess respiration, using substrates glutamate + malate (G+M), pyruvate + malate (P+M), palmitoylcarnitine + malate (Pc+M), and succinate + rotenone (S+R). The measurement of oxygen consumption from mitochondrial respiration in the State 3 indicated maximum ATP production, while State 4 referred to oxygen consumption in a resting phase, being an indirect measure of proton leak. The respiratory control ratio (RCR, State 3/State 4 ratio) indicated coupling and ATP synthesis capacity. All measurements were presented as mean ± SEM. Values were considered significant for a p < 0.05. For mitochondrial evaluation, statistical analysis was performed using two-way ANOVA and Fisher's post-hoc. Results: In the presence of S+R substrates, the RCR of the SSM in the MI MitoQ group was reduced compared to the MI group (SSM S+R: Sham 4.83 ± 0.3; Sham MitoQ 4.2 ± 0.2; IM 5.64 ± 0.9; IM MitoQ 4.31 ± 0.2; & p < 0.05 vs MI). However, the IFM was not different among groups (IFM S+R: Sham 4.63 ± 0.2; Sham MitoQ 4.27 ± 0.3; IM 4.33 ± 0.5; IM MitoQ 4.03 ± 0.2). In the presence of M+G substrates, the RCR of the SSM in the MI MitoQ group was increased compared to the MI group (SSM M+G: Sham 21.66 ± 1.7; Sham MitoQ 21.96 ± 1.7; IM 14.47 ± 1.9; IM MitoQ 19.6 ± 1.2 & ; & p < 0.05 vs MI) and the IFM as well (IFM M+G: Sham 18.4 ± 0.7; Sham MitoQ 19 ± 1.0; IM 15.2 ± 1.6; IM MitoQ 21.33 ± 1.9 & ; & p < 0.05 vs MI). In the presence of M+P substrates, the RCR of the SSM was not different between MI groups (SSM M+P: Sham 13.2 ± 0.9; Sham MitoQ 12.94 ± 0.3; IM 8.6 ± 0.6; IM MitoQ 9.73 ± 0.6 &) and the IFM as well (IFM M+G: Sham 12.18 ± 1.4; Sham MitoQ 10.67 ± 0.8; IM 9.22 ± 0.8; IM MitoQ 9.24 ± 0.7). In the presence of M+Pc substrates, the RCR of the SSM was not different between MI groups (SSM M+P: Sham 18.5 ± 1.3; Sham MitoQ 21.56 ± 1.4; IM 13.1 ± 1.3; IM MitoQ 13.97 ± 0.6) and the IFM as well (IFM M+G: Sham 17.1 ± 1.5; Sham MitoQ 18.27 ± 1.7; IM 14.02 ± 1.4; IM MitoQ 15.62 ± 1.2). Conclusion: MI impacts mitochondrial energy metabolism, with the SSM subpopulation being more susceptible to damage than the IFM subpopulation. MitoQ increased ATP synthesis and reduced proton leaks in both mitochondrial subpopulations when assessed using glutamate and malate substrates. This suggests an improvement in mitochondrial function and malate-aspartate shuttle function, leading to decreased free radicals and increased ATP production for myocardial activity, at least in the short term after MI. Support: FAPES, CAPES, CNPq, UFES Protocol: CEUA – UFES: 06 / 2023</p>



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Title	IDENTIFICATION OF ALAMANDINE-(1-5) AS A NEW ANTI-HYPERTENSIVE PEPTIDE OF THE RENIN-ANGIOTENSIN SYSTEM.
Authors	KAMYLLÉ SILVA FERRAZ, ADELSON HERIC MONTEIRO, STHÉFANIE CHAVES DE ALMEIDA GONÇALVES, CAROLINA FONSECA, NICIA PEDREIRA SOARES, ROBSON AUGUSTO SOUZA DOSSANTOS, MARIA JOSÉ CAMPAGNOLE DOS SANTOS
Affiliations	Department of Physiology and Biophysics, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: It is currently accepted that angiotensin-(1-7) [Ang-(1-7)] and alamandine [Ala1-Ang-(1-7)] are members of the counterregulatory axis of the renin-angiotensin system (RAS). Both peptides can undergo hydrolysis by angiotensin-converting enzyme and form Ang-(1-5) and Alamandine-(1-5), respectively. Recently, we have shown that Alamandine-(1-5) is present in human and mice circulation. Objective: Evaluate the cardiovascular effects induced by intravenous (i.v.) administration of Ang-(1-5) and Alamandina-(1-5). Methods: Normotensive Wistar (n=6 for each peptide) and spontaneously hypertensive rats (SHR) (n=6 for each peptide) were anesthetized with a mixture of Ketamine (50 mg/kg) and Xylazine (10 mg/kg). Polyethylene cannulas made with PE10 (4 cm for the artery and 3 cm for the vein) polymerized by heat with PE50 (aprox. 17 cm) and filled with 0.9% sterile saline containing heparin (5000UI/ml) were inserted into the abdominal aorta through the femoral artery (BP recordings) and into the femoral vein (drug injections). Twenty-four hours later, cardiovascular parameters were recorded in conscious animals. After a period of one hour for stabilization of the cardiovascular parameters, Alamandine-(1-5) or Ang-(1-5) were injected at a dose of 3µg/ 100g of b.w. A similar volume (0.1 ml/ 100g b.w.) of sterile saline was injected into SHR and Wistar rats for control. Results: Alamandine-(1-5) injection produced a progressive decrease in systolic blood pressure (SBP SHR, reaching-33±3.0 mmHg six hours after injection (Baseline SBP: 208±8 mmHg before and 175±10 mmHg, six hours after the injection). In contrast, SBP did not significantly change after the administration of Ang-(1-5) (Baseline SBP: 198±13 mmHg before and 199±8 mmHg six hours after injection). There was no significant change in heart rate (HR) in SHR after Alamandine-(1-5) (Baseline HR: 342±14 beats/min before and 341±18.8 beats/min after six hours) or after Ang-(1-5) (Baseline HR: 333±18 beats/min before and 326±19 beats/min after six hours). Alamandine-(1-5) injection in Wistar rats produced only small changes in BP (Baseline SBP: 109±10 mmHg before injection and 99±11 mmHg six hours after injection, p<0.05). No differences were observed for Ang-(1-5) injection in Wistar rats (Baseline SBP: 118±8 mmHg before injection and 115±9 mmHg six hours after injection) or in HR for Alamandine-(1-5) or Ang-(1-5). Saline injection did not change BP or HR in SHR or in Wistar rats. Conclusion: These results show that Alamandine-(1-5), but not Ang-(1-5), triggers a long-lasting fall in BP in hypertensive animals. These data indicate that we have identified a new vasodilatory peptide of the RAS, increasing our understanding of the complexity of this system and opening a possibility for a future development of a new pharmacological target for hypertension treatment. Support: Capes, Cnpq, Fapemig, and INCT Nanobiofar. Protocol: 188/2023</p>

Title	Role of the afferent renal nerves in the cardiovascular responses to acute renal ischemia-reperfusion in rats
Authors	ANA CAROLINE MARREIROS, RAFAEL SANTOS CARVALHAL, FERNANDA MANO TAGLIAPIETRA DA SILVA, MARK KNUEPFER, ERIKA EMY NISHI, CASSIA MARTA DE TOLEDO BERGAMASCHI, CRISTIANE DAMAS GIL, MAYCON IGOR DE OLIVEIRA MILANEZ, RUY RIBEIRO DE CAMPOS JÚNIOR
Affiliations	Fisiologia Cardiovascular, UNIFESP, UNIVERSIDADE FEDERAL DE SÃO PAULO
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ischemia and reperfusion (IR) injuries are still a challenge in certain clinical complications, it is known that it results from increased inflammation and apoptosis of renal tubular cells, in addition to an increase in renal sympathetic nervous activity (rSNA), however it is not yet fully clarified the role of renal afferents in response to IR. Objective: The present study aimed to evaluate how acute renal IR influences renal (rSNA) and splanchnic (sSNA) sympathetic vasomotor activation in control and in rats submitted to renal deafferentation. Methods: All experimental procedures were performed according to the guidelines recommended and approved by the Ethics in Research Committee of the Escola Paulista de Medicina – Universidade Federal de São Paulo (Protocol No. 1567290421). Two independent series of experiments were carried out in male Wistar rats (300-350 g). Control group (n=8) and renal deafferent group (RD) (n=6). Femoral vessels were catheterized before the experiments under sodium thiopental anesthesia (50 mg/kg, ip) to record mean arterial pressure (MAP) and heart rate (HR). Subsequently, a retroperitoneal incision was made to expose the splanchnic and renal nerves to record the sympathetic vasomotor activity (20 k, 100-1000 Hz, Neurolog System – Digitimer UK). Anesthesia was maintained by continuous infusion of sodium thiopental (10 mg·kg⁻¹·h⁻¹, i.v.) throughout the experiment and IR was induced by total obstruction of blood flow to the left kidney by clamping the renal artery for 60 min, followed by a period of reperfusion for 120 min. Blood collection from the femoral artery was performed in two stages, before ischemia and after 120 min of reperfusion, to perform the total and differential count of leukocyte populations. Furthermore, there were quantification of intrarenal interleukins and immunohistochemistry for CGRP were performed to confirm deafferentation. For the statistical analysis, the GraphPad Prism 7[®] program was used. Data are expressed as mean ± standard error of the mean (SEM). Differences between groups were analyzed by the One-way or Two-way ANOVA analysis of variance followed by Fisher’s posttest. In addition, when necessary, unpaired Student’s t test was used. Only values of p<0.05 (*) were considered statistically significant. Results: Renal ischemia significantly increased renal sympathetic nerve activity (rSNA) (20 min: 75% ± 38%, P<0.05), however, it did not alter splanchnic sympathetic nerve activity (sSNA). The increase in rSNA was triggered by activation of afferent fibers, since IR significantly reduced rSNA in the RD group (180 min:-73 ± 32 Δspikes/s and 180 min:-29% ± 12%, P<0.05) and induced a significantly greater drop in blood pressure (180 min:-48 ± 4 ΔmmHg, P<0.05) and bradycardia (160 min:-80 ± 7 Δbpm, P<0.05). No significant differences, however, were found between groups in the leukocyte profile. Conclusion: The results show that renal afferent nerves (capsaicin sensitive sensory nerves) triggers a preferential increase in sympathetic vasomotor activity to the kidney during acute IR. Our hypothesis is that the increase in rSNA in response to IR is triggered by renal afferent fibers since these fibers project to brain regions involved in the control of efferent sympathetic activity to the kidneys. Afferent renal nerves may be a new therapeutic target to treat acute renal lesions triggered by IR. Support: Supported by FAPESP (19/25295–0), CAPES (finance code 001), and CNPq. RRC and CTB were recipients of the CNPq fellowship. Protocol: N.A.</p>

Title	Acute effects of short-term mitoquinone treatment on vascular remodeling post-myocardial infarction
Authors	SARA BIANCA OLIVEIRA MENDES, TADEU ERITON CALIMAN ZANARDO, MARIA EDUARDA SILVA STEIN, KATYANA KALINE SILVA FERREIRA, GEORGIA AZEVEDO DE OLIVEIRA TRACHEL, ANNA KAROLINA NASCIMENTO COSTA, LAIS DE OLIVEIRA TRACHEL, IVANITA STEFANON, MAICON LANDIM-VIEIRA, AURÉLIA ARAÚJO FERNANDES
Affiliations	Department of Physiological Sciences, UFES, Department of Biomedical Sciences, FSU, Biochemistry Postgraduate Program, UFES
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Mitochondria are an important source of oxidative stress after myocardial infarction (MI). Objective: To evaluate the vascular remodeling and the effects of mitochondrial antioxidant mitoquinone (MitoQ) in the aorta from rats seven days post-MI. Methods: Wistar male rats, eight weeks old, were divided into: Sham, MI, Sham MitoQ and MI MitoQ (CEUA 06/2023). The MI was surgically induced and following the animals were treated for seven days with MitoQ (100µM/Kg/day) in drinking water. After treatment, hemodynamic analysis was performed and the thoracic aorta was collected for histological evaluation, and scanning electron microscopy (SEM). The statistical analyses are presented as mean±SEM. Two-way ANOVA followed by Tukey's post hoc test was performed. Significance values were P<0.05. Results: There were reductions in the systolic (Sham 113±3 N=10; MI 93±4* N= 9; Sham MitoQ 108±4 N=4; MI MitoQ 108±3# N=4; *p<0.05 Sham vs MI; #p<0.05 Sham MitoQ vs MI MitoQ) and diastolic (Sham 84±3 N=10; MI 68±3* N=9; Sham MitoQ 81±3 N=4; MI MitoQ 85±3 N=4; *p<0.05 Sham vs MI) arterial blood pressure in the MI compared to Sham group. We also observed an increase in the left ventricular systolic pressure (Sham 116±5 N=10; MI 79±3* N=9; Sham MitoQ 115±6 N=4; MI MitoQ 100±4# N=4; *p<0.05 Sham vs MI; #p<0.05 Sham MitoQ vs MI MitoQ) and left ventricular end diastolic pressure (Sham: 5±0.4, MI:10±1*; Sham MitoQ: 3±1; IM MitoQ: 5±0.5#; *p<0.05 Sham vs MI; #p<0.05 Sham MitoQ vs MI MitoQ). MitoQ was able to restore all these parameters. Lumen thickness and area were equal between groups (Sham 178,9±8,4 N=4; MI 116±43,1 N=4; Sham MitoQ 178,1±2,6 N=4; MI MitoQ 162,5±12,7 N=4). The number of elastin injury was significantly increased in the MI compared to the Sham (Sham 6,5±1,6 N=4; MI 13.5±1,6* N=4; *p<0.05 Sham vs MI). Elastin injury were not observed in MI MitoQ compared to Sham MitoQ (Sham MitoQ 5,8±1,1 N=4; MI MitoQ 8,18±1,7 N=4). Collagen content was increased in the MI and MitoQ did not change this alteration (Sham 13,6±0,9 N=4; MI 24,7±3,0* N=4; Sham MitoQ 16,6±0,3 N=4; MI MitoQ 25,7±1,9# N=4; *p<0.05 Sham vs MI; #p<0.05 Sham MitoQ vs MI MitoQ). SEM showed an important endothelial denudation in the MI group while this damage was rare in the MI MitoQ (Sham 0,2±0,1 N=4; MI 2,3±0,1* N=4; Sham MitoQ 0,3±0,2 N=4; MI MitoQ 1,3±0,2# N=4; *p<0.05 Sham vs MI; #p<0.05 Sham MitoQ vs MI MitoQ; & p<0.05 MI vs MI MitoQ). Conclusion: Hemodynamic alterations and adaptive remodeling have been observed seven days post-MI, MitoQ was not able to restore alterations as collagen content and elastin injury. MitoQ prevented endothelial damage. Support: FAPES, CAPES, CNPQ, UFES. Protocol: N.A.</p>

Title	ACHADOS ECOCARDIOGRÁFICOS EM UM MODELO MURINO COM MUCOPOLISSACARIDOSE TIPO 1
Authors	NANCY CARLINI VIEIRA MARTINS, ANGÉLICA SALATINO DE OLIVEIRA, ANGELA M V TAVARES, ESTEBAN ALBERTO GONZALEZ, GUILHERME BALDO
Affiliations	Fisiologia Cardiovascular, UFRGS
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Mucopolissacaridose tipo 1 (MPS-1) é uma doença rara de acúmulo lisossômico e efeitos multissistêmicos, cujos tratamentos existentes não são capazes de corrigir os danos ocasionados em artérias importantes, como a aorta e a pulmonar. A perda da capacidade elástica dessas duas artérias pode trazer consequências deletérias, não apenas para o sistema cardiovascular, mas para todo o organismo. Objective: Evidenciar a perda da função vascular em camundongos modelo para MPS-1. Methods: A amostra foi composta por 17 camundongos (mus musculus machos e fêmeas) com 6 meses de vida e aproximadamente 30 gramas (controles saudáveis n=10 e MPS-1, nocautes para o gene IDUA, n=7). Os animais foram anestesiados (isoflurano diluído em oxigênio 100%) e posicionados dorsolateralmente em uma cama aquecida. Avaliações por ecocardiografia bidimensional e análise de fluxo por Doppler foram realizadas em ecógrafo com probe linear de 12-4 MHZ, EnVisor HD System (Philips Medical, USA). Foram analisados o diâmetro da aorta e os fluxos de ambas as artérias. Os tempos de aceleração (TA) e de ejeção (TE) da artéria pulmonar também foram observados, sendo considerada a razão TA/TE para analisar sua rigidez. Para as comparações das médias entre os grupos, foi utilizado o teste t de Student. Para a análise do diâmetro da aorta foi utilizado o teste de Mann-Whitney, pois a variável não atendeu aos critérios para testes paramétricos. Valores de $p < 0,05$ foram considerados estatisticamente significativos. Results: O diâmetro da aorta foi significativamente maior no grupo MPS-1 (0,138) quando comparado com o controle saudável (0,119; $p = 0,012$), já a razão TA/TE da artéria pulmonar (controle: $0,315 \pm 0,0756$, MPS-1: $0,252 \pm 0,0542$) não diferiu estatisticamente entre os grupos ($p > 0,05$). Conclusion: Os dados preliminares desta pesquisa demonstram que, embora não tenha sido observado aumento da resistência vascular pulmonar, como relatado em outros estudos publicados pelo grupo, foi possível constatar um aumento significativo da dilatação aórtica, como consequência da perda de elasticidade desta artéria. Support: PIBIC; CNPQ; FIPE; HCPA Protocol: 2022-0631</p>

Title	Uso do software CellProfiler para aquisição automatizada de parâmetros morfológicos de cardiomiócitos isolados
Authors	DAVI EMMANUEL LISBOA LOPES, SÉRGIO SCALZO, MARCOS ELIEZECK, LUCAS MAGALHÃES, ANA CAROLINA FAGUNDES DOS SANTOS, SÍLVIA CAROLINA GUATIMOSIM FONSECA
Affiliations	Fisiologia e Biofísica, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A quantificação de parâmetros morfológicos dos cardiomiócitos é um passo importante e fundamental na compreensão dos mecanismos celulares envolvidos na patogênese da doença cardíaca. No entanto, medições rápidas e reprodutíveis são dificultadas por vários fatores inerentes à subjetividade da análise manual. Além disso, a análise manual geralmente demanda muito tempo e pode apresentar viés no processamento de imagens. Neste trabalho adaptamos o programa de processamento automático de imagens Cellprofiler para aplicação em cardiomiócitos isolados provenientes de camundongos adultos</p> <p>Objective: Otimizar a quantificação de parâmetros morfológicos de cardiomiócitos adultos por meio do uso do software Cellprofiler, reduzindo o tempo de processamento e minimizando o viés do usuário. Methods: Foram escolhidas 50 imagens de miócitos ventriculares isolados de camundongos adultos adquiridas em campo claro sob parâmetros pré-estabelecidos (célula centralizada, afastada das bordas, nenhum artefato próximo ou aderido à célula alvo, sem sobreposição de outra célula e com o maior contraste possível). As imagens foram escolhidas a partir do nosso banco de imagens do laboratório. Em seguida, montamos uma pipeline no Cellprofiler, que segmenta essas células baseando-se em variações de intensidade. Para efeito de comparação, essas mesmas imagens foram processadas pelo programa de processamento manual Fiji-imageJ (NIH) e as medidas obtidas foram exportadas para uma planilha também de maneira manual. Posteriormente, cronometramos o tempo necessário para o processamento manual completo (segmentação, medição e exportação para a planilha). O tempo total necessário para o processamento completo de todas as imagens de forma manual foi comparado com o tempo de processamento das mesmas imagens de forma automatizada. Análise estatística: Teste-T student através do software Graphpad Prism 8.0. Results: Inicialmente, comparamos o tempo médio de análise completo de cada célula pelos métodos manual (ImageJ) e automatizado (CellProfiler). Constatamos que o tempo médio de análise através do cellprofiler é significativamente mais rápido que o método convencional (em segundos: ImageJ: 54.2±1.5 vs CellProfiler 22.2±1.2. p<0.0001.) Além do menor tempo gasto nas análises automatizadas, a taxa de reconhecimento das células isoladas pelo CellProfiler foi de 100%, e ao analisarmos a média da área celular obtida pelos dois softwares, não foi observada diferença significativa (p=0.87), indicando uma boa confiabilidade do software em relação às análises convencionais. Em seguida utilizamos 4 avaliadores para analisar de forma independente a área de 50 células, e constatamos uma alta variabilidade entre os avaliadores, indicando uma alta subjetividade na análise (média em μm^2: Avaliador 1: 2562; Avaliador 2: 2794; Avaliador 3: 2419; Avaliador 4: 2805: enquanto a avaliação pelo Cellprofiler não apresentou variação entre os avaliadores: 2787). Conclusion: Nossos achados indicam que a utilização do programa Cellprofiler para análise morfométrica de cardiomiócitos isolados permite ao usuário segmentar, medir e exportar grandes quantidades de dados de maneira dinâmica, com maior sensibilidade, e um tempo de análise consideravelmente mais curto. Em conjunto estes dados mostram a importância do uso de sistemas automatizados e desenvolvimento de pipelines que garantam uma maior confiabilidade dos resultados gerados. Support: CNPq/CAPES/FAPEMIG. Protocol: N.A.</p>

Title	OVERNUTRITION DURING DEVELOPMENT AFFECTS MITOCHONDRIAL FUNCTION AND OXIDATIVE BALANCE IN THE HEART OF JUVENILE MALE RATS
Authors	JEFFERSON THADEU ARRUDA SILVA, JONATA HENRIQUE DE SANTANA, ELENILSON BERNARDO, MARIANA P. FERNANDES, CLAUDIA J. LAGRANHA
Affiliations	Pós Graduação em Nutrição, Atividade Física e Plasticidade Fenotípica, UFPE
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Overnutrition, characterized by excessive nutrient intake, can trigger an energy imbalance, paving the way for disorders like obesity. This condition might impact the developing offspring. Objective: Evaluate in the heart of male offspring, at 53 days of life, the effect of overnutrition during the lactation period, mitochondrial function, and oxidative balance. Methods: This study was approved by the ethics committee (protocol nº 117/2022). Male offspring were divided according to the nutritional insult into normonourished-NS or overnourished-OS groups on the third day of life. At 53 days of life, rats were euthanized, and hearts were collected. Data were expressed as mean \pm SEM. The significance level was maintained at 5% ($p < 0.05$) for all analyses. Statistical analyses were performed using GraphPad Prism 8.0 software. Results: Our data showed that the OS group's body weight was higher than NS's ($p = 0.04$). In association with the BW, we observed in OS an increase in ROS production ($p = 0.0026$), in parallel to the decrease in citrate synthase activity ($p = 0.0068$) and NADH levels ($p = 0.0344$), but an increase in NAD/NADH ratio ($p = 0.0236$). MDA levels were higher in the heart of OS ($p = 0.0147$). Protein oxidation was higher in OS ($p < 0.0001$). GSH levels were reduced in the OS group ($p = 0.0006$) and total SH levels in OS ($p = 0.0217$). Conclusion: Overnutrition during lactation negatively affects the male heart and increases the risk of cardiovascular disease due to the establishment of mitochondrial dysfunction and oxidative stress. Support: The authors are thankful to FACEPE and CNPq (Foundation for the Support of Science and Research from Pernambuco State—Brazil, APQ-0765-4.05/10;-1026-4.09/12; Universal-408403/16;APQ-1005-4.05/22) for the financial support to acquire the equipment and reagents used in this work. We are also grateful to UFPE, CNPq, and FACEPE that provided scholarships. This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brasil (CAPES), Finance Code 001. Protocol: Protocol nº 117/2022</p>

Title	ÁCIDO ELÁGICO ATENUA O AUMENTO DA RESPONSABILIDADE VASOCONSTRITORA EM AORTAS DE RATOS INDUZIDA PELA SOBRECARGA DE FERRO
Authors	VINÍCIUS BERMOND MARQUES, MÔNICA GOLDNER, MATEUS JOSÉ DEFANTE, BRENDA SANTOS LEITE, SABRINA BERTOLI RODRIGUES, LEONARDO DOS SANTOS, ALESSANDRA SIMÃO PADILHA
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, UFES, Faculdade Multivix, Multivix, Faculdade Novo Milênio, Faculdade Novo Milênio
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A sobrecarga crônica de ferro induz uma vasculopatia caracterizada por disfunção endotelial, sendo necessária a busca por terapias para amenizar esse dano. Nesse sentido, o ácido elágico é um polifenol com ação anti-inflamatória e antioxidante, com potencial benefício nesse contexto. Objective: Avaliar os efeitos do ácido elágico na prevenção do aumento da vasoconstrição induzida pela sobrecarga de ferro.</p> <p>Methods: Ratos Wistar machos (~200g) foram distribuídos em quatro grupos: controle (Ct), controle tratado com ácido elágico (CtEA), ferro (Fe) e ferro tratado com ácido elágico (FeEA). A sobrecarga de ferro foi induzida pela administração de ferro-dextrano (100mg/Kg/dia, 5 vezes/semana, i.p.), enquanto os controles receberam NaCl 0,9% no mesmo regime de tratamento. Simultaneamente, os grupos tratados com ácido elágico, receberam esse composto (30mg/Kg/dia) enquanto os grupos demais receberam apenas a solução diluente, ambos por gavagem. Após quatro semanas de tratamento, foram coletados o sangue para medida do ferro (N=10 por grupo) e a aorta torácica para estudo de reatividade vascular in vitro (N=6-13 por grupo). Os dados foram avaliados por ANOVA 2-vias seguida do pós-teste de Fisher, e considerado significativo $P < 0,05$. Results: O ácido elágico não interferiu no aumento do ferro sérico (Ct: 169 ± 8; CtEA: 171 ± 13; Fe: 459 ± 26 vs FeEA: $505 \pm 38 \mu\text{g/dL}$), embora tenha atenuado o aumento da responsividade vascular à fenilefrina induzida pela sobrecarga de ferro (logEC50 Ct: $-6,66 \pm 0,27$; CtEA: $-6,85 \pm 0,28$; Fe: $-7,12 \pm 0,31$ vs FeEA: $-6,77 \pm 0,23$), com prevenção do prejuízo da modulação endotelial (diferença entre as áreas sob as curvas Ct: 397 ± 42; CtEA: 413 ± 50, Fe: 272 ± 33 vs FeEA: $407 \pm 41\%$) e nitrérgica (dASC Ct: 283 ± 82; CtEA: 323 ± 90, Fe: 123 ± 77 vs FeEA: $249 \pm 141\%$), mensuradas após remoção mecânica do endotélio e incubação com L-NAME $100 \mu\text{M}$, respectivamente. Ademais, a inibição da NADPH oxidase com VAS 2870 ($10 \mu\text{M}$) reduziu a resposta contrátil apenas no grupo Fe (logEC50 Ct: $-6,6 \pm 0,1$ vs Ct- VAS2870: $-6,7 \pm 0,1$; CtEA: $-6,8 \pm 0,1$ vs CtEA-VAS2870: $-6,6 \pm 0,1$; Fe: $-7,1 \pm 0,07$ vs Fe-VAS2870: $-6,6 \pm 0,1$; FeEA: $-6,7 \pm 0,07$ vs FeEA-VAS2870: $-6,8 \pm 0,1$). Conclusion: Nossos resultados mostram que a administração oral de ácido elágico foi capaz de atenuar a resposta vasoconstritora aumentada identificada no modelo animal de sobrecarga de ferro, provavelmente pela preservação da modulação endotelial/nitrérgica e redução da ativação da NADPH oxidase. Support: CNPq, CAPES e FAPES. Protocol: CEUA-UFES no. 18/2023.</p>

Title	RESPOSTA DA ASSOCIAÇÃO DE ÓXIDO DE ROSA E EXERCÍCIO FÍSICO SOBRE SISTEMA CARDIOVASCULAR E AUTÔNOMICO
Authors	SAMUEL DE SOUSA PEREIRA ARAÚJO, JULIANA ALVES DA SILVA, ANA FLAVIA MORAES DA SILVA, JOSÉ GUILHERME VERAS DE ASSUNÇÃO, ARIELL ALVES DE OLIVEIRA, JOSÉ LOPES PEREIRA JÚNIOR, FRANCISCA VALDIRENE DE SOUSA NUNES, PÂMELA DE SENA SANTOS, CARLOS EDUARDO SALES REIS, REGINA GUIMARÃES SILVA, LIANA DE MOURA SANTANA, MARCOS ANTONIO PEREIRA DOS SANTOS, MARIA DO CARMO DE CARVALHO E MARTINS, MARCELA DA SILVA NOLETO, JOÃO PAULO JACOB SABINO
Affiliations	Biofísica e Fisiologia Humana, UFPI
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Atualmente, é evidente o aumento de pessoas acometidas por doenças cardiovasculares (DCV). Nesse cenário alarmante, a hipertensão arterial (HA), caracterizada por um marcante desequilíbrio simpatovagal, está entre as DCV mais prevalentes. Diante disso, urge a necessidade de novas terapias para mitigar esta fisiopatologia. Nesse contexto, uma subdivisão dos terpenos, os monoterpenos, tem ganhado notoriedade dada à sua diversidade, abundância e propriedades farmacológicas. Entre eles, o monoterpeno Óxido de Rosa (OR) surge como uma possível alternativa para o tratamento da HA, devido à sua atividade anti-inflamatória e hipotensora, já relatada quando administrado por via intravenosa. Ademais, além das intervenções farmacológicas, o exercício físico (EF), seja resistido ou aeróbico, é considerado uma excelente abordagem para retardar o desenvolvimento da HA e até tratá-la. Portanto, a combinação de ambas as intervenções pode potencializar a eficácia terapêutica do OR. Com base nisso, faz-se necessário utilizar um modelo apropriado para averiguar a atividade do OR sobre a HA. O modelo de ratos espontaneamente hipertensos (SHR) é uma excelente opção, pois a fisiopatologia da HA observada nos SHR se assemelha à HA essencial vista nos seres humanos. Objective: Avaliar o efeito do OR administrado cronicamente com ou sem EF de natação sobre parâmetros hemodinâmicos, além de adaptações autonômicas cardíacas em ratos SHR. Methods: Foram utilizados ratos SHR e Wistar machos com 12 semanas de vida (290-310 g), nos quais foram administrados OR, diariamente, por 34 dias consecutivos [v.o. (100 mg/kg)]. A evolução da pressão arterial sistólica (PAS) foi monitorada por meio da pletismografia com manguito de cauda [PMC (antes de iniciar o tratamento e nas semanas 1, 3 e 5)]. Vinte e quatro horas antes do término do tratamento, os animais foram anestesiados, e suas artérias e veias femorais foram canuladas para o registro da pressão arterial pulsátil (PAP) e para a administração de drogas, respectivamente. Dessa forma, foram avaliados parâmetros hemodinâmicos (PAS, PAD, PAM e FC), a sensibilidade do barorreflexo, tônus parassimpático e a frequência intrínseca de marcapasso (FIMP). Por fim, os registros da PAP também foram utilizados para a avaliação da atividade simpática e vagal, por meio da análise da variabilidade da pressão e da frequência cardíaca, tanto por meio da análise espectral quanto pela análise simbólica. Results: Os resultados obtidos após o tratamento mostraram que o OR, administrado isoladamente ou em associação com EF mostrou-se ser eficiente na redução da PAS [veículo (203 ± 3) vs OR (150 ± 3) e OR + EF (143 ± 4)], ademais, esta queda dos níveis pressóricos também foi observada na PAM [veículo (154 ± 5) vs OR (121 ± 6) e OR + EF (135 ± 4)] nos ratos SHR. No entanto, o protocolo de natação, isoladamente, não preveniu o aumento da pressão arterial, mas quando associado ao OR, foi capaz de melhorar o controle autonômico, avaliado pela variabilidade da frequência cardíaca e pelo tônus parassimpático. Em última análise, a FIMP e a sensibilidade barorreflexa estavam reduzidas nos animais SHR, e nenhuma das intervenções realizadas foram capazes de melhorar esses marcadores de regulação autonômica cardíaca. Conclusion: Portanto, a partir dos resultados apresentados no presente estudo, conclui-se que o OR é um potencial fármaco hipotensor, capaz de atenuar os parâmetros hemodinâmicos de ratos SHR, além de melhorar a função autonômica cardíaca quando associado ao exercício de natação. Support: Bolsa de mestrado n° do processo 131396/2024-2 / Universal CNPq 409109/2018-5 Protocol: 563/19</p>

Title	Serotonergic Modulation and Its Effects on Gene Expression in the Heart of Overnourished Lactating Rats
Authors	MARIA DANIELE TEIXEIRA BELTRÃO DE LEMOS, THYAGO DE OLIVEIRA RODRIGUES, OSMAR HENRIQUE DOS SANTOS JUNIOR, CLAUDIA JACQUES LAGRANHA
Affiliations	Educação Física UFPE CAV, UFPE
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Overnutrition during the neonatal period can lead to energy imbalance, mitochondrial dysfunction and, consequently, increase the risk of obesity and the development of heart disease in adult life. Objective: Investigate effects of serotonergic manipulation (by Fluoxetine) in the heart tissue of adult rats submitted or not to supernutrition overnutrition during lactation, evaluating body weight and mitochondrial function. Methods: This study was approved by the ethics committee (protocol n°0036/2022), Male Wistar rats divided on the 3rd day of life into two groups: Normonourished (n=9), Supernourished Overnourished (n=3). At 39 days of life, the groups were subdivided according to the treatment: saline (NaCl, 0.9%) or fluoxetine (10mg/kg) pharmacological treatment. At 60 days we collect the tissue. Data were expressed as mean ± SEM. The significance level was maintained at 5% (p<0.05) for all analyses. Statistical analyses were performed using GraphPad Prism 8.0 software. Results: Body weight at 21 days= (N: 40.7 + 0.68 g vs. O: 49.4 + 0.81 g, p= 0.011); 30 days= (N: 79.2 + 1.4 g vs. O: 112.9 + 3.2 g, p<0.0001); 39 days= (N: 125.9 + 3.0 g vs. O: 184.0 + 8.4 g, p<0.0001); 45 days = (N: 168.9 + 2.1 g vs. O: 226.6 + 18.8 g p=0.0003); 60 days = (N: 249.5 + 3.29 g vs. O: 289.4 + 3.70 g, p= 0.036). Treatment started at 39 days induce decrease in body weight of normofed and overfed treated with FX only at 60 days of age 60 days = (N: 249.5 + 3.3 g vs. NFX: 229.8 + 2.6 g, p= 0.0111); (O: 289.4 + 3.7 g vs. OFX: 269.0 + 3.1 g, p= 0.0111). decrease de levels of PGC-1a, TFAM and FIS1 in overfed group, but significant increase in overfed treated with fluoxetine compared to overfed. PGC1a = (O: 0.8 + 0.2 vs. OFX: 2.4 + 0.5, p=0.031); TFAM= (O: 0.1 + 0.1 vs. OFX: 3.5 + 0.6, p= 0.0003); FIS1= (O: 0.2 + 0.1 vs. OFX: 64.9 + 0.5, P<0.0001). Conclusion: Our data indicate that overnutrition, during a critical period of development in the male rat result due to the establishment of mitochondrial dysfunction in the heart. Support: CAPES, CNPq, FACEPE Protocol: n°0036/2022</p>

Title	The supplementation with lauric acid, the main component of coconut oil, promotes improvement in cardiovascular parameters in spontaneously hypertensive rats
Authors	DÉBORAH VICTÓRIA GOMES NASCIMENTO NEVES, MIRELLY CUNHA DA SILVA, JONNATHAN VINNYCIUS BENTO DA SILVA, FILIPE DE MELO BARBOSA, SIDIANE BARROS DA SILVA, MARIA DA CONCEIÇÃO CORREIA SILVA, REGINA SOUZA AIRES, THYAGO MOREIRA DE QUEIROZ
Affiliations	Programa de Pós Graduação Multicêntrico em Ciências Fisiológicas, UFPE, Programa de Pós Graduação em Nutrição, Atividade Física e Plasticidade Fenotípica, UFPE, Laboratório de Nutrição, Atividade Física e Plasticidade Fenotípica, UFPE, Núcleo de Nutrição, UFPE
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Hypertension is a multifactorial condition, and robust evidences indicate that the oxidative stress as a key mechanism in this condition. Therefore, the use of antioxidant therapy as well as dietary components with antioxidant function have been used. Objective: To investigate the effects of lauric acid, the main component of coconut oil, supplementation on cardiovascular changes in spontaneously hypertensive rats (SHR). Methods: Wistar and SHR rats, aged 16 weeks, were used and separated into four groups: Wistar and Wistar LA; SHR and SHR LA. The LA groups received gavage with a LA solution (60 mg/kg) for 14 days. Parameters such as body mass, food consumption, water intake, and blood pressure were analyzed during this period. On the 15th day of supplementation the animals were euthanized, followed by blood and organ collection for biochemical analysis and oxidative stress evaluation. The aorta was identified and mounted in an organ bath for vascular reactivity analysis. Differences were considered significant when $p < 0.05$. The statistical program used was GraphPad Prism® 8.0. All procedures were approved by CEUA/UFPE (#0091/2022). Results: LA impaired the body mass of Wistar (Wistar LA: 330.3 ± 9.8 g; $n = 8$ vs. Wistar: 383.6 ± 8.4 g; $n = 8$) and SHR (SHR LA: 222.1 ± 7.0 g $n = 8$ vs. SHR 261.9 ± 11.0 g) groups. Daily food consumption was also reduced in the SHR LA and Wistar LA animals. However daily water intake was reduced only in the SHR LA group. Using tail plethysmography analysis, the SHR group showed an increase in blood pressure levels, and treatment with AL reduced SBP (SHR AL 167.9 ± 3.7 mmHg; $n = 9$ vs. SHR 194.9 ± 2.9 mmHg; $n = 9$) and DBP (SHR AL 117.0 ± 0.9 mmHg; $n = 9$; SHR 124.4 ± 0.6 mmHg; $n = 9$). The vascular reactivity experiments showed that the treatment with LA reversed the decrease in contraction in the Wistar group in the presence of endothelium (Wistar LA MR = $92.3 \pm 7.8\%$; $n = 3$ vs. Wistar MR = $58.2 \pm 3.4\%$; $n = 6$). The SHR group showed an increase in the contractile effect compared to the control group in the presence of the endothelium (SHR MR = $106.2 \pm 7.7\%$; $n = 6$ vs. Wistar MR = $58.2 \pm 3.4\%$; 2.4%; $n = 6$ vs. Wistar MR = $112.5 \pm 3.6\%$). No changes were observed after LA treatment related to the vasorelaxant responses with either ACh or NPS. The SHR group showed an increase in the AST enzyme (SHR: 174.1 ± 22.7 U/L; $n = 2$ vs. Wistar = 118.1 ± 8.1 U/L; $n = 7$) and treatment with LA reversed this increase (SHR LA= 121.3 ± 3.2 U/L; $n = 5$ vs. SHR= 174.1 ± 22.7 U/L; $n = 2$). There was no statistical difference between the groups regarding biochemical analysis of total cholesterol, triglycerides, glucose, and ALT. LA treatment reduced MDA levels in the hepatic tissue of SHR rats (SHR LA: 0.46 ± 0.06 nmol/mg, $n = 5$ vs. SHR: 0.79 ± 0.05 nmol/mg, $n = 6$). SOD activity in the renal tissue of the SHR group was increased, being reduced by LA supplementation (SHR LA= 2.22 ± 0.06 U/mg/min; $n = 6$ vs. SHR: 2.39 ± 0.07 U/mg/min; $n = 6$). Regarding the GSH analysis, there was no statistical difference between the groups. Conclusion: In summary, we can conclude that LA represents a potential benefit for cardiovascular health and may be a promising strategy for the adjuvant treatment of hypertension. Support: FACEPE, CNPq, CAPES Protocol: 0091/2022</p>

Title	ALTERAÇÕES ELETROFISIOLÓGICAS, ECOCARDIOGRÁFICAS E DISFUNÇÃO ENDOTELIAL EM CAMUNDONGOS FÊMEAS IDOSAS.
Authors	ANA CAROLINA PEREIRA DA SILVA, YGOR SCHLEIER FRANCISCO DAS CHAGAS, GABRIEL SOUZA DE JESUS, ISLAINE SILVA DE MENEZES, ANTÔNIO CARLOS CAMPOS DE CARVALHO, CLEBER FARIAS VIEIRA, DIANA MAYRA DO CARMO COSTA, AINÁ EIRAS DOMINGOS, FREDERICO LUIZ LIMA ROSA, KARINE TAVARES DE JESUS, MARCELLY GONÇALVES PEREIRA, THAIS BARENCO-MARINS, FERNANDO DE AZEVEDO CRUZ SEARA
Affiliations	Departamento de Ciências da Saúde, Universidade Federal do Rio de Janeiro UFRJ
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Doenças cardiovasculares são as principais causas de morte no mundo, e o envelhecimento é o fator de risco dominante e ubíquo para tais doenças. As perspectivas indicam que a população idosa tende a aumentar cada vez mais, a parcela feminina envelhecida vem apresentando maiores chances de desenvolver doenças cardiovasculares em comparação com homens da mesma faixa etária que possuem estilo de vida e disfunções metabólicas semelhantes. Dessa forma se torna necessário estudos que possam identificar as alterações eletrocardiográficas, ecocardiográficas e de reatividade vascular em fêmeas idosas e a relação dessas disfunções com o envelhecimento. Objective: Avaliar a influência do processo de envelhecimento nas alterações eletrofisiológicas, ecocardiográficas e na reatividade vascular de camundongos fêmeas idosas. Methods: Todos os procedimentos foram submetidos conforme as diretrizes da Comissão de Ética No Uso de Animais (CEUA) em Experimentação Científica do Centro de Ciências da Saúde da Universidade Federal do Rio de Janeiro, Registrada no Conselho Nacional de Controle de Experimentação Animal (CONCEA) sob o número do processo n°: 01200.001568/2013-87. Para este estudo, foram utilizados camundongos fêmeas C7BL/6 em idade entre 4 a 24 meses, divididos em dois grupos de adultas (4 meses, n=5) e idosas (24 meses, n=3). Os animais foram submetidos ao registro do Eletrocardiograma (ECG) na derivação D1 de ambos os grupos, para o grupo de fêmeas adultas esses registros foram realizados com base no ciclo estral para padronizar a comparação entre os dois grupos, além disso foi realizado registros de Ecocardiograma onde será feita uma análise posterior e futuramente será realizada a eutanásia dos animais para registros de Reatividade Vascular com o objetivo de analisar o funcionamento endotelial do vaso. Results: O grupo de animais envelhecidos apresentou prolongamento da onda P ($p < 0.05$), indicando aumento da dispersão da condução elétrica atrial. A duração do intervalo PR também foi maior nesse grupo, sugerindo retardo na condução atrioventricular ($p < 0.05$). O intervalo QRS encontrou-se prolongado no grupo de animais envelhecidos, indicando dessincronização na despolarização ventricular esquerda e direita ($p < 0.05$). Por fim, a duração do intervalo QT também encontrou-se aumentada nos animais envelhecidos, indicando dispersão na condução elétrica ventricular, possivelmente por hipertrofia ventricular ($p < 0.05$). Não houve diferença significativa na duração do intervalo RR ($p > 0.05$), indicando que a frequência cardíaca estava normal. Conclusion: A partir dos resultados obtidos, podemos concluir que o envelhecimento afeta de maneira prejudicial a condução elétrica no coração de camundongos fêmeas. Os resultados indicam, particularmente, aumento na dispersão da condução elétrica atrial e ventricular, além de retardo na condução elétrica atrioventricular e dessincronização na despolarização ventricular. Support: FAPERJ, CNPq, CAPES Protocol: 01200.001568/2013-87</p>

Title	Assessment of Mitochondrial Function in Ischemic and Reperfused Hearts Treated with Heat Shock Protein 10 kDa (HSP10)
Authors	MARCELLA BORGES COUTINHO, DAHIENNE DE OLIVEIRA MENDES, JOSE HAMILTON NASCIMENTO, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Fisiologia, Universidade Federal do Rio de Janeiro
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ischemic heart disease is currently the leading cause of death in Brazil and worldwide. During infarction, the reduction or interruption of blood flow results in an imbalance between oxygen supply and demand. Immediate restoration of blood flow (reperfusion) is essential for myocardial survival, however, reperfusion itself can cause injury. One strategy to reduce ischemia and reperfusion injury is novel cardiomyokines. Recently, we described the 10 kDa heat shock protein (HSP10) as one of these cardiomyokines. This protein is secreted by ischemic preconditioning stimulation. However, it is still unclear how this protein acts to prevent these injuries. Objective: The present study aims to investigate the mechanisms of cardioprotection conferred by HSP10, focusing on the effects of this protein on the maintenance of mitochondrial function. Methods: Isolated hearts from male Wistar rats (male. 300–350 g, CCS-Central Animal Facility, Institutional Animal Care and Use Committee protocol: 154/21) were perfused with Krebs saline and then subjected to 30 minutes of global ischemia and 10 minutes of reperfusion. Before ischemia, hearts were perfused with HSP10 (1μmol-L⁻¹). At the end of reperfusion, mitochondria were isolated and mitochondrial function evaluated. In a subset of experiments mitochondria isolated from fresh hearts were incubated directly with HSP10 and subjected to hypoxia/reoxygenation in vitro. Results: The perfusion of HSP10 in isolated hearts before I/R improved mitochondrial respiration, and ATP production and prevented mitochondrial ROS formation compared to the I/R group. Incubation of HSP10 in mitochondria subjected to hypoxia and reoxygenation prevented reductions in mitochondrial respiration (91.5\pm5.1), ATP production (250.1\pm9.3), and reduced mitochondrial ROS production (219.7\pm9.0) compared to the group subjected to hypoxia/reoxygenation (n=12, 51.5\pm5.0; 187\pm21.7; 339.0\pm14.3; p<0.001, respectively). Conclusion: Mitochondria are a target for HSP10-induced cardioprotection. HSP10 can act directly on mitochondria and protect against hypoxia/reoxygenation injury. Support: Cnpq, Faperj Protocol: 01200.001568/2013-87</p>

Title	Evaluation of cardiometabolic effects induced by a high-fat diet enriched with linseed oil during the critical period of development in the female offspring of rats
Authors	VANESSA MARIA DOS SANTOS, FILIPE DE MELO BARBOSA, MIRELLY CUNHA DA SILVA, LIZANDRA HENRIQUE DE FARIAS, JONATA HENRIQUE DE SANTANA, CLAUDIA JACQUES LAGRANHA, THYAGO MOREIRA DE QUEIROZ
Affiliations	Programa de Pós Graduação em Nutrição, Atividade Física e Plasticidade Fenotípica, UFPE, Programa de Pós Graduação Multicêntrico em Ciências Fisiológicas, UFPE
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: High-fat diets during critical periods of development can induce long-lasting changes in the health of offspring, potentially increasing their susceptibility to chronic disease in adulthood. On the other hand, the consumption of a diet enriched with linseed oil, rich in omega-3, reduces the incidence of cardiometabolic diseases in adulthood. Objective: To investigate the cardiometabolic effects on the female offspring of rats at 90 days of age submitted to a high-fat diet enriched with linseed oil during pregnancy and lactation. Methods: Wistar rats of reproductive age were mated under controlled conditions, forming the following groups: control (CT); high-fat diet (HL), high-fat diet with linseed oil (HLOL). In these studies, only female offspring were used, we analyzed parameters such as body weight and pressure was measured by tail plethysmography at 60 and 90 days of age. At 90 days, the animals were euthanized, and the organs were collected for analysis. The results were expressed as mean \pm standard error of the mean. The differences were considered significant when $p < 0.05$. The statistical program used was GraphPad Prism® 8.0.) Results: The body weight of female rats in the first week of HL and HLOL was higher than that of the CT group (CT: 83.88 ± 1.91 g vs. HL: 95.20 ± 1.88 g vs. HLOL: 99.77 ± 2.33 g). Weight gain remained significant until the ninth week in the HL group compared to the CT group (CT: 232 ± 3.12 mmHg vs. HL: 249.90 ± 6.42 mmHg). In addition, we observed an increase in systolic blood pressure at 60 days of age in the HL group (HL: 157 ± 3.62 mmHg vs. CT: 128.2 ± 5.58 mmHg), but the consumption of a diet with linseed oil prevented this increase in the HLOL group (HL: 157 ± 3.62 mmHg vs. HLOL: 122.7 ± 10.39 mmHg). This effect persisted on diastolic blood pressure (CT: 82.54 ± 2.74 mmHg vs. HL: 107.70 ± 3.20 mmHg vs. HLOL: 73.55 ± 2.07 mmHg). At 90 days of age, systolic and diastolic blood pressure increased in the HL group (CT: 128.8 ± 2.06 mmHg vs. HL: 155.2 ± 5.67 mmHg) and (CT: 78.93 ± 3.09 mmHg vs. HL: 102.8 ± 3.39 mmHg), respectively. The increase in body weight and blood pressure in the HL group was accompanied by an increase in the weight of the right kidney (CT: 0.822 ± 0.03 g vs. HL: 1.045 ± 0.19 g) and heart (CT: 0.775 ± 0.02 g vs. HL: 0.929 ± 0.0 g) however oil treatment did not reduce the weight of the heart (CT: 0.775 ± 0.02 g vs. HLOL: 0.909 ± 0.02 g). Regarding cardiac hypertrophy, female HL and HLOL rats showed higher hypertrophy indices (CT: 0.222 ± 0.00 cm/g vs. HL: 0.256 ± 0.00 cm/g vs. HLOL: 0.260 ± 0.00 cm/g). We observed that serum triglyceride levels were higher in the HL group, followed by a decrease in the HLOL group (HL: 90.04 ± 7.25 mg/dL vs. HLOL: 68.34 ± 6.89 mg/dL). During the analysis of lipid peroxidation levels, there was an increase in the HL and HLOL groups in relation to the CT group in the heart (CT: 0.488 ± 0.04 mmol/mg vs. HL: 0.769 ± 0.05 mmol/mg vs. HLOL: 0.516 ± 0.05 mmol/mg). In the aorta, the HLOL group had reduced levels of this biomarker compared to the HL group (HL: 5.289 ± 0.59 mmol/mg vs. HLOL: 2.830 ± 0.55 mmol/mg). Conclusion: Therefore, it is concluded that maternal consumption of a high-fat diet can promote damage to offspring, such as increased body weight, increased blood pressure and increased lipid peroxidation, however, the supplementation with linseed oil reduces some of these parameters. Support: CNPq, CAPES, FACEPE Protocol: n° 0077/2021</p>

Title	Avaliação do perfil funcional de mitocôndrias de ratos com insuficiência cardíaca pós-infarto
Authors	ITANNA ISIS ARAÚJO DE SOUZA, MARIA EDUARDA PAVARINO, MARCELLA BORGES COUTINHO, RODRIGO VERAS DA SILVA MIRANDA, JOSÉ HAMILTON MATHEUS NASCIMENTO, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Fisiologia, UFRJ
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Aproximadamente 60 milhões de pessoas em todo mundo são afetadas pela insuficiência cardíaca. 1 em 5 pessoas desenvolverá insuficiência cardíaca após os 40 anos. Após diagnóstico, tem 30% de chance de morrer dentro de 1 ano e 70% de chances de morrer em 5 anos. A insuficiência cardíaca, além de mortal é extremamente incapacitante, reduzindo muito a qualidade de vida dos pacientes acometidos. A Insuficiência cardíaca é multifatorial e complexa, e seus mecanismos de progressão não foram completamente descritos. Contudo, há um consenso que a mitocôndria tem um papel central no desenvolvimento e progressão da insuficiência cardíaca. Objective: Caracterizar o perfil funcional das mitocôndrias em partes distintas de um coração com insuficiência cardíaca. Methods: Ratos Wistar machos foram submetidos a uma cirurgia de ligadura permanente de artéria descendente anterior esquerda (IC90) ou falso operados (SHAM). Após os 90 dias do procedimento, os animais foram anestesiados e eutanasiados (CEUA), o coração dissecado em quatro partes, sendo elas: área afetada, área limitrofe, septo cardíaco e ventrículo direito. Em seguida, as mitocôndrias foram isoladas por centrifugação diferenciada. E a função mitocondrial foi avaliada pelo consumo de O₂ nos complexos I, II e IV nos estados respiratórios I, III, III, e pela máxima desacoplada, produção de ATP, produção de ROS, potencial transmembrana e capacidade de retenção de cálcio. Results: O consumo de oxigênio das mitocôndrias no estados II do complexo I foi menor nas áreas limitrofe e no ventrículo direito vs afetada e área do septo. No estado III do complexo II o consumo de oxigênio foi maior na área afetada e no septo em comparação com as demais áreas. A produção de ATP se mostrou reduzida na área afetada quando comparada ao septo e ao ventrículo direito ($p < 0,01$) e entre os grupos SHAM e IC-90 da área afetada ($p = 0,016$). A produção de ROS foi maior na área afetada vs ventrículo direito ($p = 0,01$), o septo cardíaco também produziu mais ROS do que ventrículo direito ($p = 0,02$). É possível observar uma maior produção de ROS na área afetada do grupo IC-90 vs SHAM ($p = 0,036$) e uma maior produção de ROS no ventrículo direito IC-90 vs SHAM ($p = 0,041$). Em relação ao ATP/Consumo de O₂ o ventrículo direito e septo apresentaram aumento quando comparado a área afetada ($p > 0,01$ e $p = 0,21$, respectivamente). Com relação a capacidade de retenção de cálcio, o septo mostrou uma maior capacidade quando comparado a todas as áreas ($p = 0,001$). Conclusões: Há um comprometimento das mitocôndrias da área afetada, que apesar de estarem consumindo mais O₂ que áreas não afetadas, apresentam uma produção de ATP reduzida. Mostrando uma possível ineficiência da maquinaria fosforilativa. Além disto, a área afetada parece ter menor capacidade de reter cálcio além de produzir grandes quantidades de ROS. As mitocôndrias de outras áreas parecem estar comprometidas devido a insuficiência cardíaca, enquanto o septo parece tentar compensar o mal funcionamento das outras áreas, mas apresentando alta formação de ROS. Esses resultados parecem mostrar um contribuição clara do mal funcionamento das mitocôndrias na insuficiência e como esse mal funcionamento pode contribuir para a progressão do remodelamento patológico. Conclusion: Há um fenótipo divergente entre as mitocôndrias das diferentes áreas de um coração com insuficiência cardíaca. Sendo a área afetada pouco eficiente na relação entre consumo de O₂ e produção de ATP e a septo interventricular apresentando um comportamento mais compensatório, mas lesivo. Support: CAPES, Faperj, Cnpq Protocol: 154/21</p>

Title	COLLAGEN MATRICRYPTIN PROMOTES CARDIAC FUNCTION POST-MYOCARDIAL INFARCTION BY MEDIATING SCAR FORMATION
Authors	GABRIEL ARAUJO GRILO, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	CPMP, Centro de Pesquisa em Medicina de Precisão, UFRJ, Universidade Federal do Rio de Janeiro
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Adverse cardiac remodeling post-myocardial infarction (MI) triggers a compensatory maladaptive response that contributes to heart failure. The infarcted area is replaced by a fibrotic scar that favors collagen deposition instead of its degradation. The evolution of the scar formation depends on the interaction between cardiac cells, particularly fibroblasts, and the extracellular matrix (ECM). Matricryptins are biologically active peptides, generated from ECM proteolysis, able to regulate cell function and survival. A peptide mimetic of a collagen-derived matricryptin (p1159) was shown to stimulate left ventricle (LV) fibroblast's migration in vitro, and reduce LV dilation and fibrosis after 7 days delivery in a mouse model of MI. These suggested p1159 long-term treatment post-MI could have beneficial effects and reduce/prevent adverse LV remodeling. Objective: Our goal was to identify the fibroblast receptor and mechanism-of-action involved in p1159 induced cell migration and ECM secretion responsible for the beneficial effects on LV remodeling. Additionally, we aim to establish whether p1159 improves cardiac function using a chronic MI-mouse model. Methods: Using a permanent occlusion MI model, 4–6-month-old mice received p1159 or vehicle solution up to 28 days (n=5–6/sex SHAM; n=10–14/sex/treatment). We assessed peptide treatment effects on scar composition and structure and on systolic function. To assess peptide effects on scar vascularization, a cohort of mice were injected with isolectin-B4. To investigate p1159 mode-of-action, LV fibroblasts from naïve animals were treated with p1159 diluted in serum-free media (SFM), with 10% fetal bovine serum (FBS) as positive and SFM as negative controls, respectively. Results: Matricryptin p1159 significantly improved ejection fraction post-MI at D28 (p1159=28±14, saline=14±7, p<0.05) and reduce LV dilation (end systolic volume, p1159=85±42, saline=150±74, p<0.05) by inducing the formation of a compliant and organized infarct scar which promoted LV contractility. Specifically, infarcted scars from p1159-treated animals displayed collagen fibers aligned parallel to the epicardium to resist circumferential stretching (p1159 had more fibers aligned at -10/10°, p<0.05), with reduced levels of cross-linking (lysyl oxidase, p1159=1.4±0.2, saline=0.5±0.4, p<0.05, n=5–6/group) and improved tissue perfusion (isolectin-B4, p1159=0.5±0.1, saline=0.5±0.1, p<0.05, n=8/group). In addition, p1159 increases cardiac fibroblast migration (p1159 vs. SFM from 13h to 48h, p<0.05) by activating RhoA pathways (RhoGDI, p1159=0.1±0.01, SFM=0.58±0.08, p<0.05, n=4/group) via the membrane receptor integrin α4 (p1159=3±0.5, saline=1±0.4, n=4/group, p<0.05). Conclusion: Our data indicate p1159 treatment reduced adverse LV remodeling post-MI by modulating the deposition, arrangement, and perfusion of the fibrotic scar. Support: American Heart Association 18AIREA33960311, 19PRE34450066; National Institute of Health HL152297 Protocol: USDA 55-R-0010</p>



Title	Heart rate variability and exercise capacity in hemodialysis CKD patients: Effects of chronic β-blocker therapy.
Authors	RODRIGO CONTRERAS, NATALY SCHNEIDER, CAMILA MAUTNER, VALENTINA VERA-IVÁN ALFREDO RODRÍGUEZ NÚÑEZ
Affiliations	Physical Therapy, University of Concepcion, School of Kinesiology, San Sebastian University
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introduction Autonomic dysfunction is independently associated with an increased risk of sudden cardiac death in patients on hemodialysis. In this line, sympathetic overactivity can also reduce heart rate variability (HRV). β-blockers are drugs with well-known cardioprotective efficacy in several health conditions with an impact on physical performance. It is known that acute propranolol increases HRV in patients with chronic kidney disease (CKD). However, this group still has limited evidence regarding the effects of chronic β-blocker therapy (β-bt) on HRV and physical capacity. Objective: We aim to assess the HRV and exercise capacity in CKD patients in hemodialysis and the effect of chronic β-blocker therapy on their cardiac autonomic function. Methods: Cross-sectional study approved by the Ethical Committee in Human Research of the Health Service of Valdivia, Chile (Cod: 063). All participants signed informed consent. Patients with V-stage CKD under hemodialysis were included in the study. The control group included healthy subjects of the general population. Complementarily, a subgroup of CKD patients with β-blocker therapy (β-bt) for at least 6 months was gathered. Those with β-bt for less than 6 months were excluded. For HRV measurement iRR was recorded (Polar H7[®] HR sensor) in supine for 10 minutes. Then, data were downloaded from the manufacturer's website and exported to Kubios software version 3.3. The time and frequency domain HRV indexes were calculated utilizing 300 seconds of free artifact recordings. By the Incremental Shuttle Walking Test (ISWT) the exercise capacity was evaluated. Walking distance (WD) and the maximal VO₂ (VO₂peak) were considered as outcomes. Descriptive statistics was calculated using the mean and standard deviation (SD). The Kruskal-Wallis test (KWt) with the Dunn post hoc test was used to compare quantitative variables between groups. Additionally, the U-Mann-Whitney test (MWT) was used to compare quantitative variables between CKD patients with and without β-blocker therapy. The Chi-square test for trend was used to analyze proportions. A p-value <0.05 was considered statistically significant. Statistical analysis was performed using GraphPad Prism[®] software versión 5.00. Results: We enrolled 34 CKD patients (mean age 58±13 years) and 29 controls (mean age 57±16 years). Of CKD patients, 13 (38%) received β-bt (mean age 56±16 years). The most frequently prescribed drug was Carvedilol (n= 11). Other used β-blocker were Propanolol (n=1) and Atenolol (n=1). Patients with CKD presented a lower SDNN (-56.2% [KWt= 13.79; P= 0.001]), and RMSSD (-48.4% [KWt= 15.92; P= 0.0003]) compared to the control group. Only the RMSSD was higher in the β-bt group compared to those without β-bt (+162.5%; [MWT= 80.5; P= 0.0492]). In the frequency domain, the LF/HF ratio was lower in the β-bt group than those without β-blocker therapy (-61.2%; [MWT= 79.5; P= 0.0446]). No differences were observed between CKD and the control group. CKD exhibited decreased WD (-44.5 [KWt= 14.78; P= 0.0006]), VO₂peak (-22.7% [KWt= 11.28; P= 0.0036]), and HRpeak (-14.3 [KWt= 8.063; P= 0.0177]) as compared to the control group. No significant differences were observed in CKD with and without β-blocker therapy. Conclusion: CKD patients in hemodialysis exhibited a lower HRV and physical capacity than control. β-blocker therapy was shown to be effective in preventing autonomic dysfunction without effects on exercise capacity. Support: Grant for Installation in Academia, N^o: PAI177200011. Research and Development National Agency (ANID). Ministry of Science and Technology, Chile Protocol: Cod:063</p>

Title	Angiotensin-(2-7): A novel antihypertensive peptide of the renin-angiotensin-system
Authors	CAROLINA FONSECA DE BARROS, KAMYLLÉ FERRAZ, STHÉFANIE CHAVES DE ALMEIDA GONÇALVES, AMANDA DE SÁ MARTINS DE BESSA, URI FLEGLER VIEIRA-MACHADO, ISADORA ZHONG LIANG FERREIRA FENG, MATHEUS DE FREITAS ITABORAHY, ADELSON HÉRIC ALVES MONTEIRO, CLÓVIS NAKAIE, MARIA DE FATIMA LEITE, MARIA JOSE CAMPAGNOLE-SANTOS,- ROBSON AUGUSTO SOUZA DOS SANTOS
Affiliations	Department of Physiology and Biophysics, Federal University of Minas Gerais, Department of Biophysics, Federal University of São Paulo
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: It has been recently described that acetyl-angiotensin (2-7)-amide (Ac-Ang-(2-7)-NH₂) and angiotensin-(2-7) are potent ACE inhibitors. Objective: Investigate the effect of Ang-(2-7) in blood pressure (BP) and aortic rings of Wistar and SHR male rats. Furthermore, we evaluated whether this peptide stimulates receptors from the alternative renin-angiotensin system (RAS), including Mas, MrgD, and AT₂R using CHO-transfected cells Methods: Male Wistar and SHR, 10-16 weeks old (250-350g) were instrumented to perform cardiovascular measurements, and injection of the peptide or salina. In the baseline period, pulsatile and mean arterial pressure (MAP) and heart rate (HR) were continuously recorded for 1 hour. After that, the peptide Ang-(2-7) was injected at a doses of 30, 6, or 2.4 µg/kg, in a volume of 0,1 ml/100g in different animal and the cardiovascular parameters were recorded for 6h. Additionally, we evaluated the effect of Ang-(2-7) in isolated aortic rings from SHR and Wistar rats, pre-constricted with phenylephrine (10⁻⁷ mol. L⁻¹). The peptide effect was tested (10⁻¹² to 10⁻⁶ molar) in rings with or without pre-treatment the with the Mas/MrgD antagonist D-Pro⁷-Ang-(1-7)(10⁻⁶µmol.L⁻¹) or after endothelium removal. Finally, we used NO intracellular measurements via 4,5-diaminofluorescein-diacetate (DAF-FM diacetate) to test for the effect of Ang-(2-7) on Mas, MrgD, or AT₂ receptors using transfected-CHO cells. The human umbilical vein cell line (EA.hy926) was also used to test the effect of Ang-(2-7) in endothelial cells. Statistical analysis was performed using a one-way, two-way ANOVA or the t-test (p<0.05) were appropriated. Results: In SHR, 30 µg/kg of Ang-(2-7) induced a marked reduction in MAP reaching-40 mmHg (Baseline: 123±12mmHg, 6h vs 177± 0,50 mmHg before injection; n=3; p<0,0001). Similar result was obtained with 6µg/kg of Ang-(2-7) (Baseline MAP: 135±5 mmHg, 6h after injection vs 156±6 mmHg, before; n=3; p>0,05; and 2,4µg/kg of Ang-(2-7) (Baseline MAP: 140 ± 0,3 mmHg, 6h vs 160±2 mmHg, before, n=3; p<0,05). No significant MAP effect was observed after Ang-(2-7) injection in Wistar rats. Likewise, no significant HR effect was observed in SHR or Wistar rats after Ang-(2-7). Ang-(2-7) produced a vasorelaxing effect on aortic rings taken from SHR and Wistar rats (29,02 ±2,6% and 28,21±3%respectively) and was abolished after endothelium removal. The vasorelaxant effect of Ang-(2-7) was also abolished by pre-treatment with D-Pro⁷-Ang-(1-7).Accordingly, Ang-(2-7) induced NO production in EA.hy926 and MrgD-transfected CHO cells. In addition, Ang-(2-7) induced a slight effect on NO production in AT₂-transfected cells. Conclusion: In conclusion, we have identified a new biologically active component of the RAS with a potent antihypertensive effect in SHR. Our results suggest an important contribution of MrgD to the Ang-(2-7) cardiovascular effects. Support: CNPQ Protocol: CEUA: 113/2022.</p>

Title	ACETYL-ANGIOTENSIN (2-7)-AMIDE: A POTENT ANTI-HYPERTENSIVE PEPTIDE
Authors	URI FLEGLER VIEIRA-MACHADO, CAROLINA FONSECA DE BARROS, STHÉFANIE GONÇALVES, KAMYLLE FERRAZ, MARIA DE FATIMA LEITE, MATHEUS DE FREIRAS ITABORAHY, ISADORA ZHONG LIANG FERREIRA FENG, CLOVIS RYUICHI NAKAIE, ROGERIO SILVA, ADRIANA CARMONA, PATRÍCIA BERSANETTI, ADELSON HERIC ALVES MONTEIRO, ROBSON AUGUSTO SOUZA DOS SANTOS
Affiliations	Fisiologia e Biofísica, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The renin-angiotensin system (RAS) is a complex pathway involving several peptides with characterized biological functions. Angiotensin-(1-7), for example, is a peptide with well-established anti-hypertensive properties. A recent study identified Angiotensin-(2-7) as a smaller fragment generated from Angiotensin-(1-7). However, the biological effects of Angiotensin-(2-7) remain unknown. Objective: To investigate whether Ang (2-7) is capable of altering blood pressure. Methods: For these studies, we utilized a peptide (Ac-Ang (2-7)-NH₂) with added modifications for stability. Male spontaneously hypertensive rats (SHR) weighing 300g at 3 months old and control male Wistar rats weighing 400g at 3 months old were used. The animals were cannulated for arterial blood pressure (BP) and heart rate (HR) measurements, as well as intravenous drug injection. The protocols employed in this study received approval from the Ethics in Animal Use Committee (CEUA) of UFMG under protocol number 189/2023. BP and HR were continuously monitored for 1 hour in each animal to establish baseline levels. Subsequently, the animals received intravenous injections of Ac-Ang (2-7)-NH₂ at doses of 30 micrograms (SHR N=3; WISTAR N=3) and 6 micrograms (SHR N=3; WISTAR N=3). We recorded an additional six hours of BP and HR measurements following the injections. The statistical analysis was performed using a one-way ANOVA (analysis of variance) to compare means among baseline, 30 minutes after peptide injection, and 6 hours after peptide injection, and for comparisons between two groups, a t-test was employed ($p < 0.05$). To explore the potential role of classical RAS receptors in the effects of Ac-Ang-(2-7)-NH₂, we employed EA.hy926, an endothelial cell line, and CHO transfected cells expressing either Mas, MrgD, or AT₂ receptors. We then measured nitric oxide (NO) production in these cells following stimulation with the peptide compared to unstimulated controls. Results: Ac-Ang (2-7)-NH₂ significantly reduced blood pressure in SHR after intravenous administration at concentrations of 30µg/kg ($\Delta -40 \pm 5.7$ mmHg vs -0.3 ± 0.3 mmHg, $p < 0.01$) and 6µg/kg ($\Delta -40 \pm 5.7$ mmHg vs -0.3 ± 0.3 mmHg, $p < 0.01$). However, this peptide had no effect on the blood pressure of normotensive animals, regardless of the concentration administered. Additionally, no significant changes in heart rate were observed between the SHR group and the normotensive group. Using EA.hy926 cells, we found that Ac-Ang (2-7)-NH₂ is capable of activating the classical renin angiotensin receptors, inducing a 153% increase in NO production compared to unstimulated control ($p < 0.0001$). We further found that Ac-Ang (2-7)-NH₂ activated MrgD and AT₂ receptors in CHO cells transfected with either receptor, enhancing the NO production by 98% and 38%, respectively ($p < 0.0001$; $p < 0.001$). Notably, Ac-Ang (2-7)-NH₂ did not activate Mas transfected CHO cells ($p > 0.05$). Conclusion: Taken together, our findings suggest that Ac-Ang (2-7)-NH₂ acts as a potent antihypertensive peptide. This effect appears to be mediated through MrgD and AT₂ receptor activation. The present study supports further research exploring Ang-(2-7) as a potential therapeutic strategy for hypertension management. Support: CAPES, CNPq, Fapemig, INCT Nanobiofar. Protocol: 189/2023</p>





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 Hotel Glória Caxambu Resort & Convention

Title	CDNF induces mitochondrial protection against injuries by Ischemia/Reperfusion
Authors	EDUARDO VILLEROY CERQUEIRA, DAHIENNE OLIVEIRA MENDES, DEBORA FOGUEL, JOSE J L OLIVEIRA, LEONARDO MACIEL DE OLIVEIRA PINTO
Affiliations	Fisiologia, UFRJ, Universidade Federal do Rio de Janeiro
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ischemic preconditioning (IPC) is a noninvasive procedure against cardiac ischemia/reperfusion (I/R) injuries. The release of humoral cardioprotective factors during IPC activate membrane receptors and intracellular pathways protecting the cardiac cells. We have recently suggested CDNF(cerebral dopamine neurotrophic factor) as a new cardiomyokine in response to mitochondrial damage. Objective: Evaluate the effects of CDNF on mitochondrial function. Methods: The rat hearts were submitted to I/R on Langendorff apparatus. The mitochondria were isolated from hearts by differential centrifugation. The experimental groups, on isolated hearts, were: CTRL (control); I/R (ischemia/reperfusion); preCDNF; postCDNF; preCDNF+wort; postCDNF+wort. Mitochondrial function was assessed by ADP-stimulated respiration, swelling, transmembrane potential ($\Delta\Psi$); ROS, ATP production, oxygen consumption under simulated hypoxia/reoxygenation. Results: I/R induces a profound impact on mitochondria functioning. Interestingly, CDNF was able to prevent myocardial injury in the postischemic treatment in vivo model, as well as improved these mitochondrial functions such as the increase in respiration and ATP production, the reduction of ROS and swelling and prevention of depolarization of $\Delta\Psi$. Curiously, Wortmanin blocked the effects of the CDNF on mitochondrial function. Conclusion: Mitochondria is the target of the cardioprotection induced by CDNF. This protection is dependent on the PI3K/AKT pathway. Support: FAPERJ, CNPQ, CAPES Protocol: 154/21</p>



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Title	PROTEIN EXTRACT FROM CALOTROPIS PROCERA LATEX IMPROVES CATALASE ACTIVITY IN CARDIAC TISSUE OF ANIMALS TREATED WITH DOXORUBICIN.
Authors	IGOR DE CODES SOARES, DANIELLE CARVALHO FONSECA FALANGA DE OLIVEIRA, SAULO CHAVES MAGALHÃES, NILBERTO ROBSON FALCÃO DO NASCIMENTO, ARICLÉCIO CUNHA DE OLIVEIRA
Affiliations	Centro de Ciências da Saúde, Universidade Estadual do Ceará (UECE)
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Doxorubicin (Doxo) is a potent chemotherapeutic agent of the anthracycline class with antitumor activity against various types of cancer. Despite its significant antitumor activity, its selectivity is low, leading to adverse effects, with cardiotoxicity being one of the most notable. Although several studies have shown that this damage occurs due to redox imbalance, mitochondrial damage, and cell apoptosis through the activation of caspases by Doxo, these pathways are not yet fully elucidated. A 2019 study demonstrated adverse effects of Doxo on cardiac tissue, leading to cardiomyocyte apoptosis and consequent changes in the left ventricle, cardiomyopathy, and heart failure. They also mentioned the use of various drugs to minimize these effects, including plant extracts. Calotropis Procera (Cp) is abundant in Northeast Brazil. Evidence in the literature points to various biological effects of Cp, considering the different parts of the plant. Some highlighted pharmacological properties include pro- and anti-inflammatory and antioxidant activities. The protein extract from C. procera latex (CpLp) is composed of chitinases, proteases, lectins, enzymes related to antioxidant metabolism, and osmotin. The PII protein subfraction consists of proteases and osmotin. In previous studies conducted by our laboratory, both CpLp and the PII subfraction led to improved oxidative metabolism, with lower ROS production and increased mitochondrial density. For this reason, we believe in the cardioprotective potential of these extracts. Objective: To evaluate the acute treatment effect of Doxo and the cardioprotective effect of treatment with protein fractions of Calotropis Procera associated with the acute use of Doxo. Methods: Twenty-four Wistar rats were used, kept in an experimental vivarium under controlled temperature and lighting conditions, receiving a standard diet and water ad libitum. The animals were divided into 4 groups (n=6): Control (saline), Doxo (DX, 15 mg/kg + saline), Lp (DX, 15 mg/kg + Lp 5 mg/kg), PII (DX, 15 mg/kg + PII, 5 mg/kg). A single dose of DX or saline was administered on the first day of treatment in association with saline, Lp, or PII for 3 days. On the fourth day, the animals were euthanized, and cardiac tissue was collected for oxidative stress analysis. Results: When evaluating the Thiol groups, a significant decrease was observed in the Doxo group (0.4358 ± 0.05) compared to the Control group (0.762 ± 0.13). Regarding antioxidant enzymes, there was no difference in SOD, and Catalase significantly increased in the LP group (3.816 ± 0.9) compared to the Doxo (1.88 ± 0.3) and Control (1.38 ± 0.2) groups. Conclusion: We observed that treatment associated with the LP protein extract increases catalase activity in cardiac tissue. However, further data analysis and ongoing experiments are needed to better elucidate the cardioprotective effect. Support: CAPES Protocol: 05198059/2019</p>

Title	A estimulação da via Gi seletivamente nos cardiomiócitos atenua o remodelamento patológico induzido pela ovariectomia.
Authors	LUCAS ALEX MAGALHÃES DE SOUZA, MARCOS ELIEZECK, SÉRGIO RICARDO ALUOTTO SCALZO JÚNIOR, KIANY MIRANDA, TAMIREZ AMORIM, MATEUS CHAVES, RAPHAEL SZAWKA, SILVIA CAROLINA GUATIMOSIM FONSECA-
Affiliations	Fisiologia e Farmacologia, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Após a menopausa, há um aumento significativo na incidência de doenças cardiovasculares, atribuído principalmente à diminuição dos níveis de estrógeno, conhecido por ser um agente cardioprotetor. Além do estrógeno, a acetilcolina (ACh) também é reconhecida por seus efeitos benéficos no coração; no entanto em fêmeas ovariectomizadas nosso grupo demonstrou que a estimulação colinérgica sistêmica exacerba a disfunção cardíaca, tendo assim efeitos deletérios (TEIXEIRA et al., 2021). Objective: Neste estudo, investigamos o impacto da ativação seletiva da via colinérgica em cardiomiócitos (CMs) por meio do modelo DREADD Myh6-hM4Di e avaliar o impacto dessa ativação seletiva no remodelamento cardíaco induzido pela OVX. Methods: Para ativar seletivamente a via Gi nos CMs, cruzamos o modelo R26-LSL-Gi-hMD4i (DREADD-Gi) com Myh6-CRE para gerar camundongos Myh6-hM4Di, permitindo a ativação de Gi exclusivamente nos CMs por meio do tratamento com CNO. Subsequentemente, fêmeas de 8 semanas foram submetidas à remoção bilateral dos ovários e aguardaram-se 28 dias. Após este período, foram tratadas com CNO (0,5 mg/kg/dia) por 7 dias consecutivos, seguido da coleta dos corações no oitavo dia. Os grupos foram divididos em Sham, Sham+CNO, OVX e OVX+CNO. Results: Confirmamos o sucesso da cirurgia pela redução significativa do peso uterino nos grupos OVX (UW/TL mg/cm: Sham 19.8±1.7 vs Sham+CNO 21.7±2.8 vs OVX 8.1±0.8 vs OVX+CNO 7.4±0.7, n=9 camundongos por grupo). Em sequência observamos que a OVX induziu hipertrofia cardíaca, que não foi mitigada no grupo OVX+CNO (HW/TL mg/cm: Sham 74.3±1.8 vs Sham+CNO 77.2±2.2 vs OVX 87.4±0.8 vs OVX+CNO 86.0±1.1; n= 9 corações por grupo). Entretanto, quando avaliamos a largura dos CMs, observamos um aumento no grupo OVX em relação aos demais (µm: Sham 31.4±0.4 vs Sham+CNO 30.2±0.5 vs OVX 33.5±0.6 vs OVX+CNO 31.3±0.5; n=170 células por grupo). Realizamos então análises de morfometria cardíaca e constatamos aumento na área de secção transversal do ventrículo esquerdo e na espessura do septo interventricular nos animais OVX, a qual foi restaurada a níveis normais no grupo OVX+CNO (em mm²: Sham 10.1±0.3 vs Sham+CNO 10.5±0.3 vs OVX 13.4±0.4 vs OVX+CNO 11.3±0.3). Adicionalmente, encontramos maior deposição de colágeno nos grupos OVX pelo método de picosirius-red (deposição de colágeno em %: Sham 1.7±0.1 vs Sham+CNO 1.4±0,08 vs OVX 3.3±0.4 vs OVX+CNO 1.8±0.3). Por fim, avaliamos a funcionalidade dos CMs, e observamos significativa redução na contratilidade dos CMs oriundos de animais OVX, que foi restaurada no grupo OVX+CNO (área de encurtamento em µm²: Sham 575.2±30.3 vs Sham+CNO 564.8±31.4 vs OVX 393.4±20.4vs OVX+CNO 501.4±28.5, n=100 células por grupo.). Conclusion: Nossos achados indicam que a ativação seletiva da via Gi nos CMs atenua o remodelamento cardíaco induzido pela OVX. Isso sugere que o efeito cardiodeletério observado previamente pode ser causado por efeitos sistêmicos do modelo de hiperativação colinérgica e ter origem em outros tipos celulares. Support: CNPq/CAPES/FAPEMIG Protocol: CEUA: 102/2022</p>

Title	EFFECTS OF INSPIRATORY MUSCLE TRAINING ON CARDIAC AUTONOMIC CONTROL IN ASYMPTOMATIC POST-COVID-19 SUBJECTS
Authors	THAIS DILLINGER CONWAY SANTANNA, ANDRÉ LUIZ MUSMANNO BRANCO OLIVEIRA, ELISSA SILVA DE FARIAS MELLO, PEDRO PAULO DA SILVA SOARES, GABRIEL DIAS RODRIGUES
Affiliations	Department of Clinical Sciences and Community Health, UNIMI, Department of Physiology and Pharmacology, UFF
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introduction: The coronavirus disease (COVID-19) may induce a systemic inflammatory process affecting the cardiovascular and respiratory systems. The autonomic dysfunction seems to be a consequence, at least partially, of the “cytokine storm” that may extend to later phases of the infection. In addition, respiratory muscle weakness was reported in COVID-19 patients. An evidence-based strategy to improve respiratory muscle strength and autonomic function in several diseases is inspiratory muscle training (IMT). However, whether IMT may improve cardiac autonomic control in asymptomatic post-covid subjects remains unexplored. Objective: Objective: We aimed to investigate the effects of IMT on inspiratory muscle strength and cardiac autonomic modulation in post-covid subjects. Methods: Methods: Eight (3 women) asymptomatic post-covid subjects (33 ± 11 years; 1.71 ± 0.09 m; 69.50 ± 11.20 kg) were recruited to the laboratory measurements (EKG, and MIP test) before (t0) and after (t1) IMT. In the first week of IMT, the training started at 50% of maximal inspiratory pressure (MIP). Then, a 10% load increment was added every week, reaching 80% of MIP by the end of the 5th week of IMT. Heart rate variability was employed to evaluate cardiac autonomic modulation in the frequency domain, where low-frequency bands (LF: 0.04–0.15 Hz) indicate sympathetic predominance, while high-frequency (HF: 0.15–0.40 Hz) means respiratory and vagal modulation. All procedures were approved by the Federal Fluminense University ethics committee (CAAE:49273321.4.0000.5243). Results: Results: The preliminary data indicates that five weeks of IMT effectively increased MIP (t0: 86 ± 15 vs t1: 115 ± 28 cmH2O; p=0,01). Also, after IMT, cardiac vagally-related index (HF) was increased (t0: 21.7 ± 4.6 vs. t1: 28.9 ± 16.9 n.u; p=0.03). However, the sympathetic-related index (LF) was unchanged (t0: 58.8 ± 21.8 vs. t1: 58.9 ± 16.4 n.u; p=0,98). Conclusion: Conclusion: Although the preliminary nature of this study, IMT may improve MIP and cardiac vagal modulation in asymptomatic post-covid subjects. A larger sample size and the inclusion of a placebo group are required to validate our findings. Support: Funding: FAPERJ, CNPq and CAPES. Protocol: CAAE:49273321.4.0000.5243</p>



Title	COMPARAÇÃO DOS EFEITOS DA KETAMINA E XILAZINA SOBRE ANÁLISES ESPECTRAL E SIMBÓLICA DE RATOS SHR E WISTAR.
Authors	MARCELA DA SILVA NOLETO, PÂMELA DE SENA SANTOS, JOSÉ PEREIRA LOPES JÚNIOR, SAMUEL DE SOUSA ARAÚJO, JULIANA ALVES DA SILVA, ANA FLÁVIA MORAES DA SILVA, JOSÉ GUILHERME VERAS DE ASSUNÇÃO, REGINA GUIMARÃES SILVA, ARIELL ALVES DE OLIVEIRA, FRANCISCA VALDIRENE DE SOUSA NUNES, JOÃO PAULO JACOB SABINO
Affiliations	Departamento de Biofísica e Fisiologia, UFPI, Programa de pós graduação em Ciências Farmacêuticas, UFPI
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A escolha do anestésico mais adequado é crucial para qualquer pesquisa experimental, pois o mesmo pode afetar o sistema cardiovascular e autonômico, comprometendo a interpretação dos resultados do estudo. Nesse contexto, as análises espectral e simbólica vem recebendo grande visibilidade como ferramentas capazes de avaliar a modulação autonômica sobre o sistema cardiovascular. No entanto, não está claro quais desses dois métodos são mais suscetíveis aos efeitos colaterais observados pós anestesia.</p> <p>Objective: Avaliar as repercussões da mistura anestésica ketamina e xilazina (KX) sobre dois diferentes métodos de análise da variabilidade da frequência cardíaca (FC) e da pressão arterial (PA) em ratos Wistar e SHR, no pós-cirúrgico de 24 e 48 horas. Methods: Foram incluídos no estudo, ratos machos da linhagem Wistar (n=22) e SHR (n=28). Os animais foram anestesiados com ketamina (33,33 mg/kg) e xilazina (13,3 mg/kg), via i.m., e submetidos ao procedimento cirúrgico de canulação da artéria e veia femorais para registro da pressão arterial pulsátil e administração de fármacos, respectivamente. O software utilizado para o processamento do registro da pressão arterial pulsátil foi o LabChart 7.0, enquanto que para a análise da variabilidade da pressão arterial sistólica (VPAS) e da frequência cardíaca (VFC) utilizou-se o CardioSeries®.</p> <p>Results: Os resultados do presente estudo indicam que o anestésico KX parece alterar de forma significativa o sistema nervoso autônomo e cardiovascular, após 24 horas de sua administração, causando diminuição da pressão arterial média (PAM) em ambas as linhagens estudadas, quando comparado ao monitoramento de 48 horas. Esse resultado é corroborado pela análise da atividade simpática para leito vascular, onde também observamos um aumento da potência da banda de LF (nu) da PAS, após 48 horas da cirurgia de canulação. Além disso, após 48h foi observado, apenas nos ratos Wistar, uma atenuação dos índices RMSSD e HF (nu), ou seja, redução da atividade parassimpática sobre o IP, aliado ao aumento da atividade simpática devido a elevação dos parâmetros LF (nu) e LF/HF. Além disso, na nossa condição experimental, a análise espectral consistiu em um método mais confiável para avaliar a modulação simpática e parassimpática sobre a FC e PA, quando comparado a análise simbólica. Conclusion: Portanto, para diminuir os efeitos colaterais do anestésico KX, recomenda-se o monitoramento do sistema cardiovascular após 48 horas da cirurgia de cateterização dos vasos sanguíneos, de modo a diminuir a interferência do anestésico sobre o sistema cardiovascular e autonômico. Support: Universal CNPQ 409109/2018-5, bolsista de mestrado 88887.956000/2024-00 Protocol: 563/19</p>

Title	PAPEL DA CICLOXIGENASE NO AUMENTO DA VASOREATIVIDADE DE AORTAS DE RATOS COM SOBRECARGA CRONICA DE FERRO.
Authors	MÔNICA GOLDNER, LARISSA LORETE BARBOSA, MATEUS JOSÉ DEFANTE, BRENDA SANTOS LEITE, VINÍCIUS BERMOND MARQUES, ALESSANDRA SIMÃO PADILHA, LEONARDO DOS SANTOS
Affiliations	Graduação em Fisioterapia, Novo Milênio (Vila Velha/ES), Programa de Pós Graduação em Ciências Fisiológicas, UFES (Vitória/ES), Graduação em Biomedicina, Multifix (Cariacica/ES)
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A sobrecarga de ferro induz vasculopatia caracterizada por disfunção endotelial, estresse oxidativo e aterosclerose. Todavia, a via ácido araquidônico/ciclooxigenase, muito envolvida em processos inflamatórios, ainda não foi investigada na sobrecarga de ferro. Objective: Testar se a via da ciclooxigenase (COX) está envolvida na hiper-reatividade vascular induzida pela sobrecarga crônica de ferro em ratos. Methods: Ratos Wistar machos (~200g) foram distribuídos em dois grupos: controle (Ct, n=15) e ferro (Fe, n=14). O ferro foi administrado por injeções IP (100mg/Kg/dia, 5 vezes/semana), enquanto os controles receberam NaCl 0,9% no mesmo regime de tratamento. Após quatro semanas, foi coletado a aorta torácica para estudos de reatividade vascular in vitro. Os dados foram avaliados por teste t de Student ou ANOVA 2- vias, e considerado significativo $P < 0,05$. Results: Como esperado, o grupo Fe cursou com aumento da resposta contrátil à fenilefrina ($R_{max} \text{ Fe: } 118,6 \pm 3,4$ vs $\text{Ct: } 74,5 \pm 7,1$) e a análise de segmentos após remoção mecânica do endotélio confirmou prejuízo na modulação endotelial ($dASC \text{ Ct: } 397 \pm 42$ vs $\text{Fe: } 272 \pm 33\%$). A incubação com inibidor inespecífico da COX indometacina ($10 \mu\text{M}$) reduziu parcialmente a hiper-reatividade do grupo Fe ($dASC: 154 \pm 35\%$) sem alteração no grupo Ct, indicando papel desta via. Ademais, enquanto o uso do antagonista de receptor para tromboxano A2 (SQ-29548, $1 \mu\text{M}$) não modificou a resposta, assim com a indometacina, o antagonista de receptor para PGE2 (SC-19220, $10 \mu\text{M}$) foi capaz de atenuar o aumento de reatividade do grupo Fe ($R_{max} \text{ Fe: } 110,5 \pm 3,8$ vs $\text{Fe+SC: } 80,3 \pm 5,7$). Conclusion: Nossos resultados confirmam que a sobrecarga de ferro causa prejuízo na modulação endotelial da aorta, e sugerem que este efeito seja, ao menos em parte, dependente da PGE2 derivada da COX. Support: CNPq, CAPES e FAPES Protocol: CEUA-UFES no. 18/2023</p>

Title	Efeito do Ferulato de Etila sobre parâmetros hemodinâmicos em fêmeas SHR e Wistar
Authors	FRANCISCA VALDIRENE DE SOUSA NUNES, ARIELL ALVES DE OLIVEIRA, CARLOS EDUARDO RODRIGUES DOURADO, PAMELA DE SENA SANTOS, JOSÉ PEREIRA LOPES JUNIOR, SAMUEL DE SOUSA ARAÚJO, JULIANA ALVES DA SILVA, ANA FLAVIA MORAES DA SILVA, JOSÉ GUILHERME VERAS DE ASSUNÇÃO, REGINA GUIMARÃES SILVA, JOÃO PAULO JACOB SABINO
Affiliations	Departamento de Biofísica/fisiologia, UFPI, Programa de Pós Graduação em Ciências Farmacêuticas, UFPI
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Os mecanismos de regulação da pressão arterial no sexo feminino apresenta algumas diferenças, as quais parecem ser, parcialmente, dependentes do hormônio reprodutivo estradiol. Assim, antes da menopausa, as mulheres apresentam um risco significativamente menor para o desenvolvimento da hipertensão arterial sistêmica (HAS) em comparação com homens de idade e estado de saúde semelhantes. Entre os compostos com possível ação anti-hipertensiva, está o ferulato de etila (FE), que é um produto natural pertencente à classe dos fenilpropanóides com atividade anti-inflamatória, antioxidante e neuroprotetora descrita na literatura, e apesar de haver relatos sugerindo ação cardioprotetora, não há evidências sobre o efeito do FE na modulação cardiovascular em ratas espontaneamente hipertensas (SHR).</p> <p>Objective: Avaliar o efeito agudo do Ferulato de Etila sobre parâmetros hemodinâmicos de ratas SHR e Wistar. Methods: As ratas (12 semanas de vida) foram submetidas a avaliação citológica vaginal para determinar a fase do ciclo estral. Em seguida, os animais foram anestesiados com cetamina (75 mg/kg) e xilazina (10mg/kg) e submetidos ao procedimento de canulação da artéria e veia femoral. Quarenta e oito horas após a canulação, os animais foram conectados a um transdutor de pressão acoplado a um amplificador para registro da pressão arterial pulsátil (PAP) e frequência cardíaca (FC). Após o período de adaptação (60 min) e o registro basal (30 min), iniciou-se a administração de Nitroprussiato de sódio (NPS, 8 µg/kg, i.v.) para confirmar a canulação venosa. Após 30 minutos, os animais foram tratados com salina (0,1 mL/100 g; i.v.) ou FE (7,5; 15; 30 mg/kg; i.v.) para avaliar a resposta sobre pressão arterial média (PAM) e frequência cardíaca (FC). Ao final do experimento, foram realizadas novamente citologias vaginais para determinar a fase do ciclo estral. Results: Com relação as ratas Wistar, os resultados mostraram que o FE na dose de 7,5 mg/kg não promoveu alteração na PAM ($\Delta = -2 \pm 1$ vs -2 ± 4, mmHg) e FC ($\Delta = -17 \pm 17$ vs -13 ± 24, mmHg) quando comparado ao grupo Salina e o basal. Já na dose de 15 mg/kg foi observado que o FE promoveu uma diminuição da PAM ($\Delta = -23 \pm 4$ vs -1 ± 2, mmHg) e FC ($\Delta = -221 \pm 45$ vs -2 ± 20, bpm) em comparação ao grupos Salina e 7,5 mg/kg. Do mesmo modo, a dose de 30 mg/kg também foi capaz de promover uma redução na PAM ($\Delta = -28 \pm 2$ vs $\Delta = -2 \pm 4$, mmHg) e FC ($\Delta = -205 \pm 10$ vs $\Delta = -2 \pm 20$, bpm) em comparação aos dois grupos supracitados. Com relação as ratas SHR, o FE na dose de 7,5 mg/kg também não promoveu alteração na PAM ($\Delta = -3 \pm 5$ vs $\Delta = 3 \pm 4$, mmHg) e FC ($\Delta = -9 \pm 8$ vs $\Delta = -22 \pm 16$, bpm), quando comparado ao grupo controle. Já na dose de 15 mg/kg observou-se uma diminuição tanto na PAM ($\Delta = -22 \pm 9$ vs $\Delta = -2 \pm 3$, mmHg) quanto na FC ($\Delta = -57 \pm 20$ vs $\Delta = -31 \pm 17$, bpm) em comparação aos grupos Salina e 7,5 mg/kg. Da mesma forma, a dose de 30 mg/kg foi capaz de promover uma redução significativa da PAM ($\Delta = -31 \pm 10$ vs $\Delta = -3 \pm 2$, mmHg) e da FC ($\Delta = -51 \pm 26$ vs $\Delta = -31 \pm 17$, bpm) quando comparado ao grupo controle e 7,5 mg.kg. Conclusion: Podemos concluir que o FE foi capaz de promover uma diminuição da PAM e FC em fêmeas Wistar e SHR. Assim, o FE surge como um possível candidato a fármaco anti-hipertensivo. Entretanto, ainda são necessários estudos posteriores que elucidem os possíveis mecanismos de ação pelos quais essa substância promove seus efeitos sobre o sistema cardiovascular. Support: Bolsa de Mestrado CAPES: 88887956008/2024-00 Protocol: 804/2023</p>

Title	Effects of Capsinoids on Adiposity and Cardiac Oxidative Stress in Obese Rats
Authors	KÉSSIA CRISTINA CARVALHO SANTOS, FABIANE MERIGUETI NUNES, LUCAS FURTADO DOMINGOS, LUISA MARTINS SIMMER, DANIEL ANDRES GOMEZ SAIZ, EVELLYN RODRIGUES CORDEIRO, CAMILA RENATA CORRÊA, ANA PAULA LIMA-LEOPOLDO, ANDRÉ SOARES LEOPOLDO
Affiliations	Programa de Pós Graduação em Nutrição e Saúde, Universidade Federal do Espírito Santo, Programa de Pós Graduação em Ciências Fisiológicas, Universidade Federal do Espírito Santo, Unidade de Pesquisa Experimental, Universidade Estadual Paulista "Júlio de Mesquita Filho", Programa de Pós Graduação em Educação Física, Universidade Federal do Espírito Santo
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The excessive body fat accumulation induces the formation of pro-oxidant body environments. In the heart, oxidative stress is related to cardiovascular complications. In view of this, capsinoids (CAP), emerge as potential antioxidant agents capable of reducing oxidative damage and the consequent complications triggered by obesity. Objective: the purpose was to investigate the administration effects of CAP on adiposity and biomarkers of cardiac oxidative stress in obese rats. Objective: To investigate the administration effects of CAP on adiposity and biomarkers of cardiac oxidative stress in obese rats. Methods: 30-day-old male Wistar rats were subjected to the standard (n=17; 148±18 g of body mass) or high-fat diet (n=27; 147±17 g of body mass) for 20 weeks. Subsequently, the animals were distributed into control group (C; n=11), obese (Ob; n=13) and obese groups treated with CAP (ObCap; n=14). During treatment (8 weeks), ObCap animals received 10 mg/kg CAP diluted in water (1 mL/kg). The other groups received the vehicle during the same period. The evolution of body mass was monitored, as well as body adiposity, and, in the left ventricle (C: n=5; Ob: n=6; ObCap: n=7), the total antioxidant capacity (FRAP), lipid peroxidation (MDA), advanced oxidation of proteins products (AOPP) and protein carbonylation (CBO) was measured. For statistical analysis, the Student t test and two-way ANOVA with Bonferroni post hoc were used. Results: It was observed that, after the treatment, the final body weight in the Ob (583±51 g) was similar to C (543±43 g) and ObCap (623±69 g). Furthermore, it was observed that the treatment was not effective in reducing epididymal (Ob: 11.6±1.8 g; ObCap: 13.4±2.5 g) and retroperitoneal pads (Ob: 20.6±4.8 g; ObCap: 27.7±9.7 g), and total body fat (Ob: 43.9±7.9 g; ObCap: 54.2±14.0 g) in relation to the Ob group. However, no difference was found between Ob and ObCap for the adiposity index (Ob: 7.52±1.11 %; 8.67±1.83 %). Finally, in relation to biomarkers of cardiac oxidative stress, no difference was observed for CBO, AOPP and FRAP between the Ob and ObCap groups. However, after treatment it was found that there was an increase in lipid peroxidation (C: 21.76±5.88 nmol/mg of protein; Ob: 21.08±9.53 nmol/mg of protein; ObCap: 32.90±7.80 nmol/mg of protein) in the ObCap group compared to Ob. Conclusion: The CAP treatment was unable to contain or reduce excessive fat accumulation. Furthermore, there were no significant results capable of indicating benefits of this treatment for the prevention of cardiac oxidative stress and its damage. Support: Espírito Santo Research and Innovation Support Foundation – FAPES Protocol: N.A.</p>



14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	BK CHANNEL ACTIVATION INDUCES MITOCHONDRIAL PROTECTION AGAINST HYPOXIA/REOXYGENATION INJURY
Authors	DOMENIQUE KALI MARCONI PEREIRA RABOeira, ITANNA ISIS DE SOUZA, THAIS BARENCO, JOSÉ HAMILTON MATHEUS NASCIMENTO, CRISTIANO PONTES, LEONARDO MACIEL
Affiliations	Laboratório de Eletrofisiologia Cardíaca Antonio Paes de Carvalho, UFRJ
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ischemic heart disease remains a significant cause of mortality globally. When a myocardial infarction occurs, the reduction or interruption of blood flow leads to an imbalance between the supply and demand of oxygen in the affected area. Restoring blood flow promptly through reperfusion is crucial for the survival of the heart muscle. However, it is worth noting that reperfusion itself can cause injury to the myocardium. In recent research, the cardioprotective potential of an agonist of the large-conductance calcium-activated potassium channel (BK channel) has been explored. The BK channel is involved in regulating vascular tone, cardiac contractility, and ischemic preconditioning, which are all important factors in myocardial protection. Objective: The present study aims to investigate the mechanisms of cardioprotection conferred by BK channel activation, focusing on the effects on the maintenance of mitochondrial function. Methods: For this study, a total of 14 animals were involved, protocol CEUA number 119/21, 4-week-old male C57BL/6 mice, with 25-30 grams, were euthanized by cervical dislocation. Hearts were quickly removed and mitochondria were isolated by a differential centrifugation method. Immediately after isolation, mitochondrial function was evaluated by measurement of O₂ consumption in different respiratory states, ATP production, ROS production, and transmembrane potential. The mitochondria isolated from fresh hearts were incubated directly with BK channel agonist and subjected to hypoxia/reoxygenation in vitro. Results: Incubation of BK channel agonist in mitochondria subjected to hypoxia and reoxygenation prevented reductions in mitochondrial respiration (102±8), ATP production (211±4), and reduced mitochondrial ROS production (278±11) compared to the group subjected to hypoxia/reoxygenation (43±3; 167±41; 341±4; p<0.001, respectively). Conclusion: The activation of the BK channel could protect mitochondrial function against hypoxia/reoxygenation injuries, putatively through manipulation of the mitochondrial membrane potential. Support: FAPERJ, CNPQ, CAPES Protocol: Protocol CEUA number 119/21</p>



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Title	Analysis of sympathetic nerve activity complexity in spontaneous hypertension rats (SHR)
Authors	RODRIGO LANTYER MARQUES DANTAS, STEPHANIE FURTADO GEROLIN, GUSTAVO DOS REIS MARTINS, JOÃO RICARDO MARTINEZ BALDIN, RUY RIBEIRO CAMPOS JUNIOR, JEAN FABER, CÁSSIA DE TOLEDO BERGAMASCHI
Affiliations	Neurologia e Neurociências, UNIFESP, Fisiologia Cardiovascular, UNIFESP
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The Sympathetic Nervous System (SNS) plays a crucial role in regulating cardiovascular function and is directly linked to blood pressure control and hypertension (HTN). However, the mechanisms underlying the initiation and maintenance of elevated sympathetic activity in HTN are not fully understood. Evidence suggests that the frequency of bursts related to the electrophysiological activity of vasomotor sympathetic nerves, is the main modulator factor during the evolution of HTN. Objective: To unveil the mechanisms subjacent to this modulation, we quantify the recorded electrophysiological activity to characterize prevalent patterns of sympathetic vasomotor nerve activity (SNA) in spontaneously hypertensive (SHR) in different ages. We applied Multiscale Entropy (MSE) technique to estimate the complexity of the SNA dynamics. Assuming the complexity of a time series is related to the increase of its entropy – which is linked to its amplitude variation over different time scales – by hypothesis, as the physiological system becomes less complex during HTN evolution, their informational content degrades, increasing its entropy. Methods: We conducted experiments on 3 Wistar control (CTRL) rats (12 weeks, 350-400g), 5 adult spontaneously hypertensive rats (SHRs) (10 to 15 weeks, 210-320g), and 5 young SHRs (5 to 7 weeks, 90-150g). Under urethane anesthesia, we recorded direct measurements of blood pressure, heart rate, and renal and splenic sympathetic nerve activity (SNAr and SNAs). The electrophysiological signals were captured using Neurolog equipment (Digitimer UK, 20K, bandwidth 100-100 Hz, acquisition rate 4 kHz). Signal processing included the Hilbert Transform for envelope calculation and Welch's method for power spectral density (PSD) analysis to identify the predominant frequency bands modulating the bursts. We also assessed signal coherence to differentiate modulation patterns between groups. Signal complexity was analyzed using the MSE method, which quantifies entropy over various time scales through coarse-graining. Statistical analysis included Mann-Whitney and Kruskal-Wallis tests (significance level, $\alpha=5\%$). Data processing and analysis were conducted using Matlab® (2019). Results: Spectral analysis revealed differences in burst modulation bands between groups. In adult SHRs, the predominant band was 6-7 Hz, while in young rats, it was 7-8 Hz. This difference is linked to the higher heart rate in young rats compared to adults, corroborating the association between heart rate values and modulation of sympathetic bursts. The median complexity indices for SNAr and SNAs in the adult and young group were respectively: 17.11 ± 0.52 and 18.9 ± 0.31 ($p=0.0286$), and 16.42 ± 0.15 and 26.29 ± 0.2 ($p=0.0001$), showing the loss of complexity. Comparing the complexity of the SHR adult with the Wistar CTRL, which had more comparable ages, we obtained the following results, respectively – SNAr: 17.11 ± 0.52 and 21.13 ± 0.92 ($p=0.0042$); SNAs: 16.42 ± 0.15 and 32 ± 0.13 ($p=0.00001$), indicating that HTN in adult rats appears to reduce the ability to respond well to the system. Analysis of complexity in the young group is a future step in our analyses. Conclusion: Reduced complexity in SNAr and SNAs in SHR adult compared to the control suggests that physiological systems become less adaptable for homeostatic balance, corroborating the hypothesis that the adaptability of physiological systems decreases possibly with HTN. Further comparative analysis with age-matched controls is essential to confirm these findings. Support: CAPES (financial code 001), FAPESP (19/25295-0), and CNPq Protocol: CEUA-Unifesp No. 835908322</p>



Title	EFEITO DA ADMINISTRAÇÃO DE CARBENDAZIM NAS PROPRIEDADES ELTROCONTRÁTEIS EM RATOS WISTAR MACHOS
Authors	IVAN LOBO DE SOUSA MARQUES, MAYCON DOUGLAS MARQUES, DOUGLAS LAMOUNIER DE ALMEIDA, JADER DOS SANTOS CRUZ, ARTUR SANTOS MIRANDA
Affiliations	Fisiologia e Farmacologia, UFMG, Bioquímica e Imunologia, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Carbendazim (CAR) é um fungicida amplamente utilizado na agricultura, porém ainda há lacunas sobre sua toxicidade cardiovascular. Apesar da sua utilização ser proibida pela Agência de Vigilância Sanitária (ANVISA) em 2022, a comercialização e uso de produtos técnicos e formulados vem ocorrendo de forma gradual e contínua no país. Desse modo, busca-se observar efeitos a exposição crônica desse pesticida pela dose diária máxima permitida. Objective: Avaliar possíveis alterações eletrocontráteis e estruturais do coração e cardiomiócitos isolados de ratos wistar após a administração crônica de CAR. Methods: Ratos Wistar machos (~250 g), foram submetidos à gavagem com óleo de milho contendo (n=7) ou não (n=3) o pesticida (0,02 mg/kg), durante vinte e oito dias. Os corações desses animais foram retirados para análises histológicas ou digestão enzimática para isolamento de cardiomiócitos. As contrações celulares foram medidas por celulares detecção de bordas (Ionoptix, EUA). As células foram estimuladas nas frequências de 1 e 3 Hz por 5 ms. Comparação entre os dois grupos experimentais Controle e CAR foi realizada utilizando o teste t de Student não pareado (paramétrico) ou o teste de Mann-Whitney (não paramétrico) foram feitas usando o software GraphPad Prism 8.0. Results: Análises preliminares de ECG, como complexo QRS, onda T e intervalo Qt apresentaram não ter relação causal entre o tratamento e controle na duração e dose estabelecida. No que tange a contratilidade, não houve alterações sobre a amplitude de contração em 1Hz ($p>0,8103$) e 3 Hz ($p>0,9221$); para o tempo de 50% do pico de contração em 1 Hz ($p>0,0676$) e 3 Hz ($p>0,5643$) e o tempo para 50% do relaxamento em 1 Hz ($p>0,7845$) e 3 Hz ($p>0,8560$) em dos cardiomiócitos isolados. Conclusion: Análises iniciais indicam não haver relação causal entre o tratamento com Carbendazim, na duração e dose administrada, com alterações eletrocontráteis do coração e células isoladas. Support: FAPEMIG, CAPES Protocol: 289/2022</p>

Title	CARDIOVASCULAR EFFECTS INDUCED BY CENTRAL INFUSION OF ALAMANDINE-(1-5) IN HYPERTENSIVE ANIMALS
Authors	ADELSON HÉRIC ALVES MONTEIRO, KAMYLLE SILVA FERRAZ, CAROLINA FONSECA DE BARROS, MARIA JOSÉ CAMPAGNOLE DOS SANTOS, ANDREA SIQUEIRA HAIBARA, ROBSON AUGUSTO SOUZA DOS SANTOS
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The renin-angiotensin system (RAS) is a cascade system involving enzyme-substrate interactions that result in the production of several biologically active peptides. These peptides play an important role in controlling blood pressure, the homeostasis of body fluids and electrolytes, and cellular function. Alamandine-(1-5) is synthesized through the hydrolysis of alamandine [Ala¹-Ang-(1-7)], an heptapeptide of the RAS counterregulatory axis. It was recently demonstrated that this peptide is present in human and mice circulation, and its biological actions have begun to be investigated. Objective: To investigate the cardiovascular effects of intracerebroventricular infusion (ICV) of Ala-(1-5) in normotensive and hypertensive animals. Methods: In this study, rats (Wistar and SHR, 12-14 weeks old) were underwent stereotaxic implantation of a metallic cannula into the lateral ventricle and cannulation of the femoral artery and vein. The evaluation of cardiovascular parameters [mean arterial pressure (MAP), heart rate (HR), baroreflex sensitivity, and cardiac autonomic tone] was performed in conscious freely moving animals before and after intracerebroventricular infusion (ICV, 4 µg/12 µL/h, for 90 min) of alamandine-(1-5) or saline. Results: ICV infusion of alamandine-(1-5) did not produce a significant change in baseline values of MAP or HR in normotensive or hypertensive rats. As expected, SHR animals presented a marked attenuation of the baroreflex control of HR compared with Wistar rats. Alamandine-(1-5)-infused SHR animals showed significant improvement in the sensitivity of the baroreflex bradycardia compared with the same animals before alamandine-(1-5) infusion. In contrast in Wistar rats, alamandine-(1-5) ICV infusion did not change the baroreflex control. Interestingly, central infusion of alamandine-(1-5) did not produce significant changes in cardiac autonomic balance both in normotensive or hypertensive rats. Conclusion: Our data demonstrate for the first time that ICV infusion of alamandine-(1-5) improves baroreflex sensitivity in hypertensive animals and reinforces the importance of the brain RAS, highlighting the pentapeptide alamandine-(1-5) as a biologically active peptide of the RAS. Support: INCT Nanobiofar and CNPq. Protocol: 113/2022</p>

Title	Incubação com agonista seletivo do GPER atenua a vasoconstrição em artérias mesentéricas de resistência de fêmeas SHR
Authors	DANIEL MACEDO DE ASSIS, NATHALIE TRISTÃO BANHOS DELGADO, WENDREA KAYLAINE BURGARELLI DANIELLI MUSINI, WENDER DO NASCIMENTO ROUVER, ROGER LYRIO DOS SANTOS
Affiliations	Ciências Fisiológicas, UFES
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: É descrito que a ativação do receptor de estrogênio acoplado à proteína G (GPER) por seu agonista seletivo (G-1) induz relaxamento de artérias mesentéricas de resistência de animais normotensos e hipertensos. Entretanto, não são conhecidos os efeitos de uma pré-incubação com esse agonista nessas artérias, principalmente na hipertensão. Em virtude disso, o presente estudo avaliou a influência da pré-incubação com o G-1 no relaxamento e contração de artérias mesentéricas de resistência de fêmeas SHR.</p> <p>Objective: Avaliar o efeito exercido pela pré-incubação com o agonista do GPER na reatividade de artérias mesentéricas de resistência de fêmeas SHR. Methods: Curvas concentração-resposta à acetilcolina (ACh) (0,1 nM – 10 µM) e à noradrenalina (NOR) (10 nM – 30 µM) foram realizadas em artérias mesentéricas de fêmeas SHR, com 10-12 semanas de idade e uma média de 180 gramas. As respostas foram avaliadas antes e após a incubação por 30 minutos com 1 e 10 µM de G-1. As curvas concentração-resposta à NOR (10 nM – 30 µM) também foram avaliadas antes e após incubação com 10 µM de G-1 na presença de: inibidor não seletivo da enzima óxido nítrico sintase (L-NAME, 300 µM), inibidor não seletivo da ciclooxigenase (Indometacina, 10 µM), inibição conjugada de L-NAME com Indometacina, degradador de H₂O₂ (Catalase, 1000 und./mL) e varredor de ânion superóxido (O₂-•) (Tiron, 1 mM). A análise estatística foi realizada por meio da análise de variância de duas vias (two-way ANOVA) seguida pelo teste pós hoc de Tukey (P < 0,05).</p> <p>Results: As incubações com G-1 não alteraram a resposta máxima da curva de ACh. Apenas a concentração de 10 µM de G-1 atenuou a resposta máxima de contração em comparação à curva controle (Controle: 3,118 ± 0,14 vs. G-1: 2,443 ± 0,08 mN/mm), sendo que a remoção endotelial também diminuiu essa resposta (1,663 ± 0,2699 mN/mm). A presença do L-NAME potencializou a resposta máxima contrátil (3,771 ± 0,25) e a incubação com G-1 preveniu essa potencialização (2,867 ± 0,22 mN/mm). A incubação com Indometacina + G-1 (2,580 ± 0,25 mN/mm), assim como a inibição conjugada com L-NAME + Indometacina + G-1 (3,300 ± 0,26 mN/mm) não foram capazes de alterar a resposta máxima. No entanto, a incubação com catalase + G-1 potencializou a resposta contrátil (3,700 ± 0,1 mN/mm), assim como a presença de Tiron + G-1 (3,600 ± 0,3 mN/mm), indicando que o efeito anticontrátil do G-1 pode estar relacionado à produção de H₂O₂ via dismutação do O₂-• no endotélio. Conclusion: A ativação do GPER reduz a contração induzida pela NOR em artérias mesentéricas de resistência de fêmeas SHR, efeito dependente do endotélio. O GPER não promove diferenças significativas no relaxamento induzido pela ACh. Estes resultados geram evidências funcionais que contribuem para um melhor entendimento sobre a ativação do GPER em um contexto de hipertensão.</p> <p>Support: Fundação de Amparo à Pesquisa e Inovação do Espírito Santo (FAPES) – EDITAL FAPES Nº 15/2022, Processo Nº 2022WKM7. Fundação de Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Processo Nº 88887.966851/2024-00. Protocol: N.A.</p>

Title	PRECLINICAL EVALUATION OF THE ANTI-HYPERTENSIVE EFFECTS OF ERYTHOXYLUM SUBEROSUM EXTRACT
Authors	LETÍCIA HENRIQUE DANTAS GOMES DE LIMA, STEFANNE MADALENA MARQUES, GIULIANA MUNIZ VILA VERDE, JAMES O FAJEMIROYE, GUSTAVO RODRIGUES PEDRINO
Affiliations	Ciências Fisiológicas, UFG, Bioprodutos, UEG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The investigation of the bioactivity of plant-derived products is crucial for the development of selective substances and the improvement of public health, especially in regions with diverse flora. This study focused on the cardiovascular analysis of <i>Erythroxylum campestre</i> A. St. Hil., a species within the Erythroxylaceae family that has been relatively understudied. Objective: To evaluate the antihypertensive effects of the methanolic fraction of <i>E. suberosum</i> extract on cardiovascular responses such as heart rate (HR), mean arterial pressure (MAP), aortic blood flow (ABF), renal blood flow (RBF), renal vascular resistance (RVR), and aortic vascular resistance (AVR) in normotensive Wistar rats and spontaneously hypertensive rats (SHR). Methods: Male rats (weighing 250-350g) were anesthetized with urethane (1.2 g/kg; after anesthesia induction with 2% isoflurane in 100% O₂) and subjected to surgical procedures to record HR, MAP, ABF, and RBF. They received four randomized intravenous doses of the extract (1, 2, 3, and 6 mg/kg). CEUA 064/17 Results: None of the doses altered the cardiovascular parameters in normotensive animals. In hypertensive animals, only the lowest dose did not affect MAP. The 6 mg/kg dose produced significant differences compared to the normotensive rats (Δ WISTAR: -6.8 ± 1.4 vs. Δ SHR: $-14.5 \pm 2.7\%$ from baseline; $p < 0.05$). In HR, only the highest dose of the extract induced bradycardia compared to the vehicle (Δ vehicle: -0.2 ± 1.0 vs. $-5.2 \pm 4.6\%$ from baseline; $p < 0.05$). No significant differences were observed in ABF or RBF; however, RVR was reduced in hypertensive rats compared to normotensive rats (Δ WISTAR: -1.5 ± 2.3 and $-7.3 \pm 1.5\%$ from baseline vs. Δ SHR: -12.3 ± 3.6 and $-18.8 \pm 2.2\%$ from baseline after 3 mg/kg and 6 mg/kg doses respectively; $p < 0.05$). For AVR, only the highest dose of the extract produced a significant reduction compared to normotensive rats (Δ WISTAR: $-7.3 \pm 2.1\%$ from baseline vs. Δ SHR: $-14.1 \pm 2\%$ from baseline after 6 mg/kg dose; $p < 0.05$). Conclusion: Collectively, these data indicate that the methanolic fraction of <i>E. suberosum</i> extract can reduce MAP in spontaneously hypertensive rats, and this response is attributed to its vasorelaxant action on renal and aortic vascular beds. Support: CNPq and FAPEG Protocol: CEUA 064/17</p>

Title	Influência do dimorfismo sexual nas alterações cardiovasculares em animais sobreviventes à sepse.
Authors	JAUQUELINE APARECIDA DE SOUZA, NAIARA RIBEIRO, NATÁLIA DE ARAÚJO, KARLA DE OLIVEIRA, IVAN LOBO MARQUES, RAQUEL FERREIRA, MARINA ANDRADE, ARTUR SANTOS, JADER DOS SANTOS CRUZ, STÉFANY CAU, DANIELLA BONAVENTURA
Affiliations	Farmacologia, UFMG, Fisiologia, UFMG, Clínica e cirurgia veterinárias, UFMG, Bioquímica e Imunologia, UFMG
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Sepse é uma condição de disfunção orgânica causada por uma resposta desregulada do hospedeiro à infecção. Pacientes que sobrevivem à sepse aguda tem maiores riscos de desenvolver doenças cardiovasculares e essas respostas podem ser diferentes entre os sexos. Objective: Investigar os impactos cardiovasculares em camundongos sobreviventes à sepse, bem como a influência do dimorfismo sexual.</p> <p>Methods: Foram utilizados camundongos Balb/C com 8 semanas de idade (Biotério Central da UFMG) (20-25g) e estes foram divididos em 4 grupos: NAIVE e Sobreviventes à sepse (machos e fêmeas). CLP foi o modelo de sepse usado. 15 dias após a indução da sepse foram realizados experimentos em cardiomiócitos isolados, análise de função cardíaca (Langendorff) e estudos de reatividade vascular em aortas com e sem PVAT. Na reatividade avaliou-se a contração vascular para fenilefrina (PHE) na ausência ou presença de inibidores das enzimas óxido nítrico sintase (NOS-L-NAME) e ciclooxigenases (COX-Ibuprofeno) e em presença de Catalase. Avaliou-se também o relaxamento vascular para acetilcolina (ACh). Results: Nos cardiomiócitos isolados a sepse promoveu, em machos e fêmeas, o aumento da fração de encurtamento (M-N $6,79 \pm 0,50$ [n=94 células]; M-CLP $8,72 \pm 0,51$ [n=65 células]; F-N $5,67 \pm 0,36$ [n=111 células]; F-CLP $7,33 \pm 0,50$ [n=84 células], 1Hz); diminuição do tempo para iniciar o relaxamento (M-N $152,9 \pm 5,4$; M-CLP $139,6 \pm 5,3$; F-N $162,9 \pm 6,4$; F-CLP $143,2 \pm 4,7$, 3Hz) e o tempo até 50% da linha de base (M-N $157,9 \pm 4,8$; M-CLP $144,2 \pm 4,6$; F-N $166,6 \pm 5,8$; F-CLP $149,2 \pm 4,2$). A sepse também promoveu, somente em machos, alteração na razão da derivada da pressão pela derivada do tempo (dP/dT) máxima (dP/dT máx) e mínima (dP/dT min) basal (dP/dT máx basal: [M-N $741,1 \pm 169,3$; M-CLP $1625,0 \pm 206,2$ [n=05], dP/dT min basal: M-N $379,1 \pm 63,8$; M-CLP $845,0 \pm 133,8$]) e após estímulo com isoprenalina (dP/dT máx: M-N $1401,4 \pm 160,0$; M-CLP $3184,4 \pm 457,6$, dP/dT min: M-N $835,5 \pm 109,7$; M-CLP $1754,8 \pm 255,3$), aumentou a PDVE após curva de isoprenalina (PDVE: M-N $38,17 \pm 2,51$; M-CLP $51,88 \pm 10,86$) e diminuiu o tempo até 90% da linha de base (M-N $208,2 \pm 6,0$; M-CLP $188,4 \pm 5,5$). Em fêmeas, a sepse reduziu o tempo até o pico máximo de contração (F-N $96,01 \pm 2,5$; F-CLP $86,5 \pm 2,3$) e reduziu o tempo até 10% da linha de base (F-N $128,8 \pm 4,2$; F-CLP $114,1 \pm 3,2$). Nas respostas vasculares a sepse não promoveu nenhuma alteração na resposta vasodilatadora à ACh, nem no papel do PVAT, em machos e fêmeas. Somente no grupo M-CLP a sepse promoveu hiporreatividade vascular (Emáx: M-N PVAT- $3,7 \pm 0,2$; M-CLP PVAT- $2,2 \pm 0,3$ [n=08]) com envolvimento das enzimas NOS (Emax: CLP $2,0 \pm 0,2$ [n=12]; CLP + L-NAME $3,4 \pm 0,2$ [n=04]) e COX (Emax: CLP $2,8 \pm 0,2$ [n=12]; CLP + Ibuprofeno $3,9 \pm 0,5$ [n=04]). Observou-se a influência do dimorfismo sexual sobre o efeito anti-contrátil do PVAT apenas no grupo M-NAIVE. Conclusion: O presente estudo mostrou que machos sobreviventes à sepse tem mais prejuízos cardiovasculares do que fêmeas, confirmando a influência do dimorfismo sexual. Houve prejuízos na função cardíaca, na contratilidade de cardiomiócitos isolados, bem como hiporreatividade vascular envolvendo as enzimas NOS e COX. Support: CNPq, CAPES e FAPEMIG Protocol: (39/2022)</p>

Title	CARDIOMETABOLIC DYSFUNCTION IN THE OFFSPRING OF FRUCTOSE-OVERLOADED RATS: ROLE OF THE CHOLINERGIC ANTI-INFLAMMATORY REFLEX
Authors	VICTOR HUGO MARTINS DE MIRANDA, CAMILA PAIXÃO, PIETRA PETRICA NEVES, ANTONIO V. NASCIMENTO-FILHO, MARINA R. H. DUTRA, NATHALIA BERNARDES, LEANDRO EZEQUIEL, ROBSON CAMPOS GUITIERRE, MARIA CLÁUDIA IRIGOYEN, PROFA DRA. KÁTIA DE ANGELIS
Affiliations	Fisiologia, Unifesp
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Studies have reported an increase in the consumption of processed foods high in fructose (F), which has been associated with the development of metabolic syndrome. The cholinergic anti-inflammatory reflex (CAT) pathway appears to play an important role in this condition. Objective: The present study investigated the role of the CAT pathway by splenic and vagal denervation (D) and treatment with galantamine (GAL) on cardiometabolic and autonomic parameters in the offspring of rats subjected to chronic fructose consumption. Methods: Wistar rats (parents: male and female) were given fructose (10% in drinking water) or water for 60 days. The rats were then mated and the fructose overload was maintained in females until the end of lactation. At the end of lactation, the offspring were randomised into 4 groups (n=10/5 per sex, 30-50 g): Control (C), F, F+GAL and F+D+GAL. GAL (5 mg/kg,) an acetylcholinesterase inhibitor, was administered by gavage for 30 days. D was performed at 21 days. Offspring were evaluated at day 51. All experimental procedures and protocols were approved by the Ethics Committee of UNIFESP (protocol number: 4791091019). Results: Compared to the C group (3.63±0.24 mg/dl/%/min), the F and F+D+GAL groups (2.8±0.20 and 2.9±0.14 mg/dl/%/min) showed an impairment of insulin sensitivity, which was not observed in the F+GAL group. The F and F+D+GAL groups (vs. C group) had increased mean arterial pressure (AP) (114±1.9 and 115±1.4 vs. 101±2.2 mmHg), heart rate (381±5 and 369±5 vs. 343±10 bpm), low frequency component of systolic AP (4.95±0.49 and 3.33±0.23 vs. 1.62±0.2 mmHg²) and tachycardic response of the baroreflex (-3.24±0.26 and -3.48±0.1 vs. -3.93±0.1 bpm/mmHg); these impairments were not seen in the F+GAL group. However, the F+GAL and F+D+GAL groups showed an increase in cardiac vagal modulation indices (HF-PI and RMSSD). Splanchnic TNF-alpha was increased only in F and F+D+GAL groups compared to C group. Conclusion: Our data provide evidence for the involvement of CAT in cardiometabolic dysfunction in offspring of parents exposed to chronic fructose consumption. Such findings highlight the importance of therapeutic strategies that improve autonomic modulation to prevent early changes in the offspring of metabolically overburdened parents. Support: FAPESP (2022/04050-1), CNPq, CAPES-PROSUP Protocol: 4791091019</p>



Title	Protective effect of caloric restriction on monocrotaline-induced right ventricular hypertrophy in Wistar rats
Authors	FABRÍCIO TABELIÃO DEGRANDIS, JÚLIA CASSURIAGA DA SILVA VILELA LEMES, FERNANDO DIÓGENES TEIXEIRA MEYER, SÉRGIO ALBERTO RAZERA DE MATOS JÚNIOR, PAULO CAVALHEIRO SCHENKEL
Affiliations	Departamento de Fisiologia e Farmacologia, UFPel
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Monocrotaline administration is a classic method used to induce rodents` pulmonary arterial hypertension (PAH). It causes severe impairment of pulmonary vessel function with a significant increase in pulmonary vascular resistance due to the thickening of arteriolar walls. In this context, the increased afterload on the right ventricle (RV) necessitates compensatory cardiac chamber remodeling. It has been shown that such changes are associated, among other factors, with oxidative stress. Accordingly, caloric restriction appears promising in preventing its establishment. Objective: To evaluate whether caloric restriction attenuates cardiac hypertrophy in a monocrotaline-induced PAH model. Methods: Thirty-six male Wistar rats ($\pm 250g$) were divided into three experimental groups (n=12 each): 1) Control (CTRL), animals with a free diet; 2) Caloric Restriction (CR), animals subjected to a 30% caloric restriction compared to controls; 3) Caloric Restriction + Monocrotaline (CR+MCT), animals subjected to CR and administered monocrotaline to induce PAH. The CTRL group animals were housed in the central animal facility at the Federal University of Pelotas, receiving food and water ad libitum, and their weight and intake were measured weekly. Animals subjected to caloric restriction had their food intake reduced by 30% compared to the CTRL group over 12 experimental weeks. At the beginning of the tenth week, the CR+MCT group animals received a single dose of monocrotaline (60mg/kg, i.p.) to induce PAH and continued on their respective pre-established diets for three more weeks. At the end of this period, the animals were anesthetized with ketamine (90mg/kg) and xylazine (10mg/kg), tracheostomized for bronchoalveolar lavage sample collection, and euthanized by decapitation for tissue collection for morphometric analysis. Results: Caloric restriction significantly reduced weight gain (22% and 23%) and naso-anal growth (14 and 17%) in the RC and RC+MCT groups, respectively, when compared to the CTRL group. However, the body mass, assessed by the Lee index, was not different between groups. These body parameters, as well as RV hypertrophy and pulmonary arteriole thickness, were not significantly altered following monocrotaline administration. Conclusion: Our findings suggest that caloric restriction may be beneficial in preventing the structural pulmonary and cardiac changes typically observed in PAH. Looking ahead, we will evaluate oxidative and nitrosative stress parameters. Support: CAPES Protocol: 038178/2022-03</p>



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Title	O TRATAMENTO PADRÃO DE REPOSIÇÃO HORMONAL COM L-TIROXINA PROMOVE HIPERSENSIBILIDADE ADRENÉRGICA EM CORAÇÕES ISOLADOS DE RATOS HIPOTIREOIDEOS
Authors	RONALDO ANDRÉ CASTELO DOS SANTOS DE ALMEIDA, JÉSSICA DA SILVA SANTOS, AYRON MOTTA, BEATRIZ CAMPANHÃ CRUZ, LETÍCIA DE SOUSA AMORIM, LUCAS RODRIGUES SILVA, ANDERSON LUIZ BEZERRA DA SILVEIRA, EMERSON LOPES OLIVARES
Affiliations	Departamento de Ciências Fisiológicas, UFRRJ, UNIVERSIDADE FEDERAL RURAL DO RIO DE JANEIRO, Departamento de educação física e desportos, UFRRJ, UNIVERSIDADE FEDERAL RURAL DO RIO DE JANEIRO
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O tratamento padrão do hipotireoidismo é a reposição hormonal com L-Tiroxina (L-T4), no entanto, uma fração substancial dos pacientes exibem alta relação T4/T3 no plasma(Wiersinga et al, Eur Thyroid J 1 (2):55-71, 2012) com consequências desconhecidas a longo prazo. Isto é relevante, dado que estudos clínicos indicam que 5% a 10% dos pacientes com hipotireoidismo tratados com L-T4, exibem T4 e tireotrofina séricos normais à despeito dos sintomas persistentes de hipotireoidismo(Wiersinga et al, Eur Thyroid J 1 (2):55-71, 2012) . No sistema cardiovascular, o hipotireoidismo pode aumentar a resistência vascular sistêmica, diminuir a contratilidade miocárdica e o débito cardíaco(Klein and Danzi, Circulation 116 (15):1725-1735, 2007 and Kahaly and Dillmann, Endocr Rev 26 (5):704-728, 2005) , bem como levar a disfunção diastólica. Quanto ao sistema adrenérgico, já foram descritas diminuição da expressão dos receptores beta-adrenérgicos e sensibilidade adrenérgica no coração, além de bradicardia e desenvolvimento de insuficiência cardíaca(Iervasi et al, Circulation 107 (5):708-713, 2003 and Polikar et al, Circulation 87 (5):1435-1441, 1993). Objective: Estudar a sensibilidade adrenérgica e os possíveis efeitos do tratamento padrão de reposição hormonal (TRH) com L-T4 em corações isolados de ratos hipotireoideos.</p> <p>Methods: Vinte ratos Wistar machos (320±22,5g) foram divididos em 3 grupos: 1.falso-operados e sem implante (SHAM, n=8) e hipotireoideos (induzidos por tireoidectomia) implantados com pellet SC contendo 2. veículo (Tx, n=6) ou 3. L-T4 (TxT4, n=6). Após 30 dias, os animais foram submetidos à eutanásia e os corações foram isolados pelo método de Langendorff. A função ventricular esquerda foi registrada por 10 min em condições basais e em seguida desafiados por meio da administração de adrenalina (Adl) em doses crescentes (0,1;0,2 e 0,3 mg/mL). Results: Houve redução da massa cardíaca em Tx (0,793±0,03g) e TxT4 (1,01±0,04) comparados ao SHAM (1,35±0,05, p<0,01) embora o TxT4 tenha aumentado em relação ao Tx (p<0,01). A pressão desenvolvida pelo ventrículo esquerdo (PDVE) basal não foi diferente entre os grupos, no entanto o desafio adrenérgico aumentou a PDVE no TxT4 em relação ao Tx (122,5±5,69 vs 89,69±3,81 mmHg) e ao SHAM (112,1±0,51 mmHg), p=0,028. Resultados similares foram observados nas derivadas positivas (+dP/dT) e negativas (-dP/dT) da pressão na unidade de tempo, sendo maior no TxT4 vs. Tx (4505±288,4 vs 2841±152 mmHg/s) e no TxT4 vs. SHAM (4505±288,4 vs 3437±158,3 mmHg/s) na +dP/dT à partir de 4min. de infusão com Adl (p<0,01) e menor no TxT4 vs. Tx (-2068±82,15 vs. -1231±73,32 mmHg/s) e no TxT4 vs. SHAM (-2068 ± 82,15 vs. -1926±116,3) na -dP/dT à partir de 2 min. de infusão com Adl. (p<0,01).</p> <p>Conclusion: O TRH com L-T4 atenuou a perda de massa cardíaca e promoveu hipersensibilidade adrenérgica nas funções sistólica e diastólica cardíacas. Estudos futuros são imperativos para avaliar as consequências fisiológicas desses achados. Support: Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPQ; Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro – FAPERJ Protocol: 14/2022 – ICBS/UFRRJ</p>



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Title	Set7 pharmacological inhibition attenuates isoproterenol-induced cardiac remodeling and dysfunction
Authors	GUILHERME LUNARDON, TÁBATHA DE OLIVEIRA SILVA, AMANDA DE ALMEIDA SILVA, WENDDY WYLLIE DAMASCENA SOUGEY, MARIA CLAUDIA COSTA IRIGOYEN, MARIA LUIZA MORAIS BARRETO-CHAVES, DA-ZHI WANG, GABRIELA PLACONÁ DINIZ
Affiliations	Department of Anatomy, USP, Department of Cardiopneumology, USP, Center for Regenerative Medicine, USF
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Set7 is a methyltransferase that regulates the expression of several genes through the methylation of histones and modulates the activity of non-histone proteins. Recently, we demonstrated that Set7 deletion attenuates isoproterenol-induced cardiac fibrosis and delays heart dysfunction. However, whether the pharmacological inhibition of Set7 exerts beneficial effects to counteract the isoproterenol-induced cardiac disorders is unknown. Objective: To investigate the effect of a Set7 pharmacological inhibitor (sinefungin) in cardiac remodeling and dysfunction induced by isoproterenol. Methods: Eight-week-old male C56BL/6 mice were injected subcutaneously with vehicle (Veh, saline), isoproterenol (Iso, 40 mg/kg/day) for 14 days, or isoproterenol for 7 days followed by combined treatment with isoproterenol and sinefungin (10 mg/kg/day) for additional 7 days (Iso+Sine). Statistical significance ($p \leq 0.05$) was calculated by one-way ANOVA followed by Tukey's post hoc test. Results: Our preliminary data showed that Iso mice exhibited higher heart weight to tibia length ratio (HW/TL) and cardiomyocyte area compared to Veh mice, indicating development of cardiac hypertrophy. Interestingly, the sinefungin injection prevented the increase in HW/TL in Iso+Sine mice compared to Iso mice. In line with these findings, the Iso+Sine mice did not exhibit increase in cardiomyocyte area compared to Veh mice. Moreover, Sirius Red staining revealed that Iso mice had increased cardiac fibrosis compared with Veh mice. Notably, sinefungin injection in Iso+Sine mice prevented the myocardial fibrosis induced by isoproterenol. Echocardiogram analysis showed that Iso mice had reduced ejection fraction and fractional shortening compared with Veh mice, indicating systolic dysfunction. However, the Iso+Sine mice displayed a trend of increase in ejection fraction and fractional shortening compared to Iso mice. Moreover, the Iso and Iso+Sine mice presented a higher IVRT compared with Veh mice, indicating diastolic dysfunction. In addition, the Iso mice had an increase in E/e' ratio compared to Veh mice. On the other hand, the Iso+Sine mice displayed a E/e' ratio similar to that observed in Veh mice. Conclusion: Collectively, our preliminary data suggest that Set7 pharmacological inhibition may attenuate isoproterenol-induced cardiac hypertrophy, fibrosis, and systolic dysfunction. Further experiments are required to corroborate these preliminary findings and to determine by which mechanisms sinefungin influences the cardiac remodeling and dysfunction in response to isoproterenol. Support: FAPESP 2022/10060-0; 2020/13211-3 Protocol: CEUA ICB/USP 9344271022</p>



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Title	Avaliação da reatividade vascular em diferentes períodos de deficiência hormonal em ratas ovariectomia
Authors	WILLIAN BERGAMO DE MOURA, TAGANA ROSA DA CUNHA, JOCIMAR JOSÉ PITOL, ROGER LYRIO DOS SANTOS
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, UFES
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O modelo experimental de ovariectomia é comumente utilizado para mimetizar a disfunção hormonal ocorrida após a menopausa. No entanto, ainda não há um consenso sobre o tempo necessário para verificar possíveis alterações funcionais na aorta após o declínio hormonal. Objective: Identificar a partir de qual período após a ovariectomia, eventuais prejuízos em segmentos isolados de aorta de ratas Wistar começariam a ocorrer. Methods: Os protocolos realizados foram aprovados (CEUA-UFES #18/2022). Ratas adultas com 8 semanas foram separadas aleatoriamente em quatro grupos conforme o tempo, em dias, após a ovariectomia: OVX 07, OVX 15, OVX 21 e OVX 30. E, em seguida foram eutanasiadas e aorta torácica foi retirada, dissecada e cortada em anéis, que foram montados no sistema de banho de órgãos para a análise de reatividade. Foram realizadas curvas de concentração-resposta à fenilefrina (PE, 0,1 nM – 0,3 mM) na presença de inibidores não seletivos da óxido nítrico sintase (L-NAME, 100 µM), ou da ciclooxigenase (indometacina-INDO, 10 µM), e curvas à acetilcolina (ACh, 0.1 nM, 300 µM) e nitroprussiato de sódio (NPS, 0.01 nM, 0.3 µM). Os dados foram expressos em média ± EPM, e analisados por ANOVA de 2 vias, seguidos do post hoc de Tukey (p < 0,05). Results: Ocorreu uma diminuição progressiva na resposta contrátil à PE entre os grupos de acordo com o tempo de ovariectomia, exceto entre os grupos OVX 15 e OVX 21 (OVX 07: 3,5 ± 0,3; OVX 15: 3,6 ± 0,4; OVX 21: 3,0 ± 0,2 e OVX 30: 2,8 ± 0,2 g) No entanto, após a incubação com L-NAME, verificamos um aumento progressivo da resposta contrátil a partir do grupos OVX 15 (07: 3,5 ± 0,1; OVX 15: 2,7 ± 0,1; OVX 21: 4,1 ± 0,1; OVX 30: 4,3 ± 0,3 g), sugerindo uma participação mais significativa do óxido nítrico nos grupos de acordo com a progressão temporal. Após a incubação com INDO, verificamos uma diminuição da resposta contrátil nos grupos OVX 21 (3,6 ± 0,4 g) e OVX 30 (1,7 ± 0,1). Ao avaliar o relaxamento mediado pelo endotélio em resposta à ACh, observamos uma redução no grupo OVX 30 quando comparado ao grupo OVX 21 (OVX 21: 2,2 ± 0,3; OVX 30: 1,6 ± 0,1 g). O relaxamento independente do endotélio sofreu uma redução progressiva a partir do grupo OVX 15 (OVX 15: 2,7 ± 0,2; OVX 21: 2,0 ± 0,1; OVX 30: 1,8 ± 0,08 g). Conclusion: Os danos causados pela deficiência hormonal na aorta são observados após os 15 dias da ovariectomia. Contudo, alterações nas respostas contráteis são maiores a partir de 21 dias, enquanto, as respostas ao relaxamento são mais prejudicadas aos 30 dias. Support: CAPES e FAPES. Protocol: CEUA-UFES #18/2022</p>

Title	EFFECTS OF CHOLINERGIC STIMULATION WITH PYRIDOSTIGMINE ON CARDIOVASCULAR AUTONOMIC CONTROL AND INFLAMMATORY RESPONSE AFTER AMI IN SHR
Authors	MANUELLA DA SILVA TEIXEIRA, MARIA HELENA PORTER, PAMELA NITHZI BRICHER CHOQUE, HUMBERTO DELLÊ, FERNANDA MARCIANO CONSOLIM-COLOMBO, MARIA CLAUDIA COSTA IRIGOYEN
Affiliations	Unidade de Hipertensão, FMUSP, Laboratório de Biotecnologia, UNINOVE
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cardiovascular autonomic dysfunction impairs the cardiac response after acute myocardial infarction (AMI). Increased vagal modulation can influence the inflammatory response after AMI in spontaneously hypertensive rats (SHR). Recently, it was described that direct stimulation of the vagus nerve or the use of anticholinesterase drugs (pyridostigmine, PY) can affect immune responses, however little is known about the impact of PY on renal inflammation after AMI in the SHR model. Objective: To investigate whether cholinergic stimulation by administration of pyridostigmine modulates the autonomic response and the infiltration of inflammatory cells in the kidney after AMI in the SHR model. Methods: Adult male SHR rats were divided into 3 groups (8 animals/group): SHAM (submitted to thoracotomy), AMI (infarcted: thoracotomy with left coronary artery ligation) and AMI+PY (infarcted + treated with PY at a dose of 40 mg/kg/day, by gavage, for 7 days). On the sixth day, blood pressure curves and heart rate variability components (RMSSD, HF, LF, LF/HF) were analyzed after direct recording by femoral artery catheterization. After euthanasia on the 7th day, the kidneys were removed for histological analysis of infiltration of CD68+ and CD206+ macrophages and CD3+ and CD4+ T lymphocytes using the immunohistochemistry technique. We used the ANOVA test for analyses between groups. Results: The AMI group compared to SHAM showed an increase in sympathetic modulation and sympatho-vagal balance (LF/HF 0.5 ± 0.2 vs 0.2 ± 0.1). The AMI+PY group compared to the AMI group showed an increase in vagal activity (RMSSD 9.1 ± 2.1 vs 5.8 ± 2.2, and HF 22.7 ± 9.0 vs 6.0 ± 3.0) and BRS (0.98 ± 0.5 vs 0.6 ± 0.2). The AMI + PY group showed greater infiltration of total CD3+ T lymphocytes when compared to the SHAM group ($p < 0.05$). Conclusion: Cholinergic stimulation improves autonomic control and modulates the infiltration of inflammatory cells in renal tissue after AMI in SHR. Support: Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) Protocol: 1791/2022</p>



Title	OUTCOMES IN HYPERTENSION DISORDERS OF PREGNANCY: BABIES`BODY WEIGHT IS DIFFERENT BETWEEN CHRONIC HIPERTENTION AND PREECLAMPTIC GROUPS.
Authors	ROGER RODRÍGUEZ-GUZMÁN, SILVIA, NELSON SASS, ANDRÉ DE SOUZA MECAWI
Affiliations	Biofísica, UNIFESP, Obstetrícia Clínica, UNIFESP, Obstetrícia Fisiológica e Experimental, UNIFESP
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Hypertensive disorders of pregnancy (HDP) are the most prevalent conditions during pregnancy and one of the primary causes of maternal-fetal mortality worldwide. However, their physiopathology remains unclear. Objective: To study the outcomes of hypertension disorders of pregnancy. Methods: A prospective cohort study is being executed in São Paulo Hospital, São Paulo, Brazil where volunteers have been classified as control (C), preeclampsia (PE), and chronic hypertension (CH), and their clinical data have been obtained from their clinical reports. Results: To date, 30 volunteers have been included whose distribution in groups is: 11 C, 12 CH, and 7 PE. No significant differences were observed related to outcomes like placenta's weight, Apgar score, amniotic fluid index, pH of the umbilical cord or in variables like glycemia, TSH, FT4, total white cell count (TWCC), platelets count, and hemoglobin count. Interestingly, gestational age at birth was different between C and hypertensive groups (C = 38.50 wk ± 1.08, PE = 35.16 wk ± 1.49, CH = 36.57 wk ± 2.65) (p = 0.002) but not between CH and PE (p = 0.25). In addition, PE and CH were different according to babies` weight (PE = 2014 g ± 532.6 vs CH = 2928 g ± 852, p = 0,018) and diastolic blood pressure delta (PE = 33.67 ± 8.02 vs CH = 2.20 ± 16.06, p = 0.013). Moreover, a moderately significant correlation between TWCC before 20wk and diastolic blood pressure at the end of pregnancy was obtained (Rho = 0.48, p = 0.037). Conclusion: Hypertension in pregnancy due to PE contributes to lower weight in babies when compared to CH. Maybe some mechanism such as high diastolic blood pressure delta in PE is enrolled and it could be related to immunological profile of PE. Support: FAPESP (2019/27581-0), CAPES/PEC-PG (88881.599037/2021-01) e CNPq: 309882/2020-6. Protocol: N.A.</p>



Title	Efeitos da administração de extratos de linhaça ou amoreira na função vascular contrátil de ratas com baixa ação estrogênica
Authors	BEATRIZ MENEGATE SANTOS, ANA LUIZA MACIEL DE OLIVEIRA SILVA, ALINE CARVALHO PEREIRA, BRUNO DEL BIANCO BORGES
Affiliations	Departamento de Medicina, Universidade Federal de Lavras
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A deficiência ou diminuição da ação estrogênica no organismo feminino está associada ao aumento do risco de doenças cardiovasculares. A administração de estrogênios em roedores ovariectomizados promove cardioproteção. Entretanto, a terapia de reposição hormonal em mulheres com baixa ação estrogênica tem sido controversa nas últimas décadas, com estudos associando o uso de hormônios estrogênicos a aumento na prevalência de doença coronariana, infarto agudo do miocárdio não fatal, morte por doença coronariana e câncer de mama invasivo. Assim, a busca por produtos naturais com potenciais respostas antioxidantes, anti-inflamatórias, antiproliferativas e vasodilatadoras, tem sido de grande interesse, com intuito de trazer benefícios para o organismo com deficiência estrogênica e consequentemente cardioproteção. Objective: Avaliar os compostos fenólicos presentes nos extratos de linhaça e amoreira, e analisar os efeitos dessa suplementação na função vascular contrátil de ratas Wistar com deficiência estrogênica. Methods: A cromatografia líquida de alta eficiência (HPLC) foi utilizada para determinar os compostos fenólicos presentes nos extratos de linhaça e amoreira. Ratas Wistar adultas + 250g, foram divididas em cinco grupos experimentais, sendo um grupo com animais com cirurgia simulada tratado com salina (SHAM) e 04 grupos ovariectomizados (ovx) tratado com salina (OVX); estradiol (E2); extrato de linhaça (L); ou extrato de amoreira (A). O projeto foi aprovado pela CEUA-UFLA sob o número de protocolo 071/19. As soluções foram administradas via gavagem por 60 dias. As dosagens das soluções foram: 5 µg/kg/dia de estradiol; 400 mg/kg/dia de extrato de linhaça ou amoreira. Ao final do experimento, os animais foram anestesiados com isoflurano e decapitados. A artéria aorta torácica foi retirada, dissecada, e cortada em anéis com cerca de 04mm. Os anéis foram suspensos em banho de órgão contendo solução de Krebs-Henseleit a 37 °C, pH 7,4 e aerado com carbogênio sob tensão de repouso de 1g. A integridade endotelial foi avaliada com acetilcolina (ach, 10⁻⁶) em anéis contraídos previamente com fenilefrina (phe, 10⁻⁷). Os anéis foram considerados íntegros quando o relaxamento foi superior a 70%. Foram realizadas curvas de concentração-resposta à phe (10⁻¹⁰-10⁻⁷). Os dados foram analisados utilizando a ANOVA two-way seguido pelo teste de Bonferroni, e foram considerados estatisticamente significativos se p<0,05. Results: Por meio do HPLC foi observado a presença de trigonelina, ácido gálico e ácido p-cumárico no extrato de linhaça, enquanto no extrato de amoreira foram identificados ácido gálico, teobromina, ácido clorogênico e ácido siríngico. Animais deficientes de estrógenos demonstraram aumento na contração induzida por fenilefrina em relação aos animais SHAM (OVX: 56,9%, n=8; SHAM: 44,1%, N=5; p<0,5), enquanto os animais tratados com E2 (43,2%, n= 8; p<0,01) e extratos de linhaça (28,8%, n=8; p<0,001) ou amoreira (A: 40,9%, n=7; p<0,001) demonstraram redução na contração induzida por fenilefrina em relação aos animais OVX. Além disso, os animais tratados com extrato de amoreira apresentaram resposta semelhante aos grupos SHAM e E2, enquanto o tratamento com extrato de linhaça demonstrou menor contração em relação aos grupos SHAM (p<0,01), E2 (p<0,001) e A (p<0,01). Conclusion: Os resultados sugerem que a suplementação com extratos de linhaça ou amoreira foi capaz de prevenir o aumento da contração vascular induzida pela baixa ação estrogênica. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais; Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior Protocol: 071/19</p>

Title	Relationship between Lower Limb Perfusion Asymmetries and Anthropometric Factors in Different Age Groups
Authors	MARGARIDA FLORINDO, AND LUIS ANTONIO MONTEIRO RODRIGUES
Affiliations	1 Universidade Lusófona CBIOS –Research Center for Biosciences & Health Technologies 2 ESSCVP— Department of Physiotherapy, The Portuguese Red Cross Health School, Av. de Ceuta, 1350 125 Lisbon, Portugal
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The development of perfusion asymmetries in the lower limbs has been studied in the context of vascular morphology and hemodynamic, with potential importance for the prognosis and prevention of central and peripheral vascular diseases. Although physiologically these asymmetries are not significant in healthy young individuals, they become more evident with aging, and it is unclear if other determinants are related to this condition. Objective: This study aimed to investigate the relationship between the presence of lower limb perfusion asymmetries and factors such as age, weight, and body mass index (BMI). Methods: Twelve healthy individuals of both sexes (six men and six women), divided into two groups by age group, participated in this study: one group (n=6), aged over 50 years (average 60.5± 1.5), and one group (n=6), aged between 20 and 30 years (average of 23.0±3.3). Anthropometric data (weight: 81.3±6.1 and 62.4±10.1), BMI: 27.9±1.0 and 21.5±1.6) were collected, followed by a 15-minute stabilization period in the standing position. Lower limb perfusion was assessed using non-invasive optical techniques (Laser Doppler Flowmetry, LDF; and Polarized Light Spectroscopy, PSp). Results: The results indicated a normal distribution of perfusion by group and identified the ratios between limbs. Perfusion asymmetries measured with LDF were more evident in the elderly group (41.7%) compared to the young group (2.7%), with the right limb showing higher values. Differences measured with PSp were 15% in the elderly and 1.7% in the young. Significant positive correlations were found between perfusion ratios and age (p=0.002), weight (p=0.015), and BMI (p=0.001) in the elderly group. Conclusion: These findings contribute to the understanding of perfusion asymmetries, suggesting that age, weight, and BMI are determining factors in the development of these asymmetries. Support: This research was funded by national funds through FCT, Foundation for Science and Technology, I.P. (Portugal), under the [UIDB/04567/2020] and [UIDP/ 04567/2020] programs. Protocol: The study was previously approved by the Ethics Committee of the School of Sciences and Health Technologies from Universidade Lusófona (EC.ECTS/P03.20)</p>

Title	Cardiovascular 10-Year Risk: Analysis of Vegetarian and Omnivorous Diets
Authors	CÍNTIA FERREIRA-PÊGO, TATIANA FONTES, MARTA ESGALHADO, SOFIA LOPES, REGINA MENEZES, LUIS ANTONIO MONTEIRO RODRIGUES
Affiliations	a Sociedade Portuguesa de Fisiologia 1 Universidade Lusófona CBIOS –Research Center for Biosciences & Health Technologies Av. Campo Grande 376, 1749 024 Lisboa, Portugal
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The impact of dietary choices on cardiovascular health has attracted significant attention, with vegetarianism emerging as a dietary pattern of particular interest. While emerging evidence suggests potential cardiovascular benefits associated with a vegetarian diet, the precise nature of these associations requires further elucidation. Objective: To compare the 10-year cardiovascular risk (CVR) and its related factors between individuals following a vegetarian (VG) or omnivorous (OM) diet pattern. Methods: A cross-sectional analysis was conducted, involving 110 participants of both sexes, with a mean age of 49,17 (6,91) years, comprising 55 OM and 55 VG individuals. Metabolic markers were measured from capillary blood sampling, and the 10-year CVR was calculated using the SCORE2 algorithm. Results: Our findings revealed no statistically significant differences in 10-year CVR between the two dietary patterns. Nevertheless, slightly higher CVR values were noted among OM compared to VG (3.16% vs. 2.60%). Additionally, the OM group exhibited significantly higher levels of total cholesterol (199.00 mg/dL vs. 172.00 mg/dL), c-LDL (117.87 mg/dL vs. 99.85 mg/dL), and non-HDL cholesterol (138.00 mg/dL vs. 116.00 mg/dL), compared to the VG group. These lipid parameters are well-established indicators of an increased risk for both fatal and non-fatal cardiovascular events over 10 years. Regarding dietary habits, the consumption of sweets, sugar-sweetened beverages (SSB), and fast food proved to be risk factors for a high-risk SCORE2 for cardiovascular events at 10 years, with prevalence rates of 1.6%, 2.6%, and 2.1%, respectively. On the other hand, consumption of vegetables (1%) and fruits (0.3%), high adherence to the Mediterranean diet among OM (41%), and maintenance of a high-quality diet among VG (13.9%) were identified as protective factors against a high-risk SCORE2 for cardiovascular events over 10 years ($p < 0.05$). Conclusion: This study suggests that 10-year CVR is influenced by the quality of the diet rather than the dietary pattern alone, as no differences were observed for lifestyle variables such as smoking status and physical activity. It is important to note that the intake of sweets, SSB, fast food, and an unhealthy diet appear to increase the risk of cardiovascular diseases regardless of the specific dietary pattern followed (OM or VG). These findings underscore the critical role that individual dietary components play in shaping long-term cardiovascular health and emphasize the importance of further research to refine dietary recommendations and enhance cardiovascular outcomes.</p> <p>Support: This research was funded by national funds through FCT—Foundation for Science and Technology, I.P. (Portugal), under the [DOI 10.54499/UIDB/04567/2020] and [DOI 10.54499/UIDP/04567/2020] projects, and by COFAC/ILIND—Cooperativa De Formação e Animação Cultural CRL/Instituto Lusófono de Investigação e Desenvolvimento (grant COFAC/ILIND/CBIOS/2/2021). R.M. is funded by the FCT, Foundation for Science and Technology, I.P. (Portugal) Scientific Employment Stimulus contract [reference number CEEC/04567/CBIOS/2020]. C.F.-P. is funded by the FCT—Foundation for Science and Technology, I.P. (Portugal) Scientific Employment Stimulus contract [reference number DOI 10.54499/CEECINST/00147/2018/CP1498/CT0009]. Protocol: The study was previously approved by the Ethics Committee of the School of Sciences and Health Technologies from Universidade Lusófona (EC.ECTS/P05.21).</p>

Title	Ativação seletiva da via Gi nos cardiomiócitos: Efeitos positivos no remodelamento cardíaco e função contrátil
Authors	RAYSSA LIMA RODRIGUES, MARCOS ELIEZECK-MATEUS CHAVES DA COSTA, SERGIO SCALZO, VICTOR MOURA VIDAL, SILVIA GUATIMOSIM
Affiliations	Departamento de Fisiologia e Biofísica, Instituto de Ciências Biológicas, Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais, Brasil
Session	2-Fisiologia Cardiovascular
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Os receptores acoplados à proteína G (GPCRs) formam uma vasta família de receptores transmembrana, desempenhando um papel crucial na transdução de sinais celulares. No contexto cardiovascular, a via Gi é especialmente importante, regulando funções essenciais como a frequência cardíaca e a contratilidade. Essas funções cardíacas podem ser otimizadas com o que chamamos de remodelamento cardíaco fisiológico, promovendo adaptações benéficas que aumentam a eficiência funcional do coração, sem comprometer a saúde. Mostramos anteriormente que a ativação seletiva da via Gi em cardiomiócitos, através do modelo DREADD, foi suficiente para proteger o coração da cardiomiopatia induzida pela hiperativação adrenérgica. Especulamos aqui que essa ativação seletiva da via Gi nos cardiomiócitos poderia condicionar o coração. Objective: Methods: Utilizamos para esses experimentos animais de ambos os sexos, com idades entre 6 e 8 semanas (CEUA 102/2022). Para ativação seletiva da via Gi, cruzamos camundongos R26-LSL-Gi-hM4Di com Myh6-CRE, gerando a linhagem Myh6-hM4Di. Estes animais expressam o receptor DREADD-Gi (Designer Receptors Exclusively Activated by Designer Drugs), permitindo a ativação exclusiva da via Gi nos cardiomiócitos. Esse receptor não é ativado por ligantes endógenos, respondendo apenas ao ligante exógeno CNO. O tratamento com CNO consistiu em 7 doses diárias de 0,5 mg/kg. Após o tratamento, os corações foram submetidos a análises de imunofluorescência, contratilidade e estatística. Results: Inicialmente, observamos que o tratamento com CNO por 7 dias induziu um remodelamento cardíaco que melhorou a contratilidade (área de encurtamento em um2: CTR 509±17 vs CNO 633±29) e aumentou a largura (em um: CTR 23±0.3 vs CNO 24±0.4) e área dos cardiomiócitos isolados (em um2: CTR 2621±47 vs CNO 2790±66). Avaliamos em seguida se a hipertrofia cardíaca ocorria às custas de um remodelamento patológico. Para isso, investigamos a morte celular por Evans Blue Dye (EBD) (em % da área marcada: CTR 0.2±0.0 vs CNO 0.3±0.1), o infiltrado inflamatório cardíaco por imunofluorescência para macrófagos CD68+, a diferenciação de fibroblastos cardíacos em miofibroblastos por imunofluorescência de α-SMA (número de células por campo 40X: CTR 10.3±0.4 vs CNO 10.8±1.5 e CTR 7.0±0.8 vs CNO 4.6±0.5 respectivamente) e a expressão de colágeno tipo I e III por PCR em tempo real (expressão do mRNA: CTR 0.9±0.08 vs CNO 0.9±0.15 e CTR 1.0±0.64 vs CNO 0.9±0.19 respectivamente) Embora a funcionalidade tenha sido melhorada e o tamanho do cardiomiócito tenha aumentado, não observamos qualquer diferença na morte celular, no infiltrado inflamatório, na ativação de fibroblastos e na expressão do mRNA para colágeno. Conclusion: Os dados obtidos sugerem um possível efeito benéfico da via Gi na melhora da função dos cardiomiócitos. Curiosamente, essas alterações morfofuncionais não induzem qualquer efeito característico do remodelamento cardíaco patológico, caracterizando-se possivelmente como um remodelamento fisiológico. As perspectivas futuras incluem investigar as alterações moleculares associadas a esses remodelamento cardíaco fisiológico e avaliar o papel desse condicionamento diante de eventos cardiovasculares agressivos e cardiodeletérios. Support: CNPq, CAPES, FAPEMIG, PRPq-UFMG Protocol: CEUA: 102/2022</p>

Title	BIOSCIENCES MUSEUM PROFESSOR ELISARDO VASQUEZ: Popularizing of Physiology Connecting the Past to the Present and Aiming for the Future
Authors	ELISARDO CORRAL VASQUEZ, RADAEL R. RODRIGUES JUNIOR, ROGER LYRIO DOS SANTOS, SILVANA SANTOS MEYRELLES
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, UFES, Programa de Pós Graduação em Ciências Farmacêuticas, UVV
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: We are facing a time in which researchers are challenged to promote openness, transparency, and credibility in the knowledge produced within their scientific fields. Therefore, it is urgent to promote the dissemination of science to the general society. Objective: The aim of this work is to report on what has been done by the Biosciences Museum to popularize science. Methods: The museum was established in April 2022, aiming to provide knowledge in physiological sciences through the understanding of body function in health and disease. To achieve this goal, a collection of equipment and documents, acquired during the career of professor Elisardo Vasquez and some apparatus donate by UFES, health professionals and medical companies, were organized and exhibited in a commercial room of approximately 30 m2. This space allowed visitors to look inside each device and learn about the history of physiology. Additionally, we received support from the Profix Call (2022), through the State Research Foundation (Fapes) to have a postdoctoral student with a background in design, who is responsible for the to the museum’s web version. Results: First, the museum elicited interest and received visits from representative individuals of society, such as managers of education, healthcare and governmental funding agencies, students and professors from all levels of education, administrative and laboratory technicians from higher education institutions, journalists, and workers from diverse areas. Second, the web version of the museum, www.museudebiociencias.com.br, was a huge success, being visited by hundreds of people and appearing as the top result when a Google search is made using the words “museum” and “Vasquez”. Third, with the museum’s success, there was an increase in equipment donations, which necessitated the search for a larger space to accommodate everything. To solve this problem, we asked for help from UVV, which agreed to build an adequate space at their Biomedical Campus to host our museum. Finally, the museum motivated a scientist from Federal Fluminense University to present the history of Professor Vasquez and his Biosciences Museum at the Mercosur Anthropology Meeting in 2023. The museum also had a great impact at the Southeast Regional Conference at UVV, promoted by the Science, Technology, and Innovation Ministry. Conclusion: We conclude that the methodology used is effective, the results achieved are significant, and they may have an impact on the SBFis congress. The Biosciences Museum demonstrates that by connecting current knowledge to the inventions of the past, we will be able to achieve better conditions in the future and effectively promote the popularization of physiological science. Support: Fapes/PROFIX Grant nº 15/2022 #643/2022 P: 2022-70C49 and CNPq Scholarship-Grant nº 312911/2023-8 Protocol: not applicable</p>

Title	ACTIVE RECALL: A TEACHING-LEARNING STRATEGY IN HUMAN PHYSIOLOGY
Authors	LÍVIA CRISTINA FIDELIX DA SILVA, HELLEN KARINE DA SILVA ALVES, LEILANY DANTAS VARELA, MARIA MISRELMA MOURA BESSA, FRANCISCO FÁBIO BEZERRA DE OLIVEIRA
Affiliations	Departamento de Enfermagem, URCA Iguatu, Faculdade de Medicina, FAP ARARIPINA, Centro Universitário Paraíso, UniFAP
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A pedagogical approach that has gained prominence is the method of active recall, which is based on the active retrieval of knowledge to consolidate and retain information in long-term memory.</p> <p>Objective: The objective of this research was to investigate and evaluate the active recall method as a teaching-learning strategy in Human Physiology. Methods: This action research study was conducted with students from the Human Physiology course in the Nursing, Pharmacy, Physiotherapy, and Nutrition programs at Centro Universitário Paraíso. The sample consisted of 118 students. Data collection was done using a questionnaire to assess the students' perceptions of the active recall method. Additionally, the grades obtained by the students in the first partial assessment (without applying the active recall method) were compared with the grades from the second partial assessment (with the active recall method applied). The data was tabulated and analyzed using GraphPad Prism, version 9.0. The grades from the first partial assessment were compared with those from the second partial assessment using the paired Student's t-test, with a significance level of $p < 0.05$. Scores are presented as mean \pm standard deviation. Results: The data showed that 87.2% ($n = 103$) of the students agreed that solving questions (active recall testing) addressing the subject of the previous lesson at the beginning of classes contributed to their learning in Human Physiology, and 86.4% ($n = 102$) confirmed that the activity contributed to their understanding of the content. For 62.7% ($n = 74$), the dynamic of solving questions (active recall testing) helped increase their study frequency, and for 83.8% ($n = 99$), the activity helped them identify their difficulties in understanding the content. For 22% ($n = 26$) of the students, the activity encouraged them to develop the habit of studying or reviewing the content of the previous lesson to prepare for the problem-solving activities (active recall testing). The data showed that the majority of the students partially developed this habit, totaling 64.4% ($n = 76$) of the sample. The majority of the students (78.8%, $n = 93$) confirmed that solving questions addressing the subject of the previous lesson (active recall testing) helped increase their learning. The students also agreed (82.2%, $n = 97$) that the difficulty level of the questions used in the active recall method was normal. For 93.2% ($n = 110$), this active recall method is an interesting tool to use in teaching Human Physiology. Most of the students also stated that they would recommend the inclusion of the active recall method for other subjects (88.1%, $n = 104$). It was also found that students obtained better grades after using the active recall method compared to the grades obtained before applying the method. Comparing the results of the first partial assessment (AVP-1), before applying the method, with the second partial assessment (AVP-2), after applying the method, the data show a significant increase ($p < 0.05$) in scores in AVP-2 compared to AVP-1. The average scores in the assessments increased from 4.966 in AVP-1 to 5.703 in AVP-2, a difference of 0.7371 ± 0.2 between the means of AVP-2 and AVP-1. Conclusion: The results of this study demonstrate that it is possible to achieve more effective learning, increase student participation, and enhance their ability to recall and apply physiological concepts in a practical and meaningful way through the Active Recall Method. Support: UniFAP; URCA and FACEPE. Protocol: CEP-UNIJUAZEIRO, n. 6.152.219</p>

Title	Women Who Inspire: Disseminating and popularizing women`s scientific and social contributions throughout humanity`s history
Authors	MARISELE DOS SANTOS SOARES, ANA CAROLINA DE SOUZA DA ROSA, PÂMELLA ANDREA MACHADO DA SILVA LARANJA PINTO, NELSON GUSTAVO NOVAIS MARINHO, BIBIANA FRASSON ETCHVERRY, PÂMELA BILLIG MELLO CARPES
Affiliations	Fisiologia, UNIPAMPA
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Publicizing the participation of women in different areas of society is important, as there are still barriers that limit female representation in various spaces. The use of social networks, especially Instagram, has the potential to disseminate and popularize knowledge due to its broad reach. Objective: To present and evaluate the impact of the second season of the web series “Women Who Inspire”, linked to the Physiology Research Group (GPFis) and the Institutional Gender and Sexuality Committee of the Federal University of Pampa, on the dissemination and popularization of female personalities who have contributed to the history of humanity. Methods: The web series entitled “Women Who Inspire” was conceived in 2021 in the context of social distancing. With the changes imposed by the pandemic, our group saw on Instagram the possibility of expanding knowledge and creating new forms of scientific dissemination, initially as a way of promoting outreach actions to the population on a relevant topic involving students. The production and dissemination of the web series took place in the following stages: 1) Research into the lives and works of female personalities. 2) Planning, where we defined the personalities that would be addressed (Simone de Beauvoir, Hedy Lamar, Viola Davis, Nise Da Silveira, Eliane Potiguara, Rosalind Franklin, Kathrine Switzer, and Toni Morrison). 3) Production of the script and audio recording. 4) Audiovisual creation on the Canva platform (canva.com). 5) Review of the video by the team. 6) Dissemination of the video on the Instagram social network (instagram.com) on the GPFis profile (instagram.com/gpfisunipampa). To evaluate the published material, we used the statistics that Instagram provides to page administrators free of charge. We collected the number of likes and comments, as well as the reach (which consists of the number of accounts that viewed the posts) and the impressions of the posts (how many times the posts were viewed). The data was collected in May 2024, before the production of the third season of the series, to verify the reach and impact of the second season. Data was expressed as mean \pm standard deviation. Results: Considering data from the 8 published episodes, we found 1476 ± 678.8 views per episode. In addition, the episodes had 37.25 ± 15.23 likes and were shared about 39.13 ± 49.57 times each. We also verified that each episode reached 1196 ± 486.9 accounts, of which $31.66\% \pm 8.76\%$ were followers of the GPFis Instagram profile and $68.34\% \pm 8.76\%$ were not followers. Conclusion: The dissemination and popularization of women have the potential to break down barriers and positively inspire girls and women to insert themselves to act as agents of social transformation in different areas of society. Support: National Council for Scientific and Technological Development, Pro-Rectorcy of Extension and Culture of the Federal University of Pampa. Protocol: N.A.</p>

Title	Aliando a Neurofisiologia ao Entretenimento: Como as Séries de TV podem gerar discussões sobre a Neurobiologia das drogas no Ensino Médio
Authors	GABRIEL VICTORIANO DOS SANTOS- CARLOS HENRIQUE CONTE, TAMARA TURINI GOMES, NITICIA RAQUEL CUCATO CHRISTIANINI, MILENA ALVES
Affiliations	Diretoria de Ensino de Jaú, SEDUCSP
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O ensino de neurofisiologia no ensino médio tem sido discutido nos últimos anos ao nível da Base Nacional Comum Curricular (BNCC). Diante da reorganização curricular no Estado de São Paulo, foi implementado o material digital (MD) com o intuito de organizar os conteúdos em consonância com a BNCC na Educação Básica. O MD aborda os tópicos de neurofisiologia, mas pouco compreendido pelos alunos. Nesse sentido, as metodologias ativas surgem como estratégias didáticas com o intuito de estimular a aprendizagem e contextualizar os conteúdos para a realidade dos estudantes. Entre as estratégias didáticas utilizadas na educação, pode-se citar o uso de Séries de TV a partir da problematização de questões cotidianas como uma ferramenta incentivadora no ensino de fisiologia. Objective: Apresentar um Relato de experiência sobre o uso de Séries de TV como incentivadoras da discussão sobre o tema de Neurobiologia de drogas na 2ª Série do Ensino Médio. Methods: Foi aplicada a metodologia de Faces.2:126,2022 com o uso de séries a partir das etapas: 1ª Etapa, Levantamento de conceitos prévios: Discussão oral das questões: “As drogas de abuso agem no Sistema Nervoso?”; “Como é sua ação?”; 2ª Etapa – Aula expositiva: 1 Aula expositiva de 45 minutos sobre sinapse química e mecanismo de ação das drogas; 3ª Etapa – Transmissão de cenas. Foram discutidos os seguintes tópicos relacionados a dependência: Energéticos – Série: The Big Bang Theory – Temporada 10, episódio 3 (“A Transcendência da Dependência”); Cafeína – Série: Grey’s Anatomy – Temporada 7, episódio 14 (“A gatinha”); Opióide – Série: Euphoria. 4ª Etapa – Aplicação de questionário com as seguintes questões: 1. Os energéticos e cafeína são substâncias estimulantes, depressoras ou perturbadoras? Discuta a partir do que você observou na série; 2. Essas drogas apresentadas nas séries agem no sistema nervoso? Como isso pode ser notado?; 3. Essas cenas te ajudaram a compreender o efeito dessas substâncias? Comente. Results: Esse relato de experiência baseia-se na aplicação de sequência didática numa turma de 2ª Série do Ensino Médio, com a participação de 20 estudantes. Cerca de 90% dos estudantes identificaram o uso de substâncias relacionadas ao abuso nas cenas exibidas, mas sem discriminá-las. Todos os estudantes salientaram o efeito estimulante do energético, levantando questões sobre o seu uso. Todos os estudantes também reconheceram a ação dessas drogas no sistema nervoso devido ao fato das alterações comportamentais, no entanto, 75% desconhecem como esses processos ocorrem no encéfalo. De acordo com o levantamento da discussão feita com os alunos, as cenas auxiliaram na compreensão do efeito das drogas de abuso, sobretudo nas alterações comportamentais, entretanto seria relevante também mostrar os mecanismos fisiológicos. Conclusion: O tema de dependência de substâncias é um tópico sensível para se discutir no Ensino Médio, e as séries facilitaram a sua discussão em âmbito comportamentais, sociais e até mesmo fisiológicos, facilitando o entendimento de neurônios e sinapses. Support: Não houve Protocol: N.A.</p>



14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	The Potential of Including Neuroeducation in Teacher Training: Impact of a neuroscience of learning course on schoolteachers` comprehension of neuroscience concepts
Authors	PÂMELLA ANDRÉA MACHADO DA SILVA LARANJA PINTO, ANA LUIZA TROMBINI TADIELO, PÂMELA BILLIG MELLO CARPES
Affiliations	Grupo de Pesquisa em Fisiologia, UNIPAMPA Universidade federal do Pampa
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Adequate teacher training is critical to improving education. The POPNEURO Program integrates neuroscience into teacher training, enabling the understanding of the neurobiological needs of students and promoting effective and inclusive learning environments. Objective: This research evaluates the impact of a neuroscience of learning course on school teachers` comprehension of neuroscience applied to education concepts. Methods: In June 2023, 40 primary school teachers were introduced to essential neuroscience concepts related to learning, memory, attention, and the adolescent brain, through a 20-hour course. The course, balanced between theory and practical application, involved hands-on activities, experiments, and exercises on the online platform Lt (AD Instruments), encouraging the integration of neuroscientific principles into teaching strategies. The effectiveness of the course was assessed through a pre-and-post questionnaire, answered by all 40 participants initially and by 26 at the conclusion. Results: Results indicated significant improvements in neuroscience understanding. For instance, knowledge about the brain regions linked to impulse control increased from 92.5% to 100% correctness, understanding of neuroplasticity improved from 72.5% to 96.15%, and awareness of brain structures involved in emotional processing rose from 17.5% to 88.46%. Overall, the correct response rate jumped from 62% to 90%. Conclusion: These outcomes underscore the value of incorporating neuroscience into teacher training, as the course enhanced the teachers` grasp of critical educational neuroscience concepts, suggesting a potential improvement in teaching practices and a resultant elevation of learning environments. The results also highlight the significance of the program in fostering more informed and effective educational methods. Support: FAPERGS Protocol: N.A.</p>



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Title	QUE HORMÔNIO É ESSE? UMA PROPOSTA LÚDICA PARA O ENSINO DA FIOLOGIA ENDÓCRINA.
Authors	CAMILLY BANDEIRA AMARAL, ISLEIDE DIAS TOMÉ, EDUARDA ESQUELBECK DIAS, FABIANA LUCA ALVES
Affiliations	Saúde, Unifacear
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A Fisiologia Humana é um importante componente curricular para os mais variados cursos da área da saúde. Todavia, a carga horária dessa disciplina é baixa, existe uma grande quantidade de conteúdos que devem ser ministrados e esses conceitos fisiológicos são complexos, dificultando a aprendizagem dos estudantes. Nesse contexto, várias metodologias ativas vêm sendo utilizadas em sala de aula, pois elas dão ênfase ao papel protagonista do aluno, ao seu envolvimento direto, participativo e reflexivo em todas as etapas do processo, experimentando e criando. Objective: Assim o objetivo desse trabalho foi elaborar um jogo didático sobre o Sistema Endócrino para ser aplicado nas aulas de Fisiologia Humana, de cursos de graduação na área de saúde. Methods: Para a realização do jogo foi feita uma lista com 24 hormônios e foram pesquisadas as principais características deles. As ilustrações foram desenvolvidas por uma das alunas de iniciação científica, com base nas informações. Os materiais utilizados para a confecção do jogo foram: pedaços de madeira, impressora, papel e tesoura. Os cards depois de prontos, foram encaminhados para uma gráfica para que pudessem ser plastificados. Foram desenvolvidos 24 cards e 24 peças de madeira. Results: O jogo didático: Que hormônio é esse? consiste em adivinhar, antes do seu adversário, qual foi o hormônio secreto, sorteado por ele, por meio de perguntas sobre as suas características. Cada participante recebe 6 placas de madeira com o nome dos hormônios. Elas devem ser colocadas de frente para cada jogador. Além disso, cada jogador recebe seis cards. Cada card contém cinco dicas a respeito dos mecanismos de ação do hormônio. Se o jogador acerta qual é o hormônio, a peça do adversário é baixada. Já se o jogador erra, a peça é virada para o jogador que errou. O ganhador do jogo é aquele que derrubar mais peças do seu oponente. Foram desenvolvidas três formas de se jogar, das quais tem-se: (1) Nível Fácil: Cada jogador tem direito a três dicas; (2) Nível Difícil: Cada jogador tem direito a uma dica e duas tentativas para tentar adivinhar o hormônio do jogador adversário e (3) Nível competitivo: Nessa forma de se jogar, existe um ranking de pontuação:, se acertar com uma dica: 5 pontos, se acertar com duas dicas: 3 pontos; se acertar com três dicas: 1 ponto e se errar: menos dois pontos. O jogo foi testado inicialmente na Feira de Profissões da Unifacear e para saber a opinião das pessoas que participaram da atividade, foi criado um formulário no Google Forms. Os participantes disseram que esse material contribuiu para lembrar e aprender novos hormônios. Conclusion: Com isso, nota-se que esse jogo pode ser um recurso didático lúdico que favoreça uma aprendizagem mais significativa por parte dos alunos sobre a Fisiologia Endócrina, tornando as aulas mais dinâmicas e criativas. Support: Unifacear Protocol: N.A.</p>

Title	How our Body Works? Understanding Physiological Basis of Daily Events
Authors	PAULA ZANONI FREIRE, SILVANA DOS SANTOS MEYRELLES, AGATA LAGES GAVA
Affiliations	Departamento de Ciências Fisiológicas, UFES
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The enrichment of scientific knowledge is a social construction, based on previous reports and disclosure among pairs. However, to reach regular society and non-academic individuals, the use of a non-formal language and social embracing tools are required. Furthermore, it is necessary the simplify data to a better understanding of the experimental findings. Within this context, the use of social medias and websites are very effective in attaining a larger group of the society and are usually used to spread scientific knowledge. Objective: To propagate the physiology of human body in daily events to general population, as well as to show to initial undergraduate students the importance of physiology on their future clinical practices. Methods: On July 31st, 2023, the supervisor of the present work created an Instagram account under @fisiologianodiaadia identification. Initial undergraduate students from Health Sciences Center, Federal University of Espírito Santo, developed a carrousel of information using the physiological basis of ordinary daily events or routine clinical practices in easy and accessible language. After correction and layouts adjustments, the content is published in a post format on the Instagram account. Results: Up to the present moment the Instagram account has 14 posts and 364 followers. In the past 90 days, 736 accounts were reached, composed by 303 followers and 433 by non-followers. Within the same period, the number of interactions with publications was 608, showing a satisfactory extent of spreading of the scientific knowledge. We also noticed that contents related to aesthetic and women’s beauty were the most accessed and had a higher number of interactions. The undergraduate students that have created an Instagram post considered that the development of the material have greatly contributed to their professional skills. Conclusion: The use of casual language in social medias is an effective tool to properly inform general population about scientific findings, enhancing the critical judgment and preventing the spreading of misinformation. Our work helped both nonacademic people to comprehend how the human body works, as well as showed initial undergraduate students the importance of human physiology knowledge supporting clinical practice. Support: None Protocol: N.A.</p>



14 a 17 de Setembro de 2024
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Title	Question-based learning in the near-peer education: experience report
Authors	ANA CLARA CÂNDIDO SILVEIRA, RICHARD BOARATO DAVID, CAMILA FERREIRA RONCARI
Affiliations	Departamento de Fisiologia e Farmacologia, UFC
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Human physiology is a science that extends the knowledge of intracellular mechanisms to the integrated functioning of systems throughout the living organism. Therefore, it is as complex as it is important in the training of future health professionals. In this context, the institutional teacher initiation scholarship program plays an important role of supporting teachers by using different methodologies that can significantly improve the learning process. The question-based learning (QBL) is a methodological strategy that uses questions to structure the learning process. Objective: Report the experience of the near-peer tutor applying the QBL method on the institutional teacher initiation scholarship program. Methods: The near-peer tutor created questionnaires that were applied to human physiology students of 3 different graduate courses (dentistry, nursing and pharmacy). The questions encompassed topics from cellular and muscular physiology and were made available using Google Forms. Results: The QBL method is a quick and practical way for students to verify their knowledge, review topics studied in class and prepare for the exam, making them familiar with questions that are often found in the exams and highlighting the topics that need to be better studied. Besides this, this method brought up a lot of questions about application of the physiology concepts, allowing the near-peer tutor to delve deeper into the explanation according to the doubts. Conclusion: The near-peer tutoring using the QBL method is a beneficial alternative to complement the classes. However, this method has some shortcomings as the difficulty of covering the entire content and the risk of content memorization without effective learning. Therefore, the QBL method should be used with caution and improved for greater effectiveness. Support: Institutional teacher initiation scholarship program Protocol: N.A.</p>



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Title	Impact of Using 3D Models of Membrane Proteins Associated with an Interactive Online Platform on Cellular Physiology Learning
Authors	NELSON GUSTAVO NOVAIS MARINHO, GIULIA AZEVEDO MARTINEZ, ANNA CECÍLIA PERRETTO VIEIRA DE SOUZA, LARISSA DE ALMEIDA DIAS, ANA CAROLINA DE SOUZA DA ROSA, CLÁUDIO FELIPE KOLLING DA ROCHA, PÂMELA BILLIG MELLO CARPES,-
Affiliations	Grupo de Pesquisa em Fisiologia da UNIPAMPA SBFis UNIPAMPA, Universidade Federal do Pampa (UNIPAMPA), Grupo de Tecnologia Educacionais, FEEVALE
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Human physiology is considered one of the most complex courses in health careers. Often, traditional teaching methods fail to engage students significantly. Visualizing the microscopic world in physiology is challenging, as essential details are invisible to the naked eye. To enhance this process, educators have sought new strategies, including educational games, online platforms, and 3D models, promoting active and participatory learning. Objective: This study aimed to investigate the impact of using a 3D model of the cell membrane and its proteins on the health science undergraduates` learning of cellular physiology. Methods: The research was approved by the Research Ethics Committee of the Federal University of Pampa (protocol 3.102.158). Forty-three students from Nursing and Physiotherapy careers, all enrolled in the Human Physiology course, participated. The study included a practical class with the membrane 3D model (M3D), where students should follow a guide available on the Lt platform from AdInstruments. The guide provided step-by-step instructions on the procedures that students should follow using the M3D, which were associated with discussion questions on the theme. At the start, a pre-test of 4 questions was administered to assess previous learning. Students followed the guide, completed the activity, and took a post-test. Pre and post-test questions 1 and 2 addressed the students` self-perception about their knowledge, while 3 and 4 focused on content. Shapiro Wilk and Wilcoxon tests were used to analyze the students` self-perception questions, and Chi-Square to analyze the content-related questions. Results: In the pre-test, 34.88% (n=15) of students consider themselves able to differentiate the kinds of membrane proteins confidently, 58.14% (n=25) with difficulty, and 6.98% (n=3) consider that they cannot differentiate. After activities, 86.05% (n=37) confidently affirmed that they could differentiate proteins, and 13.95% (n=6) that they could, but with difficulty. The students` self-perceived knowledge increased after the activity with M3D (p<0.0001). In the second question, regarding explaining the Na⁺/K⁺ATPase function, in the pre-test, 9.30% (n=4) affirmed that they could explain confidently, 48.84% (n=21) with difficulty, and 41.86% (n=18) could not. After intervention, 74.42% (n=32) explained confidently, 23.56% (n=10) with difficulty, and 2.33% (n=1) could not, also significant (p<0.0001). In the learning assessment, no differences were observed between the pre and post-test (p=0.2804 – question about the protein types; 58.14% answered correctly in pre-test and 46.51% in post-test; p=0.2890 – question about active transport; 25.58% answered correctly in pre-test and 16.28% in post-test. Conclusion: The intervention with the 3D puzzle and Lt/AdInstruments platform improved students` self-perceived knowledge but did not significantly impact effectively their performance in the knowledge tests. This indicates the need for adjustments in the lesson`s planning to address areas of difficulty and optimize student learning, highlighting the importance of research investigating the impact of innovative teaching strategies on learning. Support: UNIPAMPA, CAPES, CNPq Protocol: N.A.</p>



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Title	Contribuição de metodologia ativa híbrida para o aprendizado sobre fisiologia renal
Authors	AMANDHA CHRISTINE DA SILVA SOUZA, ANA LUISA BETIOLLI, MICHELLE FRANZ MONTAN BRAGA LEITE, MARIA ANTONIA RAMOS DE AZEVEDO, FERNANDA KLEIN MARCONDES
Affiliations	Biociências, UNICAMP, Educação, UNESP
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Na área da saúde, a disciplina de Fisiologia Humana é ministrada no 1º ou 2º ano dos cursos de graduação, sendo considerada difícil pelos alunos. E, dentre os temas de maior dificuldade, está a Fisiologia Renal. Somado a isso, o aluno mais jovem, acostumado com as tecnologias de informação e comunicação desde cedo, pode enfrentar dificuldades em manter a atenção e o interesse durante longas aulas teóricas tradicionais. Por outro lado, as metodologias de aprendizagem ativa favorecem o desenvolvimento da autonomia e engajamento dos alunos, resultando em um efeito positivo no ganho cognitivo, que é definido como o crescimento no conhecimento, compreensão e habilidades cognitivas associadas aos objetivos de aprendizagem do curso. E, associadas a avaliações formativas, as metodologias ativas contribuem para o aprendizado, pois o aluno pode identificar suas dúvidas ao longo do processo ensino-aprendizagem, e não somente no momento de uma prova. Objective: O objetivo deste estudo foi avaliar se a utilização de metodologia de aprendizagem ativa híbrida pode contribuir para o aprendizado sobre fisiologia renal, de alunos ingressantes em um curso de Odontologia. Methods: Participaram do estudo 36 alunos matriculados em disciplina básica do 2º semestre do curso de Odontologia de uma universidade pública, que assinaram o Termo de Consentimento Livre e Esclarecido. Para o ensino de fisiologia renal foram utilizadas as seguintes estratégias de ensino e avaliação: aulas teóricas presenciais dialogadas combinadas com discussões em grupo, atividades com jogos educacionais e aplicação de quizzes via aplicativo de celular. Como atividade extraclasse individual, foram disponibilizadas aulas interativas na plataforma online Lt-Kuracloud com textos, esquemas e figuras explicativas, seguidos de exercícios com feedback imediato. Estas lições interativas e as atividades em classe incluíam momentos de avaliação formativa, para que os alunos e professor pudessem identificar as dúvidas e retomar o processo ensino-aprendizagem. O aprendizado foi avaliado por meio do ganho cognitivo, a partir das notas obtidas no pré e pós-teste, aplicados respectivamente na primeira aula e quinze dias após a última aula de fisiologia renal. Estas notas foram comparadas por meio de teste t de Student pareado, e foi considerado o nível de significância de 5%. Results: A média das notas no pós-teste ($8,03 \pm 1,52$) foi maior do que no pré-teste ($6,38 \pm 1,08$; $p < 0,05$) e o ganho cognitivo foi classificado como médio ($0,47 \pm 0,36$). Conclusion: Conclui-se que a metodologia ativa híbrida utilizada contribuiu para o aprendizado dos alunos sobre fisiologia renal e pode ter contribuído para organização de seus estudos. Support: FAPESP 2023/07742-4 Protocol: N.A.</p>



14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	TEACHING IN HEALTHCARE: THE USE OF A SERIOUS GAME ABOUT THE RESPIRATORY SYSTEM
Authors	FRANCIELI BONFANTI, VICTOR SARINHO, MARCIA ROSA DA COSTA, LUCILA LUDMILA PAULA GUTIERREZ
Affiliations	DCBS, UFCSPA
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Active learning approaches have been widely recognized as valuable tools for improving student engagement and understanding of content. Therefore, it is essential to create tools that can help teachers teach physiology. With this in mind, a serious game was developed about the human respiratory system called Oxygen, with the aim of contributing to learning in the classroom. Objective: So, the objective of this work was to analyze the perception of students of the Technical Nursing Course in the city of Encantado/RS regarding the contribution of the OXYGEN Serious Game of the respiratory system in the teaching and learning process of human anatomophysiology. Methods: This is a qualitative-quantitative cross-sectional research and technological production, based on the development of a Serious Game about the respiratory system. The study was developed in the stages of preparing the Serious Game and making the Game available to students in the human anatomophysiology class of a Technical Nursing course, after approval by the Research Ethics Committee (CAAE 52097821.0.0000.5345). The Serious Game in this study contains the human anatomical and physiological structure of the respiratory system, with images and characters, enabling student interaction. The data were obtained through responses to the Serious Game evaluation questionnaires. Data analysis was carried out in a quantitative, descriptive way and simple percentages, with the purpose of verifying the viability of the Serious Game as a teaching tool for students, according to their perceptions. Results: Eleven students participated in the study. Participants were aged between 19 and 35 years old and 67% of them lived in the city of Encantado; the others, in the upper region of Taquari Valley. The evaluation of the OXYGEN Serious Game demonstrated that 100% of students considered it suitable for use as a learning resource, that they had fun learning, that the problems to be solved captured their attention and that they would recommend its use to other colleagues. Conclusion: It is concluded that the OXYGEN Serious Game can be another tool to be used to contribute as a health teaching instrument for Nursing Technician students. Support:- Protocol: CAAE 52097821.0.0000.5345</p>



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Title	Levantamento do impacto do Museu de Ciências Morfológicas/UFMG sobre alunos do 8º ano da rede pública municipal
Authors	CARLOS AUGUSTO DA MATA-MACHADO, LETÍCIA SELVATICI-TOLENTINO, ALICE EMANUELLE SOUZA RODRIGUES, ANA PAULA MOREIRA DA SILVA, CAIO RODRIGUES GOMES, DAVI TERRA COSTA FERREIRA, DIEGO GUIMARÃES FLORENCIO PUJONI, LAURA REGINA DE OLIVEIRA SILVA, MARIA CLARA GARCIA FRANÇA, MARIA EDUARDA CHAVES DOS SANTOS JARDIM, TAYNARA VIEIRA RODRIGUES, WELLINGTON VINICIUS DE ARAÚJO GUIMARÃES, ANNAMARIA RAVARA VAGO, GLEYDES GAMBONI PARREIRA
Affiliations	Departamento de Morfologia, UFMG, Departamento de Fisiologia e Biofísica, UFMG, Departamento de Genética, Ecologia e Evolução, UFMG
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O Museu de Ciências Morfológicas (MCM), da Universidade Federal de Minas Gerais (UFMG), é um museu formado por peças anatômicas humanas reais expostas prezando-se a distribuição anatômica e funcional dos diferentes sistemas orgânicos. A diversidade de público atendido inspirou o MCM a desenvolver diferentes projetos, dentre eles “A célula ao alcance da mão”, acervo dedicado ao ensino inclusivo, composta por peças tridimensionais confeccionadas em gesso e resina, abrangendo desde as organelas até os sistemas, que incentivam o conhecimento pela percepção tátil. Alunos do 8º ano representam o montante majoritário de visitantes, devido aos anos finais do ensino fundamental serem destinados, como definido pela Base Nacional Comum Curricular (BNCC), à interação entre os sistemas. Segundo o Censo Escolar 2023, divulgado pelo Ministério da Educação (MEC), dos 11,6 milhões de alunos dessa faixa escolar, 5,1 milhões (44%) pertencem a rede municipal, a frente da rede estadual (40%) e escolas privadas (16%). Portanto, esses fatos, somados, fazem pertinente a investigação da percepção desse público sobre o corpo humano. Objective: Este estudo propõe avaliar a percepção de alunos do 8º ano do ensino fundamental sobre seu interesse pela estrutura e função do corpo humano e sobre o incentivo da observação de peças anatômicas reais e da percepção tátil de réplicas tridimensionais de sistemas orgânicos. Methods: Formulários no formato de escala Likert foram distribuídos, do dia 3 a 13 de junho de 2024, a 155 alunos do 8º ano do ensino fundamental de escolas da rede municipal de Belo Horizonte (MG) e Betim (MG). Os dados coletados foram analisados no Microsoft Excel. Results: Dos 155 visitantes, foram registrados 81,3% com 13 anos de idade, 9,7% com 14, 7,7% com 12, e apenas 1,3% com 15. Desses, 83,2% declaram já ter estudado o corpo humano. Quando pedidos para descrever seu interesse pela morfologia, apenas 3,2% declaram “nenhum”, 7,7% “abaixo da média”, 41,9% “médio”, 30,3% “acima da média” e 15,5% “alto”. Quando solicitados que avaliem o investimento da escola no preparo para cuidar do seu próprio organismo, 4,5% marcam “ruim”, 11,6% “abaixo da média”, 38,1% “médio”, 30,3% “acima da média” e 15,5% “alto”. Na avaliação de quanto a observação de peças reais enriquece seus conhecimentos sobre o corpo humano, obtivemos o seguinte: 0,6% “nada”, 11,8% “um pouco”, 13,5% “neutro”, 34,2% “razoavelmente” e 40% “muito”. Na experiência do tato nas peças tridimensionais, 0% assinala “sem importância”, 7,7% “pouco importante”, 20% “razoavelmente importante”, 40% “importante” e 32,3% “muito importante”. Quando perguntados quanto a visita ao museu motiva a busca de conhecimentos, 12,3% marcam “um pouco”, 9,7% “neutro”, 29% “razoavelmente” e 49% “muito”. Por fim, o acompanhamento e orientação oferecidos pelos mediadores são descritos por 1,3% como “neutros”, 11,6% “bons” e 87,1% “ótimos”. Conclusion: Os resultados sugerem que a visita ao acervo didático-científico do MCM, somado do acompanhamento de mediadores, sensibiliza e desperta nos visitantes o desejo de conhecer melhor o organismo. Embora os dados obtidos sobre a visita à coleção “A célula ao alcance da mão” (peças tridimensionais) indiquem um interesse estatisticamente menor quando comparado à observação das peças humanas reais, e que a maioria dos alunos registram seu interesse pela morfologia como “médio” (41,9%), a visita ao museu incentiva a busca de novos conhecimentos sobre a estrutura e funcionamento do organismo. Support: PROEX, ICB, UFMG, Rede de Museus/UFMG, Museu de Ciências Morfológicas/UFMG Protocol: N.A.</p>

Title	Estratégias para promover o aprendizado em fisiologia humana e adaptação do aluno ingressante à rotina universitária: percepção de graduandos em Odontologia.
Authors	KARINA RECHE CASALE, MARIA ANTONIA RAMOS DE AZEVEDO, FERNANDA KLEIN MARCONDES
Affiliations	Biociências, UNICAMP, Educação, UNESP
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: No curso de Odontologia, disciplinas básicas, nos primeiros semestres, de Fisiologia Humana são consideradas difíceis pelos alunos. Isto somado a dificuldades de adaptação às novas demandas, disciplinas acadêmicas, avaliações de aprendizagem, além de questões econômicas e relacionais, podem comprometer seu rendimento acadêmico e bem estar. Para promover o engajamento dos estudantes e a aprendizagem significativa, instituições e professores têm utilizado estratégias de aprendizagem ativa, para complementar ou substituir aulas tradicionais. Objective: Avaliar a percepção discente sobre a contribuição de estratégias de aprendizagem ativa para sua rotina de estudos e para o aprendizado em Fisiologia Humana.</p> <p>Methods: Este estudo foi aprovado pelo comitê de ética institucional (CAAE: 42980515.00000.5418). Participaram 47 alunos matriculados no 1º semestre do curso de Odontologia de uma universidade pública, cursando uma disciplina básica, que incluía Fisiologia Humana. As estratégias de ensino utilizadas foram vídeos pré aula (Edpuzzle), aulas interativas online (Lt-ADInstruments) para estudo individual extraclasse, aulas dialogadas na qual a explicação oral da professora foi combinada com atividades com jogos educacionais ou questões para discussão em equipe, atribuição de notas por participação para atividades extraclasse ou em classe, além de avaliações formativas que permitiam aos alunos e docentes verificarem o que havia ou não, sido apreendido. O uso das estratégias foi explicado, à medida que eram apresentadas, com base em conceitos da neurociência aplicada à educação, a fim de que os alunos compreendessem as escolhas pedagógicas da professora, e o que era esperado deles. Para análise da percepção discente foram disponibilizadas questões, em um formulário no Google Forms, em que os alunos indicaram de 0 a 10 se a estratégia havia sido útil para seu aprendizado ou rotina de estudos, justificando sua resposta. Também responderam se as explicações da professora as estratégias de ensino e avaliação haviam sido úteis. Results: A média das respostas sobre as estratégias utilizadas foram: vídeos pré-aula ($9,32 \pm 1,18$), aulas interativas online ($9,72 \pm 0,58$), jogos educacionais ($9,43 \pm 1,06$), discussões em equipe ($9,40 \pm 0,99$), atividades com notas por participação ($9,34 \pm 1,07$) e diferentes tipos de avaliações ($9,49 \pm 1,06$). Dentre as justificativas mais frequentes, os alunos indicaram que as notas por participação e a realização de avaliações formativas motivaram-nos a estudar e auxiliaram a lembrar o que tinham estudado, contribuíram para a organização do tempo e do estudo, ajudaram a rever o conteúdo, manter a matéria em dia, e estudar para provas, desenvolvendo uma rotina de estudos. Todos os participantes responderam que as explicações da professora sobre as estratégias utilizadas foram úteis para o seu aprendizado e sua motivação, tornaram o aprendizado mais didático e que se sentiram mais motivados e confortáveis para esclarecerem suas dúvidas. Conclusion: Estes resultados indicam que, na opinião dos alunos, o uso de diferentes estratégias de ensino e avaliação do aprendizado foi útil para sua adaptação e organização do tempo, ao longo do 1º semestre acadêmico, e para seu aprendizado em Fisiologia Humana, contribuindo para a participação ativa na construção de seu conhecimento, bem como para divisão de responsabilidades com o professor, nesta construção. Support: FAPESP 2022/14201-7. Protocol: N.A.</p>



14 a 17 de Setembro de 2024
Hotel Glória Caxambu Resort & Convention

Title	Didactic model of zebrafish (<i>Danio rerio</i>) for scientific dissemination of the use of animal models in vivarium
Authors	EMILLY VITORIA LEONARDO DA SILVA, ANDRESSA RAPHAELY DE LIMA SILVA, PABYTON GONCALVES CADENA, MARILIA RIBEIRO SALES CADENA
Affiliations	Departamento de Biologia, UFRPE, Departamento de Morfologia e Fisiologia Animal, UFRPE
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Didactic models are powerful teaching and learning resources. They represent reality in an interactive manner, and foster students` engagement with scientific knowledge, that is often confined to the scientific community. An example of this is the use of zebrafish (<i>D. rerio</i>) as an animal model in research, scientific knowledge that is not widely disseminated in society. Objective: To develop a 3D educational artifact of zebrafish, encompassing the early developmental stage (1 to 128 cells), embryos at 24 hours post-fertilization (hpf), and seven-day-old larvae in both normal developmental stages and affected by FASD (Fetal Alcohol Spectrum Disorder) as tools for scientific dissemination of animal model usage in vivariums.</p> <p>Methods: Didactic models were designed based on the morphology of zebrafish embryos and larvae as described in specialized literature and observed under a microscope at the Laboratório de Fisiologia e Comportamento Animal (LECA-UFRPE). The modeling of the didactic models was conducted using Blender® software version 3.0.1. Subsequently, the 3D design was sliced using Prusa® software and 3D printed on an XYZ35 TURBO model printer (Recifemecatron) in the Laboratório Plural (Department of Biology, UFRPE), using PLA (Polylactic Acid) filament. Results: The educational artifacts developed resemble zebrafish embryos and larvae, are three-dimensional and tangible, allowing for manipulation and promoting understanding of the depicted structures. Conclusion: The zebrafish didactic models are relevant for scientific dissemination of the use of animal models in vivariums and can be employed in teaching practice, facilitating the teaching-learning process. Support:- Protocol: N.A.</p>



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Title	Proposta de atividade prática para o aprendizado de potenciais gerador e de ação utilizando circuitos eletrônicos
Authors	PAULO FERNANDO GUEDES PEREIRA MONTENEGRO, AMANDO BERNARDO DE SOUZA, PAULO FERNANDO GUEDES PEREIRA MONTENEGRO
Affiliations	Departamento de Sistemática e Ecologia, UFPB, UNIVERSIDADE FEDERAL DA PARAÍBA
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Analogias são importantes ferramentas para o ensino de conceitos científicos, pois permitem estabelecer comparações entre algo que já é conhecido (domínio base) e aquilo que se pretende conhecer (domínio alvo). Diversos autores utilizam circuitos eletrônicos como modelos analógicos (domínio base) para representar processos fisiológicos (domínio alvo) e por isso, apresentam grande potencial como ferramentas didáticas para o ensino de fisiologia. Objective: Este estudo descreve a utilização de circuitos simples, adaptados para permitir a simulação de processos de produção de potenciais gerador e de ação em células excitáveis, em contexto de ensino. Methods: O projeto fundamentou-se na Teoria do Mapeamento Estrutural, assumindo a existência de analogias entre o funcionamento de circuitos eletrônicos e células excitáveis. Para esse estudo, considerou-se como atributos do domínio alvo a) a intensidade graduada do potencial transmembrana da célula excitável frente a estímulos de intensidade variada (potencial gerador) e b) a variação de frequência de pulsos (potencial de ação) em resposta a essa gradação do potencial gerador. Inicialmente, buscou-se em páginas e repositórios de vídeos por circuitos eletrônicos que apresentassem como atributos a) a variação da intensidade da resposta de um componente à variação de um estímulo sobre ele aplicado e b) a variação da frequência de resposta de um componente à variação do estímulo sobre ele aplicado. Em uma segunda etapa, realizou-se a montagem dos circuitos selecionados em protoboard, os quais foram apresentados aos alunos durante a aula sobre atividade elétrica de células excitáveis, ministrada nos componentes “Fisiologia Humana e Animal Comparada” e “Fisiologia Animal Comparada” para os cursos de Bacharelado e Licenciatura em Ciências Biológicas da Universidade Federal da Paraíba – Campus I (João Pessoa). Os alunos receberam as instruções de como operar o circuito e, a partir das observações realizadas e de questionamentos feitos pelo professor, passou-se à discussão sobre os atributos dos potenciais gerador e de ação, mapeando-os em relação aos atributos do circuito. Results: Os circuitos selecionados são simples, pois utilizam poucos componentes (LEDs, resistores, capacitor, Circuito integrado 555, protoboard e bateria de 9V), de fácil obtenção e a baixo custo. Dessa forma, futuros professores de Biologia e fisiologia podem replicar o protótipo, contribuindo para difusão de conhecimentos em Fisiologia através do uso de uma metodologia ativa de aprendizagem. Optou-se por deixar o protótipo final montado na protoboard para que os alunos pudessem visualizar a estrutura do circuito e observar os elementos resistivos e capacitivos responsáveis pela variação da corrente que atravessa o circuito, em analogia com o modelo de circuito RC da membrana celular. Ainda que os alunos não conhecessem previamente a teoria de funcionamento de circuitos eletrônicos, a visualização e manipulação do circuito permitiu que eles entendessem os seus atributos, permitindo a compreensão dos atributos do domínio-alvo. Conclusion: Apesar de não ter sido realizada uma avaliação formal sobre a eficácia do circuito como ferramenta didática, os alunos demonstraram haver compreendido o processo de produção de potenciais gerador e de ação, o que foi avaliado informalmente através da habilidade para empregar os conceitos associados a este tema em outras situações de aprendizagem ao longo da disciplina. Support: Sem apoio financeiro Protocol: N.A.</p>

Title	O ENSINO DE FISILOGIA COMO ESTRATÉGIA PARA A PROMOÇÃO DE HÁBITOS DE VIDA SAUDÁVEIS EM ESCOLARES: DIÁLOGOS ENTRE UNIVERSIDADE E EDUCAÇÃO BÁSICA
Authors	CLARISSA S SAMPAIO, LAYLA SALUANE BARBOSA DOS SANTOS, VICTOR TRAVASSOS SARINHO, ÉRICA MARIA GRANJEIRO
Affiliations	Departamento de Biologia (DCBIO), Universidade Estadual de Feira de Santana (UEFS), Departamento de Tecnologia, Universidade Estadual de Feira de Santana (UEFS), Departamento de Saúde, Universidade Estadual de Feira de Santana (UEFS)
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O ensino de Fisiologia Humana é importante para o entendimento do funcionamento e das respostas do organismo em diferentes situações, especialmente naquelas relacionadas ao estilo de vida contemporâneo, o qual é marcado por hábitos de vida não saudáveis, sendo um fator de risco para ocorrência de doenças crônicas não transmissíveis. Considerando que o ambiente escolar é um espaço propício para implementação de ações de Divulgação Científica e Educação em Saúde, o estreitamento do diálogo entre Universidade e Escolas Básicas é uma estratégia pertinente e desafiadora para a promoção da saúde e prevenção de doenças em escolares. Objective: O presente trabalho visa relatar ações extensionistas, por meio do diálogo entre Universidade e Educação Básica, com vistas ao fortalecimento do ensino de fisiologia humana na Escola e promoção da Saúde Cardiovascular de escolares. Methods: O projeto foi aprovado pelo Comitê de Ética em Seres Humanos (4.724.985) e desenvolvido, em três etapas, por estudantes de graduação dos cursos da saúde da Universidade Estadual de Feira de Santana. Etapa 1: Aplicação de um formulário online para avaliação do estilo de vida de estudantes, com idade de 11 e 12 anos, regularmente matriculados no ensino fundamental I de uma Escola Pública do Estado da Bahia. Etapa 2: Elaboração de materiais didáticos inovadores para o Ensino de Fisiologia na Educação Básica. Etapa 3: Atividades de Educação em Saúde com os Escolares. Results: Dentre os 73 entrevistados, em relação ao sexo, 54,8% dos estudantes eram do sexo feminino. 50% disseram não realizar exames de rotina, 46,6% afirmaram não controlar o que e o quanto comem e 16,4% disseram possuir algum problema de saúde. Considerando que a inserção de um jogo didático sobre alimentação saudável no Ensino de Fisiologia tem o potencial de aprimorar o autocuidado e promover hábitos saudáveis, na segunda etapa deste trabalho, foi desenvolvido um jogo didático denominado Diversão Nutritiva, o qual aborda temas como alimentos in Natura, alimentos industrializados e bons hábitos alimentares. Ademais, foram desenvolvidas atividades de Educação em Saúde na Escola, com a utilização de diferentes materiais didáticos, realização de Palestras, rodas de conversa e murais educativos. Conclusion: Os dados coletados sugerem um controle alimentar inadequado e autocuidado deficiente entre os estudantes. Nesse contexto, as ações de divulgação científica contribuíram para o entendimento dos processos fisiológicos e dos benefícios da alimentação saudável e da atividade física para a saúde. As atividades constituíram uma forma de construção de conhecimentos e auxiliaram no ensino, aprendizado e promoção da educação em saúde na escola, além de contribuírem para a formação dos estudantes de graduação envolvidos. Support: PROEX e PPPG UEFS Protocol: N.A.</p>

Title	PERCEPTION OF STRESSORS BY TEACHERS AT THE FEDERAL UNIVERSITY OF SOUTH AND SOUTHEAST OF PARÁ, CAMPUS OF SÃO FÉLIX DO XINGU, PA, BRAZIL
Authors	JOEL GILSON PACHECO MONTEIRO, GEANE BORGES DOS SANTOS, ALINE ANDRADE MOURÃO
Affiliations	Grupo de Estudos e Pesquisas em Fisiologia e Saúde na Amazônia (GEPFSA), UNIFESSPA
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Stress can be characterized as a natural reaction of our body when it experiences situations of danger or threat. In general, stress is not considered a disease, but in several sectors of the job market, emotional exhaustion is increasingly observed among many professionals, which makes it a triggering agent for several health problems. Among the groups of professionals most affected by stressful working conditions, education employees stand out. Objective: The present study sought to evaluate stressful problems faced by professors at the Federal University of South and Southeast of Pará (Unifesspa) in São Félix do Xingu-PA, as a result of their work activities, evaluating the perception of stressors in these professors at this university and also, how these stressors affect them, both directly and indirectly. Methods: In the first part of the research, we used a semi-structured questionnaire with closed questions on the topic. The participating teachers signed the free and informed consent form. The analyzes were qualitative and the data was expressed as percentage (%). Results: Interviews with the professors at the Instituto de Estudos do Xingu (IEX/Unifesspa) highlighted dissatisfaction regarding several factors, highlighting the problems of a campus that has a limited structure, located in a small city in the southeast of Pará, like other smaller municipalities which record several social and infrastructure problems. Preliminary data obtained through interviews with 10 of the unit's total of 24 teachers showed that 66.67% are women, with the remaining 33.33% men. The results showed that there are difficulties among teachers in organizing their classes, these conditions are highlighted by a lack of spaces to carry out their activities and equipment. Among those interviewed, 42.85% confirmed that they undergo medical monitoring, which can be correlated with external factors that hinder their daily functions and also social well-being, being unanimous in responding that the municipality does not offer quality of life and adequate health. In this sense, the majority, around 85.71% of those interviewed, reported that they practice physical activities as a strategy to relieve stress. Conclusion: The next phases include carrying out socio-educational actions, proposing ideas that aim to improve quality of life and health, according to the needs highlighted after previous analysis of the interviews. In these actions, we will hold a thematic seminar, with the delivery of a folder and presentations on the topic. As a positive intervention, we intend to bring together proposals for improvements in the quality of life and health of employees not only at IEX, but throughout the municipality and direct local authorities, such as public authorities and the university rector, so that specific and appropriate interventions are carried out with the aim of improving and retaining teachers in the city. Support: GEPFSA / Unifesspa Protocol: N.A.</p>

Title	Uso de reels na divulgação científica: a experiência do perfil Café com Ciência no Instagram
Authors	BÁRBARA ELISIÁRIO OLIVEIRA, RENATA ÁVILA ANDRADE, MARIA CLARA LANDIM FABIANO, LEONARDO DOS SANTOS
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, UFES
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Café com Ciência é uma proposta de utilização do Instagram para a popularização da ciência que atua por meio do perfil @cafe.comciencia. Desde sua reativação em 2023, o perfil tem sido alimentado com postagens semanais acerca de assuntos de fisiologia humana e saúde. Entre os formatos de posts de feed disponibilizados pelo Instagram, tem-se os reels, que correspondem a publicação de vídeos com até três minutos de duração. O grande diferencial dessa modalidade está relacionado ao seu potencial de alcance, que é significativamente maior quando comparada a outros tipos de publicação, já que a plataforma do Instagram prioriza sua entrega ao público. Objective: Avaliar a disseminação de conteúdo científico através da publicação de reels no perfil @cafe.comciencia no Instagram. Methods: A partir de fevereiro de 2023 foram elaborados e publicados reels com base em artigos sobre pesquisas do Programa de Pós-Graduação em Ciências Fisiológicas da UFES (PPGCF-UFES), temas de interesse do público do perfil, e assuntos de ciências da saúde relacionados ao cotidiano. A análise de alcance foi realizada a partir de dados da própria plataforma (número de visualizações e número de contas alcançadas). Já a análise de engajamento foi realizada a partir do número de interações (curtidas, comentários, salvamentos e compartilhamentos) e do cálculo do índice de engajamento ($E = n^{\circ} \text{ total de interações} * 100 / \text{visualizações}$). Results: Entre 01/02/2023 e 07/06/2024 foram publicados, ao todo, 49 reels no perfil. Entre 01/02/2023 e 07/06/2024 foram publicados, ao todo, 49 reels no perfil @cafe.comciencia. O número total de visualizações, obtido por meio da soma de todos os reels, resultou em 86.682 visualizações com média de 1770 visualizações/vídeo. Os 5 reels mais visualizados foram: apresentação de um coração isolado pulsando, pela técnica de Langendorff (7.202 visualizações, 3.583 contas alcançadas, $E=34,7\%$); alunas de mestrado mostrando aspectos curiosos do cotidiano de cientistas (6.273 visualizações, 3.397 contas alcançadas, $E=54\%$); explicação sobre como um aluno de graduação pode fazer ciência na Universidade (4.228 visualizações, 2.521 contas alcançadas, $E=33,8\%$); origem da toxina botulínica (4.158 visualizações, 3.355 contas alcançadas, $E=66,6\%$) e apresentação do PPGCF-UFES (3.058 visualizações, 2.204 contas alcançadas, $E=61,2\%$). Conclusion: O vídeo com o maior número de visualizações exibe o experimento científico como cotidiano do laboratório, o que parece despertar curiosidade do público e, com isso, grande visibilidade dentre os usuários do Instagram. Já o maior índice de engajamento (E) foi obtido por um vídeo em que uma doutoranda explica a origem da toxina botulínica, algo que, por fazer parte do interesse do público, gera sua identificação e interação com o conteúdo. Como ambas publicações apresentaram número semelhante de contas alcançadas, é possível constatar que o alcance e as visualizações não são proporcionais ao engajamento. Conclui-se que os reels, de fato, são ferramentas eficientes para difundir o conhecimento científico, porém as interações dos seguidores com o conteúdo parecem depender da presença de elementos que despertem a identificação do público. Support: FAPES Protocol: N.A.</p>

Title	EVALUATING ADHD-RELATED TIKTOK CONTENT: QUALITY ANALYSIS IN A BRAZILIAN CONTEXT
Authors	MATHEUS AUGUSTO ARRUDA MELO, ANNA CAROLINA TAVARES DE OLIVEIRA, VICTOR RODRIGUES SANTOS
Affiliations	Morphology, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: TikTok, launched in 2016, has become a prominent platform with over one billion monthly active users. In the U.S., it has 150 million users, followed by Indonesia and Brazil. In Brazil, the platform is popular among young people, with almost 99 million users, 45% of whom are between 19 and 29 years old and 52% women. TikTok stands out for its personalized recommendation algorithm, which continuously learns about user interests. Factors like likes, shares, and views influence recommendations. The platform faces challenges such as misinformation but continues to have a significant impact on digital culture.</p> <p>Objective: The research aims to identify and analyze popular TikTok videos about ADHD, focusing on symptoms, diagnosis, personal experiences, and management. The study assesses the quality and comprehensibility of the information to ensure the reliable dissemination of knowledge on the platform.</p> <p>Methods: On May 10, 2024, the study analyzed popular TikTok videos with the hashtag `#tdah` related to ADHD. Two experts classified relevant videos as `useful`, `personal experiences`, `misleading`, or `meme.` Information quality was assessed using PEMAT-A/V criteria. Statistical analyses ensured reliability and comprehensiveness, contributing to the dissemination of accurate ADHD information. Results: A total of 400 videos were analyzed on the platform, following the established criteria. Of these, 51.75% were excluded: 2% were not related to ADHD, 3.75% had no audio or text, 15% were in a language other than Portuguese, and 31% were duplicates, either due to double-blind analysis or the same video appearing on different pages. Among the classified videos, 25% were identified as useful, 23% as personal experiences, 27% as misleading, and 25% as memes. PEMAT-A/V scores were 0.48 ± 0.02 for useful videos and 0.28 ± 0.14 for misleading videos. Results of the Student's t-test demonstrated a significant difference ($p < 0.001$).</p> <p>Conclusion: The results show that, after applying the exclusion criteria, the remaining videos were categorized to reflect the diversity of content about ADHD on the platform. The high percentage of misleading videos and the significant presence of memes indicate an urgent need for better quality control and reliable sources for disseminating information about ADHD. The significant difference ($p < 0.001$) suggests that useful videos are significantly superior in terms of quality and utility compared to misleading videos, as evaluated by PEMAT-A/V. The low variability in the scores of useful videos indicates consistently high quality among these videos. Conversely, the greater variability in the scores of misleading videos suggests a wider range in the quality and utility of this content. Support: Sem financiamento Protocol: N.A.</p>



Title	Da pesquisa à extensão: Como a pandemia de COVID-19 afetou o tratamento e o cotidiano de pacientes oncológicos
Authors	GABRIEL PEREIRA RIBEIRO, DAPHINY BARROS DA CUNHA, RICARDO DE MATTOS SANTA-RITA, RAQUEL DE SOUZA GESTINARI, CELIA YELIMAR PALMERO QUINTANA, DAIANA VIEIRA LOPES ALVES
Affiliations	Laboratório Integrado de Morfologia (LIM), Universidade Federal do Rio de Janeiro, Instituto de Ciências Médicas, Universidade Federal do Rio de Janeiro
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A pandemia de COVID-19 impactou severamente a rotina da população mundial. As incertezas acerca das complicações da doença causaram pânico, uma vez que poucos estudos eram realizados e concluídos. Assim, lockdowns foram decretados ao redor do mundo, para evitar uma maior propagação do vírus. No Brasil, o desrespeito ao lockdown, junto à sobrecarga do sistema de saúde, resultou em 685.750 vidas perdidas e mais de 34 milhões de casos confirmados em pouco mais de 2 anos. O câncer é um conjunto de doenças malignas, originado de significativas alterações genéticas e epigenéticas, que conferem vantagens às células, como resistência à morte celular, invasão e metástase. Os tratamentos mais comuns para o câncer diminuem o funcionamento do sistema imune do paciente, o que os tornam imunocomprometidos. Dessa forma, eles foram classificados como grupo de risco na pandemia e tiveram consultas, cirurgias e sessões de tratamento interrompidas e adiadas em todo o país para serem preservados da infecção por COVID-19. Objective: Analisar os impactos da pandemia de COVID-19 sobre pacientes em tratamento oncológico no Brasil através de formulários on-line. Methods: Análise quantitativa, do tipo descritiva e transversal. Foi construído um questionário autoperenchível, por meio da plataforma Google Forms, que ficou disponível de agosto de 2020 a agosto de 2023. O link do questionário foi encaminhado por e-mail e através das redes sociais do “Projeto Câncer e Covid” com a chamada aos participantes. O recorte populacional estipulado foi o de pacientes em tratamento oncológico durante a pandemia de COVID-19, maiores de 18 anos, residentes no Brasil e com acesso à internet. A pesquisa foi aprovada pelo CEP UFRJ Macaé e a participação foi anônima. Results: A maioria dos participantes era do sexo feminino e com câncer de mama. Tivemos abrangência de todo território nacional. Foram relatadas alterações na rotina como mudanças de consultas presenciais para on-line e atrasos em cirurgias. Além de grande medo das notícias, pela falta de informações sobre medidas e direitos de pacientes oncológicos durante a pandemia. Nesse contexto, desenvolvemos um projeto de extensão e divulgação científica pelas redes sociais, já que muitos voluntários nos enviaram diversas dúvidas para além do nosso questionário, reflexo da ineficiente divulgação de informações destinadas a esse público. Desse modo, nossas redes sociais passaram a ser importantes veículos de divulgação científica, pelos quais os pacientes e familiares encontravam informações de fontes de grande impacto, reformuladas à linguagem acessível. Pudemos sanar várias dúvidas quanto à vacinação desse grupo, reduzindo sensações de medo e desconforto relatados durante o estudo. Além disso, pudemos responder a perguntas e interagir por enquetes, ampliando a divulgação de informações confiáveis e reduzindo as “fake news” comuns durante a pandemia. Conclusion: Portanto, é perceptível que a pandemia de COVID-19 impactou severamente a rotina de tratamento de pacientes oncológicos, com implicações biopsicossociais. Nosso trabalho pôde identificar o problema da falta e da precariedade das informações relativas ao grupo de pacientes oncológicos durante a pandemia, e ajudar a reduzir a sensação de medo e desconforto dos mesmos. Entretanto, mais estudos acerca desse assunto se fazem necessários para entender o atual cenário da oncologia brasileira e mundial e ampliar os canais de informação seguros e de divulgação científica sobre o assunto. Support: Sem apoio financeiro Protocol: CAAE 35479520.8.0000.5699</p>

Title	Didactic Strategy with Models for Teaching Transport through cell membrane
Authors	EVELLYN CAROLINE MOTA PADILHA DE OLIVEIRA, MADNA COSTA FREITAS, GERLLANNY MARA DE SOUZA LOPES, GUILHERME LUÍS FERREIRA DA SILVA, MARIA ALICE ALBUQUERQUE, PEDRO GUILHERME SANTOS CAVALCANTI, MIRELLY KAILLANY DA SILVA PEDROSA, MARIA LAURA VIEIRA DE MELO FALCÃO, EMANUELLE SOUZA AGUIAR PIMENTA, ALINE DE FREITAS BRITO
Affiliations	Escola Superior de Educação Física, UNIVERSIDADE DE PERNAMBUCO, Enfermagem, Unibra, Instituto Superior de Ciências Biomédicas, UEC, Núcleo de Pesquisa e Desenvolvimento de Medicamentos, UFC
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Understanding the mechanisms of transport across the membrane is fundamental for understanding cellular physiology, as these processes are essential for the maintenance of homeostasis and cellular functioning (Am. J. Physiol. 311:H1653, 2016). Teaching methods that involve the construction of physical models have been effective in promoting active learning and retention of knowledge in different areas of biology. The use of models as educational tool can facilitate the visualization and understanding of these complex processes. Objective: Evaluate the effectiveness of using models in understanding the different types of transport across the cell membrane among bachelor`s degree students in Physical Education. Methods: The sample was composed of students from the Bachelor`s degree in Physical Education at University of Pernambuco (UPE), who study physiology human in the second period. The activity involved the construction of models on types of transport across the membrane and the preparation of summaries on this experience. The models were divided as follows: pair 1, Secondary active transport, double 2, Simple and facilitated diffusion, double 2 – Osmosis and double 4, Primary active transport. Materials used included cardboard, colored rubber, disposable cups, paper, juice powder, styrofoam, toothpicks, beads, straws, laminated paper, among others. Each group described the objective, materials, explanation of the process and learning experience. Results: Students reported extremely positive feedback. All agreed that the teaching strategy with models allowed for better understanding of the subject, facilitated explanation between peers, promoted collaborative learning and helped with content retention. Conclusion: A Using models as a teaching tool proved to be effective in understanding the different types of transport across the cell membrane. This one method promoted more active and collaborative learning, facilitating knowledge retention. The strategy can be applied to other topics in the cellular physiology to improve teaching and learning. Support: own financing Protocol: N.A.</p>



14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	Depicting the physiology education and research across Portuguese higher education
Authors	LUIS ANTONIO MONTEIRO RODRIGUES, IRIS GUERREIRO, VERA M.S. ISCA, JOÃO GREGÓRIO
Affiliations	1 Universidade Lusófona CBIOS –Research Center for Biosciences & Health Technologies
Session	10-Ensino e Divulgação Científica
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The direction of Physiology teaching and research has been globally discussed within Physiology societies. Within the European Higher Education Area (EHEA) after the post-Bologna harmonization process, the place of physiology is still poorly characterized. Objective: This study examines the current state of Physiology education and research in Portugal as an EHEA member Methods: A mixed-methods study was developed to identify Portuguese institutions offering Physiology in their curriculum and to evaluate faculty research performance. Data from the Portuguese Directorate-General for Higher Education (DGES) from September to November 2022 helped identify relevant programs. Detailed information on course types, hours, and ECTS credits was compiled from university websites into a database of 365 courses and 764 distinct Physiology CU/D. A bibliometric analysis of faculty publications from 2017 to 2022 was made using VOSviewer to identify major research themes Results: Significant differences exist between university and technical college programs. Technical colleges frequently introduce Physiology in the first curricular year, often linked to Anatomy, while universities have been progressively integrating Physiology throughout their programs. Regarding related research outputs, our bibliometric study revealed huge disparities among faculty, with significantly greater productivity in Medical Physiology and Lifestyle Physiology, focused in four major thematic, biomedical research, cardiovascular health, athletic performance, and wellness. Conclusion: The findings confirm that Physiology shows a robust although diverse condition in Portugal, highlighting its vital role in health sciences education. Nevertheless, this characterization should be extended to other EHEA members to better define and harmonise a European Physiology identity. Support: This work was funded by national funds through the Foundation for Science and Technology (FCT), I.P., under the UIDB/04567/2020 and UIDP/ 04567/2020 projects. João Gregório is funded by a FCT Scientific Employment Stimulus contract,reference number CEEC/CBIOS/EPH/2018. Protocol: N.A.</p>



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14 a 17 de Setembro de 2024
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Title	Electrophysiological evaluation of neuron-astrocyte interaction in the Nucleus Tractus Solitarius of mice exposed to sustained hypoxia
Authors	MICKAEL S. LUZ, DANIELA ACCORSI-MENDONÇA, BENEDITO H MACHADO
Affiliations	Fisiologia, FMRP
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The Nucleus Tractus Solitarius (NTS) is critical for cardiorespiratory regulation and astrocytes play an important modulatory role in the synaptic transmission in this nucleus. Glutamate is the main excitatory neurotransmitter and its extracellular level is regulated by astrocytic glutamate transporters (GLT-1 and GLAST). Objective: To evaluate the effect of sustained hypoxia (SH) on glutamatergic transmission in the NTS of mice and its modulation by astrocytes. Methods: NTS brainstem slices were obtained from mice after normoxia (control; FiO₂=0.21, 24h) or SH (FiO₂=0.10, 24h). Electrophysiological properties of neurons and astrocytes were evaluated using whole-cell patch clamp technique Results: In control mice, we verified that the majority of astrocyte glutamate transporter activity is mediated by GLT-1 [D-aspartate: -57.2 ± 17 pA (n=5) vs D-aspartate + Dihydrokainic acid (DHK-300 μM, GLT-1 inhibitor): -19 ± 9.6 pA (n=5)]. The neuron-astrocyte interaction is present in control mice since the inhibition of GLT-1 affected the neuronal properties, such as Resting Membrane Potential [RMP; aCSF: -83 ± 4 mV (n=15) vs DHK: -71 ± 5.1 mV (n=15)] and amplitude of glutamatergic currents in neurons evoked by Tractus Solitarius (TS) stimulation [aCSF: -87.6 ± 23 pA (n=12) vs aCSF + DHK: -139.3 ± 45 pA (n=12)]. This interaction is also present in SH mice, as the inhibition of GLT-1 affected the glutamate transporter activity in astrocytes after SH [D-aspartate: -40.6 ± 6.4 pA (n=5) vs D-aspartate + DHK: -13.2 ± 4.4 pA (n=5)], the RMP of the neurons [aCSF: -78.7 ± 5 mV (n=10) vs DHK: -70.8 ± 4 mV (n=10)] and the amplitude of glutamatergic currents in neurons evoked by Tractus Solitarius (TS) stimulation [aCSF: -99 ± 24 pA (n=9) vs aCSF + DHK: -145.4 ± 26 pA (n=9)]. SH increased the amplitude of TS-evoked glutamatergic current in NTS neurons [control: -51.6 ± 11 pA (n=23) vs SH: -77.6 ± 12 pA (n=23)], which is not related to changes in astrocyte glutamate transporter activity [control: -38 ± 6 pA (n=31) vs SH: -45.9 ± 6.5 pA (n=21)] neither to the pre-synaptic release of glutamate: 1/CV2 [control: 30.1 ± 6.6 (n=23) vs SH: 50.6 ± 14.9 (n=22)], paired pulse ratio [control: 0.72 ± 0.05 (n=23) vs SH: 0.69 ± 0.03 (n=23)] and short-term depression [fifth stimulus; control: 61.1 ± 4 % (n=24) vs 57.2 ± 4.3 % (n=24)]. Conclusion: These data provide evidence that the neuron-astrocyte interaction in the NTS of mice, via GLT-1 activity, is not affected by SH exposure. Considering that the increase in TS-evoked glutamatergic current observed after SH is not related to changes in astrocyte glutamate transporter activity nor to the pre-synaptic glutamate release, we suggest that this increase is due to changes in post-synaptic mechanisms. Support: CAPES (#88887.635569/2021-00), FAPESP (#2018/15957-2) and CNPq (#309338/2020-4) Protocol: N.A.</p>



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Title	α-Glucosidase isoform G contributes to heme detoxification in <i>Rhodnius prolixus</i> and its knockdown affects <i>Trypanosoma cruzi</i> metacyclogenesis
Authors	FERNANDA FERREIRA MAISSNER, CARINA AZEVEDO OLIVEIRA SILVA, ANDRÉ BORGES FARIAS, ELANE DA SILVA RIBEIRO, EVENILTON PESSOA COSTA, JOSÉ LUCIANO NEPOMUCENO DA SILVA, JOSÉ ROBERTO DA SILVA, FLÁVIA BORGES MURY
Affiliations	Laboratório de Biociências Translacionais, UFRJ, Laboratório Integrado de Bioquímica Hatisaburo Masuda, UFRJ, Laboratório de Computação Científica, UFRJ
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The triatomine bug <i>R. prolixus</i> is a hematophagous Hemiptera and primary vector of <i>T. cruzi</i>, the causative agent of Chagas` disease. Blood-feeding is a challenging process for these organisms, due to liberation of high doses of free heme after digestion of hemoglobin, and in this arthropod, this molecule is aggregated into hemozoin (Hz), a non-oxidative biocrystal. Two major components of this phenomenon are the perimicrovillar membranes (PMM) and its biochemical marker, the enzyme α-glucosidase. Objective: In this study, we investigated the effects of α-glucosidase isoform G knockdown in heme detoxification, on the bug physiology, and on <i>T. cruzi</i> proliferation and metacyclogenesis. Methods: For this purpose, adult females of <i>R. prolixus</i> were challenged with RNAi against Rp-αGluG (dsαGluG) or control (dsGFP). The posterior midgut epithelia used for expression analysis by RT-qPCR, α-glucosidase activity, H₂O₂ quantification, and the its content for Hz formation. The anterior midgut used for residual hemoglobin analysis, total protein quantification and the rectum for parasite load upon <i>T. cruzi</i> infection analysis. Also, bioinformatics analysis on structure prediction were performed. All animal care and experimental protocols were conducted in accordance with the guidelines of the Committee for Evaluation of Animal Use for Research (Federal University of Rio de Janeiro – NUPEM/CCS) and the protocols were approved by CCS-UFRJ, under register 01200.001568/2013-87. The experiments were performed during 2021 and 2023. Results: In silico, a 3D structure of Rp-αGluG was predicted for molecular docking with the heme molecule. Our data in vivo show that the group challenged with dsαGluG mRNA relative expression (n=18; dsGFP: 2419212,485 [10711,52 – 10472965,44]; dsαGluG: 1062,08 [392,32 – 110613,40]; n=18) and α-glucosidase activity (n=4; dsGFP: 15,82 \pm 8,99; dsαGluG: 8,56 \pm 3,35 mU/mL; n=4) were reduced, confirming the effects of Rp-αGluG knockdown. Also, this group produced less Hz (n=21; dsGFP: 121,82 \pm 28,41; dsαGluG: 99,10 \pm 24,77 nmols/mL; n=18), with more intact hemoglobin available in the digestive tract (n=4; dsGFP: 100,00 \pm 0,02; dsαGluG: 186,65 \pm 13,97 %; n=4) and higher H₂O₂ formation (n=5; dsGFP: 1,29 \pm 0,24; dsαGluG: 2,31 \pm 0,51 μM; n=5). These animals also laid fewer eggs per female (n=3; dsGFP: 14,3 \pm 3,8; dsαGluG: 6,3 \pm 2,9 eggs; n=3), which had a lower hatching rate (n=3; dsGFP: 69,8 \pm 5,0; dsαGluG: 5 \pm 10,0 %; n=4). In addition, <i>T. cruzi</i> metacyclogenesis was significantly lower in the dsαGluG group (n=4; dsGFP: 23,73 \pm 10,84; dsαGluG: 9,7 \pm 4,77 %; n=5). Conclusion: The present work demonstrates the importance of Rp-αGluG in heme detoxification and the effects on the digestive and reproductive physiology of this bug, as well as its influence on the life cycle of <i>T. cruzi</i>. Since heme neutralization is a vital process for hematophagous bugs, our study provides useful information for the development of new strategies of potentially affecting the vectorial transmission of Chagas disease. Support: FAPERJ, INCT-EM Protocol: 01200.001568/2013-87</p>

Title	Electrophysiological properties of the Nucleus Tractus Solitarius glutamatergic neurons from mice submitted to the experimental model of asthma.
Authors	ENRICO MICALI AIELLO, DANIEL PHELIPE DE SOUZA, RENATO WILLIAN MARTINS SÁ, DAVI JOSÉ DE ALMEIDA MORAES
Affiliations	Fisiologia, FMRP, Fisiologia e Biofísica, ICB
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Asthma is a global health concern, causing 1 in 250 deaths. It involves airways bronchoconstriction and mucus hypersecretion due to allergen-triggered inflammation. This process activates neurons in the Nucleus Tractus Solitarius (NTS), leading to bronchoconstriction and mucus production, via excitation of brainstem parasympathetic motoneurons. However, the impact of an experimental model of asthma on the electrophysiological properties of excitatory NTS neurons is still unknown. Herein, we tested the hypothesis that the experimental model of asthma increases the excitability of the NTS glutamatergic neurons of mice. Objective: To investigate the effects of the experimental model of asthma on the electrophysiological properties of NTS glutamatergic neurons of mice. Methods: We crossed Vglut2-ires-cre knock-in and Ai95D mice to express the fluorescent protein tdTomato in glutamatergic neurons. Male Vglut2-Ai95 animals (C57BL/6J – 7 weeks old; CEUA 087/2019) were submitted to an experimental model of asthma, which consisted of three intraperitoneal sensitizations, with an interval of seven days, and intranasal challenges, for three consecutive days of ovalbumin (OVA). The control group received only PBS. Medullary slices from mice of the PBS and OVA groups were used for the electrophysiological recordings of the NTS glutamatergic neurons, using whole cell clamp technique (current clamp). These neurons were identified by the presence of tdTomato. Data are expressed as mean \pm standard deviation. Results: We found that the blockade of fast synaptic transmission reduced the excitability of NTS glutamatergic neurons from PBS (20 pA: 3.05 ± 6 vs 12.72 ± 11; $p = 0.02$; $n=53$) and OVA (20 pA: 1.29 ± 1 vs 15.08 ± 15; $p = 0.02$; $n=19$) groups. However, the capacitance (14.64 ± 7 vs 13.03 ± 7 pF; $p = 0.51$; $n=44$), resting membrane potential (-55.18 ± 7 vs -57.50 ± 11 mV; $p = 0.19$; $n=29$), intrinsic firing frequency (1.89 ± 3 vs 0.82 ± 1 Hz; $p = 0.74$; $n=29$), input resistance (0.69 ± 0.4 vs 0.70 ± 0.6; $p = 0.63$; $n=28$) and excitability (120 pA: 3.64 ± 9 vs 1.57 ± 1; $p > 0.99$; $n=29$) of the NTS glutamatergic neurons from PBS and OVA groups were not different. Conclusion: We conclude that the experimental model of asthma does not affect the intrinsic electrophysiological properties of NTS glutamatergic neurons of mice. These findings suggest that the activation of excitatory synaptic transmission to NTS neurons, rather than changes in its intrinsic excitability, contributes to the generation of bronchoconstriction and mucus hypersecretion in asthmatic mice. Support: FAPESP (2023/02346-3; 2021/06886-7). Protocol: 087/2019</p>

Title	Genomic surveillance and serological profile of SARS-CoV-2 variants circulating in Macaé and nearby cities, Southeastern Brazil
Authors	AMANDA CRISTINA VEIGA FERNANDES DA SILVA, CARINA AZEVEDO OLIVEIRA SILVA, GRAZIELE FONSECA DE SOUSA, VIKTORIA APARECIDA GOMES SILVA COELHO, LUCAS TAVARES DA CUNHA, ARTUR NUNES PAES, ALLAN PIERRE BONETTI POZZOBON, DANIELE DAS GRAÇAS DOS SANTOS, RAPHAEL MELLO CARPES, EVENILTON PESSOA COSTA, CINTIA MONTEIRO-DE-BARROS, JOSÉ LUCIANO NEPOMUCENO-SILVA, RAQUEL DE SOUZA GESTINARI, FLÁVIA BORGES MURY
Affiliations	Laboratório Integrado de Doenças Emergentes e Negligenciadas, Universidade Federal do Rio de Janeiro
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A characteristic of the COVID-19 pandemic has been the sequential emergence and global dissemination of SARS-CoV-2 variants, noted for their enhanced transmission efficiency. These variants with mutations in the Spike glycoprotein (S-glycoprotein), which interacts with ACE2 receptors in human cells is critical for infection, affects the transmissibility of the virus, which is a matter of great concern for public health. Objective: This research analyses the effects these variants on a cohort of vaccinated and naturally infected individuals from the cities of Macaé-RJ, Rio das Ostras-RJ, and Campos dos Goytacazes-RJ, Brazil, from March 2021 to March 2023. Methods: This study was approved by the Research Ethics Committee of the National Health Council (protocol number: CAAE 57373422.8.0000.5699). This investigation encompasses the Alpha (B.1.1.7), Gamma (P.1), Delta (B.1.617.2, B.1.671.3), and Omicron (BQ.1, BQ.1.1 sublines, and BF.7) variants, focusing on their genomic surveillance and implications for the disease's epidemiology. The experimental analysis included a control group (vaccinated and uninfected subjects), and an infected group (post-vaccinated subjects). Samples from nasopharyngeal swabs underwent viral detection via RT-qPCR for diagnosis confirmation. RNase H-dependent RT-qPCR (rhAmp-PCR) and third-generation sequencing were used to detect SARS-CoV-2 variants. Anti-S-glycoprotein immunoglobulins were also evaluated for vaccinated infected and noninfected volunteers. Symptoms from infected individuals were compiled in order to reveal patterns of clinical signs associated with viral infection. Results: The study included 289 participants, with infections identified by Gamma (n = 44), Delta (n = 189), and Omicron (n = 56) variants. The prevalent symptoms among the naturally infected participants were cough, fever, sore throat, headache, and runny nose. For Omicron, cognitive symptoms such as memory loss and concentration issues were reported. Interestingly, the infected vaccinated group had higher anti-S-glycoprotein IgM production (n = 28, 0.2833 ± 0.09768 OD) compared to the uninfected vaccinated group (n = 14, 0.1035 ± 0.03625 OD). Conversely, anti-S-glycoprotein IgG production was higher in the control group (n = 12, 1.770 ± 0.1393 OD) than in the infected vaccinated group (n = 26, 1.391 ± 0.1563 OD). Conclusion: This comprehensive study enables monitoring of predominant variants and their correlation with clinical cases, providing valuable insights for public health. Our research group continues to survey circulating variants, contributing to the global understanding of the pandemic. Support: FAPERJ / CAPES Protocol: CAAE 57373422.8.0000.5699</p>



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Title	Ativação Astrocítica Modula Atividade de Neurônios Magnocelulares do Núcleo Supraóptico do Hipotálamo
Authors	MELINA PIRES DA SILVA, KAROLINE MARTINS DOS SANTOS
Affiliations	Departamento de Biofísica, UNIFESP
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A regulação da osmolaridade plasmática é crucial para manter a homeostase. Além dos mecanismos periféricos que controlam o equilíbrio hidromineral, existem osmoreceptores centrais que atuam como sensores para variações mínimas na osmolaridade plasmática. Esses osmoreceptores centrais projetam-se para núcleos que podem liberar hormônios nos vasos sanguíneos capazes de desencadear mecanismos para recuperar os níveis de normais de osmolaridade. Um desses núcleos é o núcleo supraóptico (SON), localizado no hipotálamo, composto por neurônios magnocelulares osmosensíveis que, quando ativados, liberam vasopressina e ocitocina na circulação. Evidências recentes sugerem que além dos neurônios, as células gliais, especificamente os astrócitos, também estão envolvidas na osmossensibilidade do SON e podem contribuir para a excitabilidade dos neurônios magnocelulares. No entanto, o mecanismo exato pelo qual os astrócitos modulam a atividade do SON ainda não está claro. Objective: Neste estudo, o principal objetivo é de compreender 1. Se as mudanças osmóticas impactam a função dos astrócitos, e 2. se os astrócitos podem afetar a excitabilidade dos neurônios do SON. Methods: Foi utilizada a técnica de patch clamp whole-cell combinada com o uso de camundongos geneticamente modificados, tecnologia de optogenética e registro de células em two-photon para acessar tanto astrócitos quanto neurônios do SON. Results: Inicialmente, observou-se em camundongos que expressam canais de rodopsina em astrócitos que a ativação astrocítica do SON aumentou a atividade dos neurônios magnocelulares dessa região. Além disso, a exposição a soluções hipertônicas (seja hipertonicidade por alta concentração de sódio como por presença de manitol) levou a níveis elevados de cálcio intracelular nos astrócitos do SON, um indicativo de sua ativação. Para investigar a significância fisiológica da ativação dos astrócitos pela alta concentração de sódio e se a ativação dos astrócitos modula a atividade dos neurônios do SON, foi registrada simultaneamente a atividade de um astrócito e de um neurônio do SON em um desafio osmótico com sobrecarga de sódio. Foi observada uma despolarização simultânea, com a despolarização dos astrócitos ($-89 \pm 0,5$ mV vs $-87 \pm 0,6$ mV, $n = 14$; $p < 0,005$) precedendo a ativação neuronal (60 ± 10 s vs 131 ± 19 s; $n = 6$ pares, $p < 0,006$). Conclusion: Essas descobertas destacam o papel dos astrócitos na osmorregulação central, sugerindo que estas células gliais podem agir como mediadores na resposta neuronal a situações de alta osmolaridade, corroborando a hipótese de que a regulação da osmolaridade plasmática é mantida por uma rede celular vasta e complexa. Support: FAPESP #2018/07027-5 e 2023/01652-3 Protocol: CEUA 8836280223</p>



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Title	INVESTIGATING SEIZURE PATTERNS IN TEMPORAL LOBE EPILEPSY WITH VECTOR-EEG
Authors	JOÃO PEDRO CARVALHO MOREIRA, LEONARDO DE OLIVEIRA GUARNIERI, FLÁVIO AFONSO GONÇALVES MOURÃO, EDUARDO MAZONI ANDRADE MARÇAL MENDES, MÁRCIO FLÁVIO DUTRA MORAES
Affiliations	Departamento de Engenharia Elétrica, UFMG, Departamento de Fisiologia e Biofísica, UFMG
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy, though often seen as a syndrome with diverse causes and symptoms, consistently involves a specific abnormally activated circuit during ictogenesis in each patient. Understanding the spatiotemporal propagation of seizures is crucial for accurate diagnosis, prediction, and treatment. While neural dynamics recording techniques have improved, deep brain electrical activity offers unmatched temporal resolution but limited spatial resolution. This spatial limitation is influenced by factors such as electrode quantity, size, and placement within the brain. The proposed Vector-EEG technique aims to enhance spatial information while maintaining high temporal precision, providing insights into the direction and magnitude of neural dipole activity. Objective: In this work, we first evaluated the behavior of the Vector-EEG in relation to bipolar stimuli. Next, the Vector-EEG was used to study the dynamics of status epilepticus induced by intrahippocampal kainic acid administration. Methods: In the initial phase, a single bipolar Teflon-coated stainless steel electrode was used to stimulate the CA3 region of the hippocampus, simulating dipole generation in the brain. Eight Teflon-coated stainless steel wires were used to form two sets of four spatially distributed electrodes inserted bilaterally in CA1. After electrode insertion, sequential stimulation and EEG recording were performed. In the subsequent phase, 16 Teflon-coated stainless steel wires were used to create four sets of four spatially distributed electrodes for bilateral recordings in the amygdala complex and CA1 hippocampus. Following a recovery period, a three-step protocol was conducted: (1) 30 minutes of basal recording, (2) administration of kainic acid to induce seizures, and (3) two hours of seizure recording. All stereotaxic surgeries were carried out on an 8-week-old Wistar rat (~250 g) for electrode implantation (CEUA: 116/2021) and the data were collected and stored at a 2 kHz sampling rate using an Intan RHD2132 analog-to-digital converter connected to an OpenEphys system. Results: The electrical stimuli created a unidirectional path proportional to the stimulus amplitude, and reversing the dipole's polarity reversed the Vector-EEG direction. During seizures, the Vector-EEG representation markedly differed from the basal EEG. Each electrographic epileptiform pattern produced repetitive trajectories with increasingly larger magnitudes in sequential discharges. Vectors from different recording sites aligned with expectations following unilateral KA injection, indicating the progression of circuitry propagation. The anatomical distribution was evident, with vector clusters showing the directionality of primary activity sources. The Euclidean distance between two vectors served as a comparative metric, revealing that seizure epoch distances averaged 3 ± 3.5 times greater than basal epoch distances. Conclusion: The appearance of a simulated dipole caused a correlated deflection in the Vector-EEG's trajectory, demonstrating the technique's ability to represent dynamic changes in neural circuits. Applied to seizures, different recorded sites show very distinct trajectory profiles, showing an emerging cyclic trajectory pattern throughout the epileptic seizure episodes. The Vector-EEG magnitude increased during consecutive trajectory cycles, suggesting a higher neural recruitment alongside a propagation of the ictogenic process throughout recruited neural networks. Support: This study was financed by the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: CEUA: 116/2021</p>

Title	Electrophysiological evaluation of spontaneous inhibitory synaptic currents in the nucleus tractus solitarius of C57Bl/6J mice exposed to sustained hypoxia
Authors	OCTAVIO AUGUSTO DE CARVALHO MAIA, DANIELA ACCORSI-MENDONÇA, BENEDITO HONÓRIO MACHADO
Affiliations	Fisiologia, USP
Session	11-Eletrofisiologia, Biomembranas, Transportadores e Sinalização
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The nucleus tractus solitarius (NTS) in the brainstem is the gateway where visceral information converges, including the processing and modulation of cardiovascular and respiratory reflexes. The excitatory neurotransmission of these reflexes in the NTS has been widely described, while the inhibitory neurotransmission and neuromodulation require further investigation. Objective: To investigate the impact of sustained hypoxia (SH) on the excitatory (glutamatergic) and inhibitory (GABAergic) spontaneous currents in the NTS neurons of mice. Methods: NTS brainstem slices were obtained from male mice (7 weeks old) after normoxia (FiO₂=0.21, 24h) or SH (FiO₂=0.10, 24h). The electrophysiological properties of neurons were evaluated using the patch clamp technique in whole-cell voltage-clamp mode. Spontaneous synaptic currents were evaluated in the following sequential protocols: 1) control (ACSF), 2) in the presence of the glutamatergic AMPA receptor antagonist (ACSF + DNQX) and 3) in the presence of AMPA and GABAA receptors antagonists (ACSF + DNQX + Picrotoxin). Results: No significant differences were observed between normoxia and SH groups under control condition (ACSF), in frequency [SH: 9.7 ± 3.7 Hz (n=11) vs. normoxia: 4.8 ± 1.1 Hz, (n=9), p > 0.05], amplitude (SH: 32.2 ± 5.7 vs. normoxia: 18 ± 2.3 pA, p > 0.05) and half-width (SH: 3.5 ± 0.4, vs. normoxia: 6.6 ± 0.7 ms, p > 0.05). The sequential antagonism of AMPA receptors also produced no significant changes in frequency [SH: 4.1 ± 1.6 Hz (n=9) vs. normoxia: 4 ± 1.3 Hz, (n=8), p > 0.05], amplitude (SH: 30.4 ± 7.2 vs. normoxia: 21.5 ± 4.4 pA, p > 0.05) and half-width (SH: 4 ± 0.8, vs. normoxia: 6.4 ± 0.8 ms, p > 0.05). After the subsequent antagonism of GABAA receptors, we noticed the presence of residual spontaneous inhibitory currents, which were similar in both groups: frequency [SH: 0.9 ± 0.4 Hz (n=5) vs. normoxia: 1.6 ± 0.5 Hz (n=7), p > 0.05] and in amplitude (SH: 11.8 ± 3.3, vs. normoxia: 18.8 ± 4.8 pA, p > 0.05). However, the half-width was significantly reduced in neurons of SH [SH: 2 ± 0.3 ms (n=5) vs. normoxia: 4.2 ± 0.6 ms (n=7), p < 0.0180]. Conclusion: These findings reveal that GABAergic currents are present in the NTS neurons of mice and similarly to glutamatergic currents are not affected by SH. The persistent residual inhibitory current observed after GABA antagonism is probably glycinergic, which underpins the observed changes in half-width reduction in the NTS neurons of mice exposed to SH. The role of glycinergic current in the NTS neurons of mice is still matter for further investigation. Support: FAPESP (2018/15957-2 and 2023/182698) and CNPQ (309338/2020-4) Protocol: 1109/2022R1</p>

Title	O hipotireoidismo dessincroniza a ritmicidade circadiana do consumo de oxigênio e ocasiona um arrastamento do ritmo diário da temperatura corporal em camundongos machos
Authors	YANCKA DE OLIVEIRA DAMASCENO, FELIPE EMRICH, JOÃO CARVALHO-MOREIRA, PALOMA BITTENCOURT-SILVA, LUCAS R. DRUMMOND, MÁRCIO F. D. MORAES, GLAUBER SANTOS FERREIRA DA SILVA, CÂNDIDO CELSO COIMBRA, RODRIGO ANTONIO PELICIARI-GARCIA, PAULA BARGI-SOUZA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Engenharia Eletrica, UFMG, Educação Física, UEMG, Ciências Biológicas, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Os hormônios tireoidianos (HTs) desempenham um papel importante para o desenvolvimento, crescimento, diferenciação neuronal, regulação do metabolismo e da temperatura corporal. Existe uma associação entre os HTs e os ritmos biológicos evidenciada pelas ações dos HTs na regulação de parâmetros fisiológicos como o metabolismo e a termogênese, que, por sua vez, apresentam ritmicidade circadiana. Além disso, tanto o hipotireoidismo quanto o hipertireoidismo alteram a expressão dos genes do relógio em tecidos alvos, como o coração e a adeno-hipófise, levando à dessincronização do relógio biológico nestes tecidos periféricos. Finalmente, é pertinente mencionar que as desordens tireoidianas são altamente prevalentes dentre as endocrinopatias e existe uma associação entre hipotireoidismo, diabetes mellitus e síndrome metabólica. A hipótese deste trabalho é que os HTs modulam a ritmicidade circadiana da termorregulação e do consumo de oxigênio. Objective: Caracterizar o perfil diário de atividade locomotora espontânea, temperatura corporal e consumo de oxigênio (O₂) em camundongos machos eutireoideos ou hipotireoideos. Methods: Foram utilizados 24 camundongos machos adultos C57BL/6J, com aproximadamente 20g e 6 semanas de vida. Os camundongos foram separados em caixas contendo entre 4 e 5 animais, divididos em dois grupos: eutireoideos (C – controle) e hipotireoideos (H). O hipotireoidismo foi induzido utilizando o Metimazol (0,1%) em associação com o perclorato de sódio (1%) ambos dissolvidos na água de beber. Durante todo o experimento os animais tiveram acesso ad libitum à ração e água. Parte dos animais foram submetidos a uma cirurgia para a inserção de um sensor de telemetria para a avaliação da atividade locomotora espontânea (ALE) e temperatura corporal (Tc). Estes parâmetros foram testados em condições de ciclo claro:escuro (12:12) e escuro constante. Para avaliar o perfil diário de consumo de O₂ (VO₂), os animais foram colocados, individualmente, em recipientes de acrílico vedados, com apenas uma entrada e uma saída de ar, ambas as quais eram monitoradas com um analisador de gases. Os camundongos permaneceram nos recipientes por 30 min para adaptação seguido de registro por 24h. Results: Durante a fase de atividade dos animais C, foi observado o VO₂ apresenta dois picos intercalados por uma ligeira redução entre os ZTs 19-22, o qual é abolido no grupo H. As análises de ALE e Tc ao longo das 24h demonstraram que, em condições de escuro constante a oscilação diária da atividade locomotora espontânea e da temperatura corporal apresenta um padrão com menor arraste no grupo H. O VO₂ dos animais controles apresentou um padrão circadiano com valores aumentados na fase de atividade dos camundongos, enquanto os animais H apresentaram valores reduzidos, observados praticamente ao longo das 24h. Além disso, foi observada uma perda da ritmicidade circadiana no VO₂ nos animais H. Conclusion: O hipotireoidismo altera a ritmicidade da Tc e do VO₂, levando a dessincronização destes processos. Tal dessincronização pode favorecer o desenvolvimento de outros distúrbios endócrinos como o diabetes mellitus e a síndrome metabólica em associação com o hipotireoidismo. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) (APQ-0013-22) e Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ) (403972/2021-3) Protocol: 170/2021</p>

Title	PLACENTAL ATLAS: SINGLE-CELL TRANSCRIPTOME ANALYSIS IN FULL-TERM HUMAN PLACENTAS
Authors	RAFAELA GIRAÇOL DA CRUZ, VICTOR JARDIM DUQUE, JOÃO VICTOR SILVA NANI, ANDRÉ DE SOUZA MECAWI
Affiliations	Biofísica, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Pregnancy is a period of intense changes in the maternal body, particularly in the placenta, the main component of the maternal-fetal interface. This transitional organ performs essential functions for fetal development and maternal adaptation, with great cellular heterogeneity and a critical role in secreting hormones necessary for metabolic and physiological function during pregnancy. Alterations in placental development and function can lead to various complications, such as preeclampsia (PE) and gestational diabetes mellitus (GDM). Understanding this organ is crucial, prompting the development of a single-cell transcriptomic atlas of the human term placenta by integrating different single-cell RNA sequencing (scRNA-Seq) studies under physiological and pathological conditions. Objective: The objective of this study is to develop a single-cell transcriptomic atlas of full-term human placentas, integrating data from previous studies. Methods: In this study, we conducted a literature review and utilized scRNA-Seq data from 4 studies covering data from control pregnancies (Commun Biol. 6:264,2023) and pathological pregnancies, such as PE (MolCells. 45:317,2022), GDM (Fendo. 12: 679582,2021), and advanced maternal age (AMA, Jzus. 23:747,2022). We performed quality control analysis to exclude cells with a mitochondrial RNA percentage above 10%. The cells were then integrated using the `RPCA` reduction method in the Seurat package (v5) to minimize batch effects and group them according to their transcriptomic profile. Cells were classified according to markers established in the literature (Hum Reprod Update. 2024). Differential gene marker analysis was performed using the Wilcoxon test in the Seurat package. Results: Our integration comprised 20,927 cells from healthy placentas and 40,371 cells from pathological placentas, totaling 61,298 cells. We identified 11 cell types: neutrophils (CXCL1), cytotrophoblasts (FXVD3 & SPINT1), fusing cytotrophoblasts (CSHL1 & CSH2), extravillous trophoblasts (NOTUM & FSTL3), endothelial cells (IFI2), T lymphocytes (PRF1), B lymphocytes (IGLC2), monocytes (TIMP1), perivascular cells (ACTA2 & TAGLN), mast cells (CPA3), and erythrocytes (HBG2). Analysis of genes enriched in each of them revealed unique findings such as Opsin 3 (OPN3), a G protein-coupled photosensitive receptor, in all the described trophoblast groups, and Prostaglandin E Receptor 3 (PTGER3) in extravillous trophoblasts. Conclusion: This atlas provides a comprehensive view of the transcriptomes of diverse placental cell types, offering insights into placental biology. Integrating thousands of single cells enhances the statistical power to identify cell type-specific transcripts. The improved understanding of these mechanisms offers significant potential for elucidating poorly described gestational diseases and identifying novel therapeutic targets. Support: We thank São Paulo Research Foundation (FAPESP) for the undergraduate fellowship to Rafaela Giraçol (2024/01716-4) and for research funding (2019/27581-0), as well as the Higher Education Improvement Coordination (CAPES #001). Protocol: N.A.</p>

Title	Analysis of bone microarchitecture in Wistar rats at different periods of reproductive aging
Authors	DÉBORA PRAZIAS CAVALCANTE, LUANA GALANTE DOURADINHO, RITA CÁSSIA MENEGATI DORNELLES
Affiliations	Departamento de Ciências Básicas, UNESP/FOA
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Aging can lead to the emergence of pathologies, such as bone deterioration that affects the structure, functionality and composition of the bone, predisposing to osteoporosis. The etiology of this senescence-related pathology is multifactorial in origin; the reduction in 17β-estradiol (E2) concentrations during menopause contributes to the imbalance between bone formation and resorption, inducing accelerated loss. Similar to the human, rodent exhibit characteristics in reproductive aging, such as decline in follicles, irregular cycling, irregular fertility and steroid hormone fluctuations. Objective: To analyze the cortical and trabecular structure of the femoral neck in female rodents at different ages to detect and determine the onset of bone impairment and fragility. Methods: Study carried out with 15 multiparous Wistar rats aged 9, 16, and 24 months (CEUA n. 760/2022). The rats were housed in collective boxes in an environment with a controlled temperature of $22^{\circ}\text{C} (\pm 2)$, an inverted light cycle of 12/12 hours, and humidity of $55\% (\pm 10\%)$. They had free access to water and feed. The estrous cycle was monitored by daily analysis of vaginal cytology collected by vaginal smear for 15 uninterrupted days. Only rats meeting the following criteria were included in the study: 9-month-old adult rats with a regular estrous cycle, 16-month-old middle-aged rats with an irregular estrous cycle, and 24-month-old rats that were acyclic, in estropause. After euthanasia of the rats, the femur was collected and stored in physiological solution [0.9% NaCl; w/v] freezer [-20°C] to carry out the non-destructive 3D analysis of bone microarchitecture (micro-CT). Results: In the bone microtomography analysis of the trabecular bone, the percentage of bone volume (9 vs 16: $p < 0.0001$; 9 vs 24: $p = 0.0005$) and the thickness of the trabeculae (9 vs 16: $p < 0.0001$; 9 vs 24: $p < 0.0001$) was significantly higher at 9 months compared to animals aged 16 and 24 months. However, the number of trabeculae (Tb.N) parameter did not show a statistical difference at different ages. Adult rats showed less separation of trabeculae (Tb.Sp) when compared to middle-aged rats (9 vs 16: $p = 0.0005$; 16 vs 24: $p = 0.0262$), but there was no difference in relation to animals in acyclic. Cortical bone parameters in 9-month-old animals showed greater area (9 vs 16: $p = 0.0012$; 9 vs 24: $p < 0.0001$) and cortical bone thickness (9 vs 16: $p < 0.0001$; 9 vs 24: $p < 0.0001$) when compared with 16 and 24 months, however, in the polar moment of inertia (MMI) parameter, it was not possible to observe a significant difference between the groups. Regarding the number of pores, the 9 and 16 month old rats showed fewer pores than the 24 month old rats (9 vs 24: $p = 0.0004$; 16 vs 24: $p = 0.0139$). Conclusion: During reproductive senescence, cortical and trabecular bone volume, area, and thickness decrease, while cortical porosity and trabecular separation increase. These changes can occur as early as 16 months. These data indicate significant changes in bone remodeling throughout the female life cycle. Female rodents serve as effective experimental models for studying bone fragility. Support: CAPES Protocol: CEUA n. 760/2022</p>

Title	Açaí juçara administration (<i>Euterpe edulis Martius</i>) in the preconception period did not interfere in metabolic and litter parameters of female Wistar rats at an advanced age
Authors	MAYRA DIAS RODRIGUES, BRENDA FRANCISCONI DIAZ, LARISSA RUGILA DOS SANTOS STOPA, RHAUANY PELISSON GUERGOLETTE, ERNANE TORRES UCHOA, KARLA BIGETTI GUERGOLETTTO, GRAZIELA SCALIANI CERAVOLO
Affiliations	Ciências Fisiológicas, UEL, Ciências e Tecnologia de Alimentos, UEL
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Preconception care is defined as a series of interventions to a woman's health that aim at identifying and modifying biological, behavioral and social hazards through prevention and management to avoid poor pregnancy outcomes. In this context, preconception care includes good nutrition and the consumption of açaí juçara (<i>Euterpe edulis Martius</i>), rich in antioxidants polyphenols, can be a good alternative for the inclusion in the woman's diet. However, it is still not known if the preconception treatment with açaí juçara would affect metabolic parameters in healthy advance-aged females. Objective: This study aimed to evaluate the effects of the juçara pulp administration, before pregnancy, on the maternal metabolic and litter parameters of pregnant rats at an advanced reproductive age. Methods: All animal procedures were approved by the Ethics Committee on the Use of Animals, protocol n° 33/2022. At postnatal day 168, healthy female Wistar rats were treated with juçara pulp (JU group) or tap water (control/CTR group) for six weeks and then put for mating with males. When pregnant, maternal weight gain was recorded weekly. On gestational day (GD) 19, oral glucose tolerance test was performed from which a glucose uptake curve (mg/dL) and the area under the curve were obtained (arbitrary units – AU). In the next day, the rats were euthanized, blood serum was collected, and the litter of each mother was weighed and counted. In the serum, total cholesterol, high-density lipoprotein, and triglycerides (mg/dL) were measured. For statistical analysis, the T-test was used, differences when $p < 0.05$. The results are expressed as mean\pmSEM, n=number of rats/group. Results: Preconception treatment with juçara pulp reduced basal glucose levels (CTR:89.63\pm2,80, n=8 vs JU:81.00\pm2,05 mg/dL, n=7), but didn't interfere in the other parameters evaluated. Conclusion: These results suggest that the consumption of açaí juçara pulp before pregnancy can be secure for women at an advanced age. Support: Universidade Estadual de Londrina Protocol: n° 33/2022</p>



Title	EFFECTS OF HEAT THERAPY ON BODY WEIGHT GAIN, GLUCOSE TOLERANCE TEST RESPONSE, AND PHYSICAL EXERCISE PERFORMANCE IN RATS FED A HIGH-FAT DIET
Authors	RENAN DANIEL BUENO BASSO, LUANA WEIZENMANN, LUCAS MACHADO SULZBACHER, AMANDA GULARTE GOMES, EDUARDA MARQUES DE BRUM, PAULINE BRENDLER GOETTEMES FIORIN, MATIAS NUNES FRIZZO, MIRNA STELA LUDWIG, THIAGO GOMES HECK
Affiliations	Programa de Pós Graduação em Atenção Integral à Saúde, UNIJUÍ, Curso de Medicina, UNIJUÍ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity is a health issue that affects a large portion of the global population and is associated with a pro-inflammatory profile and defective heat shock response (HSR), which means a risk for the development of type 2 diabetes mellitus (T2DM) (Cell Stress Chaperones. 29:p116, 2024). Exercise is a well-known non-pharmacological intervention with anti-inflammatory effects based on HSR (Cell Stress Chaperones. 22:p271, 2017) in treating obesity and T2DM by reducing body weight and improving physical activity performance. On the other hand, heat therapy also has anti-inflammatory effects and is considered a non-pharmacological strategy for treating obesity and T2DM (Curr. Opin. C. Nut. Met. Care 18:p374, 2015).</p> <p>Objective: We aim to test whether heat therapy can prevent body weight gain and improve glucose tolerance and physical activity performance, similar to the effects of exercise. Methods: Adult (2-month-old) male Wistar rats (n=51) were subjected to a high-fat diet (HFD, 22.8 MJ/kg, 58.3% fat) or standard diet (16.6 MJ/kg, 11.4% fat) for 10 weeks. After that, all animals were adapted to treadmill exercise (10 min/day, 8 m/min) for 5 days and then underwent a maximal treadmill exercise test (7° inclination, 5m/min, increasing 5m/min each 5 min until exhaustion). Subsequently, all groups remained with their diets for 10 weeks, and HFD animals received 8 weeks of intervention with treadmill exercise (20 min., 5x/week, 60-70% of the max. velocity) or heat therapy (20 min. of water bath at 41°C, 5x/week), or without intervention, forming the following groups: Standard diet without intervention (C, n = 13); HFD without intervention (HFD, n = 12); HFD treated with exercise (HFD+Ex, n = 13); and HFD treated with heat therapy (HFD+HT, n = 13). The bodyweight gain (BWG) was evaluated before and after interventions, and the response to the glucose tolerance test (GTT i.p.) and to the exercise test were evaluated at the end of the study. Data were expressed as mean ± s.d., analyzed by One-way or Two-way ANOVA followed by Fisher LSD multiple comparisons tests, with significance considered at P<0.05. Results: In the first ten weeks (before intervention), all HFD groups increased body weight compared to the Control Group (BWG%: C=34.5±11.9; HFD=47.8±9.3*; HFD+Ex=46.8±9.2*; HFD+HT=46.5±5.5*; *P = 0.013 vs. C, F(3, 32)=4.129). After the intervention (20thvs.10th weeks), the HFD+HT group showed the lowest body weight gain among HFD groups (BWG%: C=9.6±2.6; HFD=15.6±6.4; HFD+Ex=11.2 ± 3.7; HFD+HT=4.2±5.1*; *P = 0.0002 vs. HFD and HFD+Ex, F(3, 32)=8.892). Thus, at the end of the study, the Control and HFD+HT groups presented lower body weight gain in comparison to the HFD group (BWG%: C=47.6±15.7*; HFD=70.8±13.9; HFD+Ex=63.3±11.9; HFD+HT=52.7±9.8*; *P = 0.003 vs. HFD and HFD+Ex, F(3, 32)=5.701). Both HFD+Ex and HFD+HT groups presented higher levels of glucose during GTT in comparison with the C group (*P<0.02), but lower than the HFD group (**P<0.05), without difference between them (P = 0.937) (AUC-GTT mM.min-1: C=767±64; HFD=936±61; HFD+EX=835±68*/**; HFD+HT=811±70*/**). Only the HFD+Exercise group improved physical capacity, showing better performance than HFD and HFD+HT. (Min. to exhaustion: 10th vs. 20th week: C=19.9±2.8 vs. 17.6±3.2; HFD=16.3±9.5 vs. 16.7±5.8; HFD+Ex=17.7±3.5 vs. 19.9±2.0*, HFD+HT=18.5±2.9 vs. 16.7±1.6; *P<0.05, F=(47, 47)=2.609). Conclusion: Heat therapy has benefits in treating obesity and T2DM but does not match the benefits of exercise in terms of physical capacity. Support: CAPES, PPGAIS-UNIJUÍ, FAPERGS, CNPq, grants 307926/2022–2, and 405546/2023-8 to TGH. Protocol: CEUA-0232017</p>



Title	Resveratrol Induces Protection, While Metformin Causes Cellular Damage in Ishikawa Endometrial Adenocarcinoma Cells Lineage
Authors	HENRIQUE LEAL DE OLIVEIRA, DÉBORA BISOL, CAROLINA VACCARI BATISTA, LAURA COMASSETTO ANDRADE DUARTE, GABRIEL PENTEADO SILVEIRA, GABRIELA HACKMANN SALGADO GUIMARÃES, MÔNICA WLACH, SARA HARTKE, VICTÓRIA BORGMANN ANTONIO DE SOUZA, VÂNIA MARÍLIA SANTOS FORTES DOS REIS, EDISON CAPP, LEO ANDERSON MEIRA MARTINS, ILMA SIMONI BRUM
Affiliations	Departamento de Fisiologia, UFRGS
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Endometrial cancer (EC) is a malignant neoplasm in the uterine lining with increasing incidence in developed countries. Obesity and Diabetes Mellitus 2 are linked to EC, raising the levels of mitogenic and antiapoptotic agents such as insulin, insulin-like growth factor type 1 and estrogen. Metformin (MF) is an insulin-sensitizing drug used to treat hyperglycemia and, according to reports, reduces the proliferation of cancer cells through the PI3K/Akt-mTOR signaling pathway. Resveratrol (RSV) is a natural polyphenol found in foods and can act in this pathway. Objective: This work evaluated the effects of MF and RSV on Ishikawa endometrial adenocarcinoma lineage. Methods: Experiments were conducted with 24, 48 or 72 hour treatments, covering both the lowest (MF and RSV 0.1 μM) and highest (MF 25 μM and RSV 75 μM) individual or combined doses. Cell viability assays (MTT and Sulforhodamine B), mitochondrial function and cell death (Mitotracker and Annexin/PI), cytotoxicity and caspase activation (ApoTox) were performed, along with gene expression analysis (RT-qPCR) of important pathway genes (IGF-1, among 11 others). An in silico study was also executed using CYTOSCAPE software through the STRING database and Kyoto Encyclopedia of Genes and Genomes to understand the relationship between these genes and others important in carcinogenesis. Results: The effect on cell viability was dose- and time-dependent for MF and dose-dependent for RSV. MF 25 μM treatment caused mitochondrial damage and apoptosis through caspase activation. RSV 75 μM treatment caused a decrease in mitochondrial mass, function, cytotoxicity, and caspase activation. Combined treatment decreased metabolic and mitochondrial activity, reducing cytotoxicity and caspase activation. RSV may protect against MF's toxic effects. Although the in silico study identified interesting target molecules, the molecular results at 0.1 μM were not statistically significant. Conclusion: Future molecular studies are needed to evaluate these results' impacts on EC. Support: CNPq-PIBIC Protocol: N.A.</p>

Title	Vagus nerve and spleen modulates adiposity, metabolism, and serum iron levels in hypothalamic obese and non-obese rats
Authors	ELLEN CAROLINA ZAWOSKI GOMES, AMANDA ROCHA FUJITA, GIOVANA FANHANI TESSARO, MARIANELA DÍAZ URRUTIA, EVELINE CRISTIANE BATISTA SCHMIDT, CAROLINE DE MAMAN OLDRA, ELIZÂNGELA VANESSA DA CRUZ HOFFMANN, MATHEUS DIAS MARTINS, SANDRA LUCINEI BALBO, SABRINA GRASSIOLLI
Affiliations	Centro de Ciências Biológicas e da Saúde, Universidade Estadual do Oeste do Paraná
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity-related inflammation may play a central role in disrupting iron metabolism, increasing the risk of anemia. The spleen plays a pivotal role in iron homeostasis and the inflammatory process. The vagal anti-inflammatory reflex is spleen-dependent, but its effects on iron homeostasis are unknown.</p> <p>Objective: Here, we evaluate the effects of vagus nerve and spleen ablation on adiposity and serum iron levels in anemic, hypothalamic-obese, and non-obese rats. Methods: Ethics committee approval nº 13-22. Obesity was induced by monosodium glutamate (MSG; 4 g/Kg). Non-obese or Control group (CTRL) received saline equimolar. On post-natal day (PND) 60, the animals underwent subdiaphragmatic vagotomy (SV); splenectomy (SPL); SV+SPL; or sham surgery. On PND90, the animals were phenylhydrazine-induced anemia (PHZ; 3 doses; 40 mg/kg). The non-anemic group received saline solution (0.9%). On PND120, body weight (BW), naso-anal length (NAL), Lee index (LI), spleen size, and the weight of retroperitoneal white adipose tissue (WAT-R) and inguinal (WAT-I) were evaluated. Total blood was collected, and plasma/serum was used for the measurement of glucose (Glc), triglycerides (TG), total cholesterol (TC), and serum iron. Insulin resistance (IR) was accessed by the Triglycerides-Glucose index (TyG). Results: In CTRL-PHZ rats, higher LI (4.9%), spleen size (33%), TG (23.1%), and TyG (2.6%) were observed, along with lower serum iron (45.7%) compared to the non-anemic group. Surgical procedures influenced biometric and biochemical parameters in CTRL rats, independently of the effects of PHZ-anemia. Thus, SV rats had lower BW (6.5%) compared to SHAM; and SV+SPL rats showed lower NAL (3.8%) and a higher LI (5%), compared to the SPL group. Furthermore, WAT-R was lower in CTRL-SV (41.9%) and in CTRL-SV+SPL (51.1%) rats compared to SHAM group. The fasting Glc was higher in CTRL-SV (13.9%) and CTRL-SV+SPL (14.5%) compared to SHAM. Similar increases were observed in TG and TC in CTRL SV+SPL (60.1 and 72.7%, respectively), CTRL-SV (58.9 and 67.6%), and SPL (58.6 and 43.9%) compared to SHAM group. Moreover, TyG values were higher in SV (6.9%), SV+SPL (6.6%), and SPL (6.6%) compared to SHAM rats. The SV+SPL association reduced serum iron (38.8%) in non-obese and non-anemic group compared to SHAM. In MSG-obese rats, PHZ-anemia decreased LI (2.2%), WAT R (14.6%), and WAT I (46.4%) compared to non-anemic group. An interaction effect was observed in WAT I. Thus, PHZ-anemic group reduced WAT-I in SPL (46.9%) and SV+SPL (40%) animals. Also, PHZ-anemia reduced TC (12.4%) in MSG-obese animals. Independently of PHZ-anemia, SV with or without SPL changed biometric and biochemical parameters in MSG-obese rats. Thus, MSG-SV and MSG-SV+SPL groups had lower BW (14.7 and 14.9%, respectively), and WAT-R (39.7 and 39.4%) compared to SHAM rats. Also, MSG-SV rats showed lower TG (34.7%) and TyG (5.7%) compared to SHAM group. TC was lower in all surgical groups (SPL 33.6%; SV 40.6%; SV+SPL 41%), compared to SHAM. Finally, MSG-SV+SPL group showed higher serum iron (36.1%), than SHAM rats. Conclusion: PHZ-induced anemia promotes opposite effects on body composition and lipid profile in MSG-obese and non-obese rats. Moreover, in MSG-obese rats, vagotomy with or without splenectomy reduced adiposity and improved insulin sensitivity, independently of the effects of PHZ-anemia. Support: National Council for Scientific and Technological Development (CNPq) Protocol: 13-22</p>

Title	MODULATION OF PLASMATIC IRISIN, MITOCHONDRIAL FUNCTION AND ANTIOXIDANT ACTIVITY OF BROWN ADIPOSE TISSUE IN RESPONSE TO PHYSICAL TRAINING AND/OR CARBOHYDRATE-RESTRICTED HIGH-PROTEIN DIET IN OBESE RATS
Authors	JÚLIA DE OLIVEIRA BORGES, LUCIANO EVANGELISTA DOS SANTOS FILHO, GRAZIELLE PRATES LOURENÇO DOS SANTOS BITTENCOURT, THIAGO MACÊDO LOPES CORREIA, AMANDA ALVES DE ALMEIDA, MAIARA RAULINA DE JESUS DIAS, REGIANE RIBEIRO DIAS, DOUGLAS SANTOS BATISTA, INGRA GABRIELA DE OLIVEIRA ALMEIDA, SAMUEL SANTOS BITTENCOURT PEREIRA, AMÉLIA CRISTINA MAGALHÃES GUSMÃO, RAFAEL PEREIRA
Affiliations	Programa de Pós Graduação Multicêntrico em Ciências Fisiológicas, Universidade Federal da Bahia
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity impacts negatively metabolic health, especially due to the brown adipose tissue function impairments. Irisin is an adipomyokine with a recognized impact on the metabolic profile of many tissues, but not yet fully understood in brown adipose tissue. Dietary interventions and physical training are strategies with potential effects in reducing or reversing obesity-induced impairments, including mitochondrial dysfunction and decreased antioxidant capacity in different tissues. Objective: To evaluate the effects of a carbohydrate-restricted high-protein diet associated or not with physical training on the modulation of plasma irisin, mitochondrial activity and antioxidant capacity in brown adipose tissue of obese Wistar rats. Methods: 28 male Wistar rats were submitted to an eight-week obesity-induced hypercaloric diet (HC) and then divided into four groups/experimental protocols (n=7, each): Hypercaloric diet, sedentary (HCS), hypercaloric diet, physical training (HCT), carbohydrate-restricted hyperprotein diet, sedentary (HPS) and carbohydrate-restricted high-protein diet, physical training (HPT). At the end of 12 weeks of the experimental protocol, serum and brown adipose tissue (BAT) were collected and stored for subsequent analysis. The BAT antioxidant capacity was assessed through the activity of the enzymes: catalase, glutathione peroxidase (GPx), and superoxide dismutase (SOD). Citrate synthase enzyme activity was quantified to evaluate mitochondrial function. Serum Irisin was measured using the ELISA method, and the gene expression of its precursor (i.e., FNDC5) and UCP-1 were quantified in BAT by qPCR. This study was approved by the CEUA of IMS/CAT-UFBA (Protocol nº 053/2017). Data were analyzed by Two-Way ANOVA followed by the Bonferroni post-test. The significance level was set as $p < 0.05$. Results: Physical training promoted a significant increase in serum irisin concentration (HCS: 5.8 ± 1.1; HCT: 10.6 ± 3.2; HPS: 5.2 ± 1.6; HPT: 14.8 ± 6.7, $p = 0.0006$) and FNDC5 gene expression in BAT (HCS: 1.0 ± 0.1; HCT: 1.4 ± 0.2; HPS: 1.0 ± 0.1; HPT: 1.4 ± 0.3, $p = 0.0024$) regardless of diet. Citrate synthase activity was also influenced only by physical training (HCS: 0.1 ± 0.05; HCT: 0.4 ± 0.1; HPS: 0.2 ± 0.05; HPT: 0.4 ± 0.04, $p < 0.0001$), as well as the activities of SOD enzymes (HCS: 0.3 ± 0.2; HCT: 1.3 ± 0.4; HPS: 0.4 ± 0.2; HPT: 1.0 ± 0.2, $p < 0.0001$), Catalase (HCS: 0.5 ± 0.1; HCT: 0.8 ± 0.1; HPS: 0.3 ± 0.1; HPT: 0.7 ± 0.2, $p < 0.0001$) and GPx (HCS: 0.02 ± 0.01; HCT: 0.06 ± 0.02; HPS: 0.02 ± 0.01; HPT: 0.06 ± 0.01, $p < 0.0001$). Similar to previous results, physical training also promoted upregulation of UCP-1 gene expression in BAT (HCS: 0.9 ± 0.1; HPT: 1.3 ± 0.3; HPS: 1.1 ± 0.2; HPT: 1.4 ± 0.2, $p = 0.0030$). Conclusion: Physical training improved serum Irisin and all investigated parameters in the BAT. Furthermore, physical training also positively modulated FNDC5 and UCP-1 gene expression in BAT. Such findings may suggest possible effects of increased irisin secretion during physical exercise on the benefits observed in antioxidant capacity and mitochondrial function in BAT. Support: Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB) Protocol: 053/2017</p>

Title	AT1 receptor antagonism alleviates lipid metabolism disorders and inflammatory markers in nonalcoholic fatty liver disease by regulation the SIRT1/NF-κB pathway in high-fat-diet-fed rat
Authors	LAVÍNIA BEATRIZ HERMINIO DA SILVA, ROSA ARIEL BUSTILLO-RIVAS, GLÓRIA ISOLINA BOENTE PINTO DUARTE, LUIZA ANTAS RABELO, VALÉRIA NUNES-SOUZA
Affiliations	Department of Physiology and Pharmacology, UFPE, Institute of Biological Sciences and Health, UFAL
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The high prevalence of nonalcoholic fatty liver disease (NAFLD) represents a serious public health problem. Furthermore, evidence indicates the Angiotensin II-AT1 pathway in the development of NAFLD (Nunes-Souza et al., Oxi. Med. and Cel. Long., 2016) and the antagonistic signaling between Sirtuin 1 and NF-κB regulates energy metabolism and inflammatory response present in many chronic metabolic diseases (Kauppinen et al., Cell Signal. 25:1939,2013). Objective: To evaluate the effects of AT1 receptor antagonism in NAFLD in high-fat-diet-fed rats. Methods: 8-week-old male Wistar rats were divided into: Control group (CT, n=5), which received a standard rodent diet (11.8% kcal lipids); Obese group (HFD, n=6), which received a high fat diet (58.4% kcal lipids) for 16 weeks; Control+losartan group (CT-L, n=7) and Obese+losartan group (HFD-L, n=8) which concomitantly received pharmacological intervention with losartan (15mg.Kg-1/day-gavage) in the last 8 weeks of the dietary intervention. Body weight, white adipose tissue (WAT) index and insulin resistance were evaluated. Hepatic lipid deposition was assessed by Folch technique followed by measurement of lipid fractions using commercial kits. Relative mRNA expression in liver was determined by quantitative polymerase chain reaction (qPCR). The protocols were approved by UFPE Ethics Committee for the Use of Animals (Process 0089/2021). Results: Compared to the control, the HFD groups showed an increase in body weight (HFD= 542.6 ± 20.99 vs CT= 423.0 ± 14.00; HFD L= 493.8 ± 19.23 vs CT-L= 418.8 ± 11.02, p<0.05) accompanied by a higher adiposity index (HFD = 7.93 ± 0.59 vs CT= 4.55 ± 0.91; HFD-L= 9.74 ± 1.01 vs CT-L= 3.76 ± 0.53, p<0.05), and insulin resistance, the latter was attenuated in the HFD+LOS group. Total hepatic lipid levels were significantly higher in the HFD group compared to CT (HFD= 0.19 ± 0.01 vs CT= 0.15 ± 0.01, p=0.0298), but not among the groups treated with losartan (HFD-L vs CT-L, p=0.555). The HFD and HFD-L groups had a significant increase in hepatic triglycerides compared to the respective control group (HFD= 9.56 ± 1.36 vs CT= 4.02 ± 0.28; HFD-L= 7.85 ± 0.75 vs CT-L= 3.37 ± 0.23, p<0.01), as well as in cholesterol levels (HFD= 3.03 ± 0.28 vs CT= 1.21 ± 0.09; HFD L= 2.15 ± 0.21 vs CT-L= 1.08 ± 0.08, p<0.01). However, the treatment with losartan decreased cholesterol levels in the HFD-L group when compared with HFD (HFD-L = 2,15 ± 0.21 vs HFD= 3.03 ± 0.28, p= 0.0295). The HFD group showed an increase in relative mRNA expression for Angiotensinogen (HFD= 1.44 ± 0.15 vs CT= 1.02 ± 0.09, p= 0.0488), AT1 receptor (HFD= 1.74 ± 0.19 vs CT= 1.01 ± 0.07, p= 0.009) and CD36 (HFD= 1.88 ± 0.33 vs CT= 0.81 ± 0.23, p= 0.0392) compared to the control, but not among the HFD-L and CT-L groups, suggesting the involvement of the Angiotensin II-AT1 axis in NAFLD. Furthermore, losartan treatment increased relative mRNA expression for Sirtuin 1 in HFD-L (HFD-L= 1.45 ± 0.10 vs CT-L= 0.97 ± 0.14, p= 0.0194), accompanied by a decreased in CD68 (HFD-L= 1.19 ± 0.2 vs HFD= 2.5 ± 0.4, p= 0.0323) and NFκB (HFD-L= 1.37 ± 0.1 vs HFD= 1.85 ± 0.2, p= 0.044). Conclusion: Angiotensin II-AT1 pathway contributes to lipid accumulation and inflammation in high fat diet-induced NAFLD. In addition, AT1 receptor antagonism may attenuates such disorders by regulation of Sirtuin1/NF-κB axis. Support: Fundação do Amparo a Ciência e Tecnologia (FACEPE, Processo APQ-1038-2.07/22); National Institute of Science and Technology in Nano-Biopharmaceutics (N-BIOFAR); Bolsa DS-CAPES Protocol: 0089/2021</p>

Title	Consequências do hipotireoidismo no perfil diário de ativação neuronal dos núcleos supraquiasmático e paraventricular do hipotálamo de camundongos C57BL/6J machos
Authors	LETÍCIA SELVATICI-TOLENTINO, BRUNO HENRIQUE GOMES, FELIPE EMRICH, ROBERTA ARAÚJO LOPES, RAPHAEL ESCORSIM SZAWKA, CÂNDIDO CELSO COIMBRA, RODRIGO ANTONIO PELICIARI-GARCIA, PAULA BARGI-SOUZA
Affiliations	Fisiologia e Biofísica, UFMG, Ciências Biológicas, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O eixo tireoidiano (HPT) compreende o Hormônio Liberador de Tireotrofina (TRH), produzido no núcleo paraventricular do hipotálamo (PVN), que estimula a secreção do Hormônio Estimulador da Tireoide (TSH). O TSH estimula a síntese dos hormônios tireoidianos (HTs), os quais, então, inibem a síntese e secreção de TRH e TSH. Sabe-se que os níveis séricos de TSH e HTs oscilam ao longo do dia por influência do relógio central dos núcleos supraquiasmáticos (SCN). O hipotireoidismo, uma desordem endócrina comum, resulta em alterações na termogênese, no metabolismo e a dessincronização dos ritmos endógenos no coração e na adeno-hipófise. Contudo, a consequência do hipotireoidismo para a ritmicidade circadiana do próprio eixo ainda é desconhecida. Objective: Investigar os efeitos do hipotireoidismo na atividade dos neurônios do SCN e PVN ao longo das 24h. Methods: Camundongos machos C57BL/6J foram divididos em Controle (C) e Hipotireoideos (H). O hipotireoidismo foi induzido com 0,1% Metimazol e 1% Perclorato de Sódio na água de beber por 45 dias. Em seguida, os animais foram divididos em subgrupos, anestesiados, perfundidos com paraformaldeído (PFA) 4% e eutanasiados a cada 4 h ao longo de 24h (Zeitgeber Time (ZT) 0: 7h; n=3-4/ZT/grupo). Os cérebros foram fixados em PFA 4% por 24h, e saturados com solução de sacarose 30%, seguido de congelamento em isopentano 99% a -50°C e armazenamento a -80°C. Foram, então, fatiados a 30 µm de espessura no criostato, e os cortes submetidos a imunohistoquímica da proteína c-FOS. As imagens foram capturadas com microscópio. Os neurônios imunorreativos nas áreas bilaterais do PVN (bregma: -0,58mm ao -1,22mm) e do SCN (bregma: -0,22mm ao -0,82mm) foram contados no software ImageJ, e a quantidade foi normalizada pela área analisada de cada corte. Os dados submetidos a análise de variância (ANOVA) de uma via para testar a variação ao longo do dia, seguido de análise de ajuste de curva cosseno para 24h. ANOVA de duas vias foi utilizada para avaliar a influência dos fatores tempo e tratamento, seguido de análise de pós teste pareado para cada ZT. Os testes foram realizados no software Prism 9.3.1. Results: A atividade neuronal dos SCN apresentou variação temporal ($P < 0,001$), interação entre os fatores tempo e tratamento ($P < 0,001$), e ritmicidade circadiana (C: $P = 0,002$; H: $P = 0,002$) nos dois grupos. Os valores médios de acrofase, mesor e amplitude foram 7,73; 99,99 e 30,08, respectivamente. Com relação a atividade neuronal do PVN, foi observado variação ao longo do dia nos dois grupos (C: $P = 0,0135$; H: $P = 0,0022$), embora não sejam circadianas (C: $P = 0.4563$; H: $P = 0.2021$). Houve alterações significativas com relação ao tempo ($P < 0,0001$), tratamento ($P < 0,0001$), além de interação entre essas variáveis ($P = 0,0027$). Por último, a comparação pareada demonstrou que o hipotireoidismo aumenta a atividade neuronal do PVN nos ZTs 16 e 20, na fase de atividade dos roedores. Conclusion: O hipotireoidismo modula diferencialmente a atividade neuronal dos núcleos SCN e PVN do hipotálamo, diminuindo o número de neurônios ativos no SCN no meio da fase clara (ZT 8) e aumentando a quantidade de neurônios ativos no PVN na fase escura (ZTs 16 e 20). Entretanto, mais estudos são necessários para esclarecer as repercussões do hipotireoidismo sobre a ritmicidade do próprio eixo tireoidiano. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) (APQ-00013-22) e Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ) (403972/2021-3). Protocol: CEUA UFMG: 170/2021</p>

Title	CURCUMIN AND PHYSICAL EXERCISE PREVENT THE WHITENING OF BROWN ADIPOSE TISSUE IN OVARIECTOMIZED DIABETIC RAT
Authors	REGIANE RIBEIRO DIAS, JÚLIA DE OLIVEIRA BORGES, AMANDA ALVES DE ALMEIDA, MAIARA RAULINA DE JESUS DIAS, THIAGO MACÊDO LOPES CORREIA, DOUGLAS SANTOS BATISTA, SAMUEL SANTOS BITTENCOURT PEREIRA, LAURA SIQUEIRA SOUZA BRITO, ALICE VELOSO ROCHA SANTANA, SUZETE CARVALHO LANDULFO LUZ, TELMA DE JESUS SOARES, AMÉLIA CRISTINA MENDES DE MAGALHÃES GUSMÃO
Affiliations	Programa de Pós graduação Multicêntrico em Ciências Fisiológicas, UFBA
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Type 1 diabetes mellitus associated with ovarian hormone deprivation promotes changes in brown adipose tissue's morphology and metabolic activity, negatively impacting metabolism. Curcumin and physical training appear as non-pharmacological therapeutic strategies in managing type 1 diabetes mellitus and its complications. Objective: To evaluate the effects of curcumin and physical training on morphological parameters in brown adipose tissue (BAT) of diabetic and ovariectomized Wistar rats. Methods: 24 female Wistar rats were used, submitted to bilateral ovariectomy surgery, and type I Diabetes induced by intravenous administration of streptozotocin (STZ: 40 mg/kg) two weeks after the surgical procedure. Subsequently, the rats were randomly divided into four experimental groups (n=6): sedentary ovariectomized diabetics (DOS), trained ovariectomized diabetics (DOT), sedentary ovariectomized diabetics + Curcumin (DOS+CUR), trained ovariectomized diabetics + curcumin (DOT+ CUR). One week after the induction of type 1 diabetes mellitus, the groups began treatments with curcumin (100 mg/kg/day) via gavage diluted in natural yogurt and physical exercise on a treadmill at an intensity of 70% maximum aerobic capacity, five days/week, for 8 weeks. At the end of the experiment, the animals were euthanized, and the visceral adipose tissue (VAT) deposits (sum of mesenteric, retroperitoneal, and parametrial deposits) and brown adipose tissue were removed, weighed, and fixed. An optical microscope with a digital camera (Olympus BX51) was used to obtain photomicrographs of histological sections stained with hematoxylin and eosin, 20x magnification. The images were analyzed for the number of total, unilocular, and multilocular adipocytes per field using the ImageJ® program. This study was approved by the CEUA of IMS/CAT-UFBA (Protocol nº 096/2021). Data were analyzed using Two-Way ANOVA followed by Tukey's post-test. Differences were considered significant when $p < 0.05$. Results: TAM weight did not differ between the experimental groups, while TAV increased by physical training alone or associated with curcumin (DOS: 0.5 ± 0.1; DOT: 0.7 ± 0.1; DOS+CUR: 0.4 ± 0.04; DOT+CUR: 1.0 ± 0.2, $p < 0.0001$ and $p = 0.0496$). Physical training and curcumin increased the percentage of multilocular adipocytes (DOS: 4.9 ± 1.8; DOT: 22.2 ± 5.9; DOS+CUR: 20.1 ± 4.7; DOT+CUR: 31.5 ± 4.9, $p < 0.0001$), and the groups treated with curcumin showed a greater quantity of total adipocytes per field in the BAT (DOS: 105.8 ± 13.7; DOT: 108.9 ± 10.2; DOS+CUR: 134.7 ± 10.2; DOT+CUR: 119.2 ± 8.5, $p = 0.0003$). Conclusion: Physical training and curcumin promoted an increase in multilocular adipocytes, improving the morphology of the TAM, which presented an altered pattern predominantly unilocular due to the impacts of diabetes and ovarian hormone deprivation. Support: Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB) Protocol: 096/2021</p>

Title	EUPHORBIA TIRUCALLI (AVELOZ) LATEX INTAKE INCREASES BONE MARROW MONONUCLEAR CELLS (BMMC'S) REACTIVY OXYGEN SPECIES (ROS) PRODUCTION
Authors	MARIA EDUARDA DE SOUZA BARROSO, EDGAR HELL KAMPKE, RAFAELA AIRES, LORENA NASCIMENTO SANTOS NEVES, BIANCA PRANDI CAMPAGNARO, LUCIANA POLACO COVRE, ELISARDO CORRAL VASQUEZ, RICARDO MACHADO KUSTER, SILVANA DOS SANTOS MEYRELLES
Affiliations	Laboratory of Integrative Physiology, UFES, Laboratory of Translational Physiology and Pharmacology, UVV, Center for Infectious Diseases of UFES, UFES, Department of Chemistry, UFES
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Bone marrow mononuclear cells (BMMC's) are important source of hematopoietic stem cells, mesenchymal stem cells and endothelial progenitor cells and participates in adult tissue repair. Euphorbia tirucalli (Aveloz) latex has been widely used by Brazilian population as an adjuvant therapy for various diseases, especially cancer. Although Aveloz latex contains alkaloids that can be very caustic, no in vivo studies have been done to investigate its effects on different physiological systems and organs. Objective: Investigate the action of E. Tirucalli latex intake on the reactive oxygen species (ROS) production in the bone marrow cells of Wistar rats. Methods: Male Wistar rats were divided into two groups: Control (n=5-8) treated with water (1 mL) and Aveloz (n=5-8) treated with Aveloz latex (13.47 mg/kg/1mLH₂O) administered by gavage for 15 days. After treatment, the femur and tibia of the experimental animals were removed, and with the help of a syringe, bone marrow cells were collected (1x10⁶ cells/mL) by flushing with culture medium. Then BMMC's underwent flow cytometry, and ROS levels were quantified using fluorescent probes for superoxide anion (dihydroethidium, DHE) and hydrogen peroxide (2',7'-dichlorofluorescein diacetate, DCF). In addition, BMMC's viability was determined by the Trypan Blue dye exclusion test. Results: Aveloz treated animals showed a significant increase (p<0.05) in the superoxide anion levels compared to Control group (41574±2947 a.u. vs. 28899±4342 a.u), respectively. No difference was observed in the hydrogen peroxide levels between Control (2433±335.8 a.u.) and Aveloz (2302±240.6 a.u.) groups. A significant decrease (p<0.05) in BMMC's viability was observed in Aveloz (75.80±1.52 %) compared to Control (90.60±0.23 %) animals. Simultaneously, a significant increase in the number of dead BMMC's were verified in the Aveloz (23.78±1.58%) compared to Control (9.420±0.24%) group. Conclusion: Aveloz intake for 15 days significantly compromises BMMC's viability, which may be caused by the increased ROS production. These original and important results highlight the importance to carefully investigate the in vivo Aveloz intake effects on the different physiological systems. Support: Foundation for Research Support of Espírito Santo (FAPES), National Council for Scientific and Technological Development (CNPq), and Coordination for the Improvement of Higher Education Personnel (CAPES). Protocol: CEUA-UFES No. 01/2022</p>

Title	TRPV1 MODULATES THE HYPERTHERMIA INDUCED BY BETA-3 ADRENERGIC STIMULATION
Authors	PEDRO LUCAS CAILLAUX LUCIANO, GABRIEL DA SILVA TEODORO FARIA, LUCIANA DE SOUZA BRANDÃO MARTINS, KIANY MIRANDA, SILVIA CAROLINA GUATIMOSIM, MARIA NATHALIA DE CARVALHO M M F BORGES, MARISTELA DE OLIVEIRA POLETINI
Affiliations	Fisiologia e Biofísica, UFMG, Departamento de Ciências Biológicas, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Transient receptor potential vanilloid type 1 (TRPV1) channels are calcium channels expressed in both neuronal and non-neuronal tissues, including brown adipose tissue (BAT). Blocking TRPV1 results in hyperthermia by activating cold-defense mechanisms, which involve the stimulation of β3-adrenoreceptor signaling in BAT. However, the role of TRPV1 in thermogenesis induced by direct β3-adrenergic stimulation is not fully understood. Objective: To evaluate the participation of TRPV1 in the thermogenesis induced by β3-adrenergic stimulation. Methods: In all experiments, mice were implanted with a telemetric probe under anesthesia to monitor abdominal temperature (Ta). Mice knockout for TRPV1 (KO) in a C57BL background and their littermates' wild type (WT) were injected with the β3-adrenergic agonist CL-316,243 (1 mg/kg) or its vehicle (saline) at 12:00 PM, and Ta was monitored before and for 3 hours after the treatments. Another set of WT animals was injected with the TRPV1 agonist resiniferatoxin (RTX, dose: 500 ng/kg) or its vehicle (ethanol 1%). One hour later, both RTX and vehicle-treated animals received the β3-adrenergic agonist, and their Ta was monitored before and for up to 2 hours after treatments. At the end of the experiment, mice were euthanized by cervical dislocation, and BAT was removed for histological analysis. Two-way ANOVA followed by Sidak's post-test was used to reveal statistical differences in Ta. Results: KO mice (n=9) showed lower Ta compared to WT mice (n=9) before β3-adrenergic agonist treatment (p<0.0001), but no significant differences were observed after the treatment. The change in Ta from baseline to peak revealed that KO animals showed a greater response to β3 stimulation (p=0.0063). Furthermore, TRPV1 activation by RTX abolished the increase in Ta observed after CL-316,243 treatment (p<0.0001). The β3-adrenergic stimulation was confirmed by an increased number of BAT cells after CL-316,243 treatment (p<0.05). Conclusion: The lack of TRPV1 contributes to a greater thermogenic capacity, as TRPV1-KO mice responded similarly to WT mice despite displaying lower basal Ta. Additionally, CL-316,243 treatment was unable to increase Ta under TRPV1 stimulation. Thus, TRPV1 appears to modulate β3-adrenergic stimulation, potentially attenuating or blocking the response of β-adrenergic signaling. Support: CNPQ, CAPES, FAPEMIG Protocol: CEUA, 87/2024</p>

Title	Impact of Cashew Nut Kernel Oil on Glucose and Glycogen Metabolism
Authors	GABRIELA ARAUJO FREIRE, CAIO BRUNO RODRIGUES MARTINS, RAIMUNDO RIGOBERTO BARBOSA XAVIER-FILHO, LANDERSON LOPES PEREIRA, ANA BEATRIZ OLIVEIRA DA FONSECA, NYLANE MARIA NUNES ALENCAR, ANA PAULA DIONÍSIO, MARISA JADNA FREDERICO CANUTO
Affiliations	Departamento de Fisiologia e Farmacologia, UFC, UNIVERSIDADE FEDERAL DO CEARÁ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Functional foods may help control glucose metabolism and reverse the initial stages of Type 2 Diabetes Mellitus, improving patients` quality of life. Cashew nut kernel oil (CNKO), an innovative product, has characteristics of a functional food, but they have not yet been sufficiently explored. Objective: The aim of this study was to evaluate the effects of CNKO on glucose and glycogen metabolism. Methods: The glucose tolerance test (GTT), glycogen distributions among tissues in animals, and alpha glucosidases in vitro were performed. Glycemia was measured before any treatment or glucose overload (zero time represents fasting glycemia). C57Bl6 mice (18-25g) received CNKO (0,1; 0,5 and 1,0 g/kg), extra virgin olive oil (0,5 g/kg) and glucose (2 g/kg of body weight) was administered 90 min later. Glycemia was measured at 15, 30, 60, and 120 min after glucose overload by the glucose oxidase method. The animals were then euthanized. Results: Treatment with CNKO (0,1 g/kg) reduced serum glucose by approximately 24% and 16% at 15 min and 30 min, respectively, with CNKO (0,5 g/kg) decreased serum glucose by about 20%, 30% and 25% after 15, 30 and 60 min, respectively. The highest dose of CNKO tested (1,0 g/kg) reduced serum glucose by 11% at 15 min. The extra virgin olive oil (0,5 g/kg) increased serum glucose when compared with the hyperglycemic control group. Concentration muscle glycogen in the muscle reduced by 50% and the liver reduced by 28%. CNKO and Acarbose (5mg/ml, both) reduced intestinal enzymes (alpha-glucosidases) by 70 and 80%, respectively. Conclusion: The OACC group regulated blood glucose in vivo; unpublished effect and reduced the alpha glycosidase activity in vitro. CNKO consumption have a positive impact on glucose and glycogen metabolism. Support: FUNCAP, EMBRAPA, CNPQ e CAPES. Protocol: CEUA-NPDM 601704230</p>

Title	SHORT-TERM INTAKE OF AVELOZ (EUPHORBIA TIRUCALLI) CAUSES LIVER DYSFUNCTION AND HEPATOCYTE INFLAMMATION IN HEALTHY RATS
Authors	HELLEN SILER VASCONCELLOS, LETICIA VERONÉS MARSAGLIA, EDGAR HELL KAMPKE, ÁGATA LAGES GAVA, ELISARDO CORRAL VASQUEZ, RICARDO MACHADO KUSTER, MARIA EDUARDA DE SOUZA BARROSO, SILVANA DOS SANTOS MEYRELLES
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, UFES, Programa de Pós graduação em Ciências Farmacêuticas, UVV, Departamento de Química, UFES
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Euphorbia tirucalli (Aveloz) is a plant native to Africa, brought to Brazil where it easily adapted and has been popularly used for the treatment of a variety of infectious, tumoral, and inflammatory diseases. Although Aveloz is widely used by the population, its effects on different organs and physiological systems are not well understood. Objective: To evaluate in healthy rats the effects of short-term Aveloz administration on the liver function and hepatocyte inflammatory response. Methods: Male Wistar rats were divided into two groups: Control (CT, n=5-8) treated with water (1 mL) and Aveloz (AV, n=5-8) treated with Euphorbia tirucalli latex (13.47 mg/kg/1mLH₂O) administered by gavage for 15 days. The effects of Aveloz on liver function were assessed by blood measurements of glutamic-pyruvic transaminase (GPT) and glutamic-oxaloacetic transaminase (GOT) activities. Furthermore, the inflammatory response was measured through the activity of the enzyme myeloperoxidase (MPO) in the liver tissue homogenate. Results: Fifteen days of Aveloz treatment produced a significant increase ($p < 0.05$) in blood levels of GOT (128.4 ± 22.1 U/L) and GPT (65.83 ± 7.05 U/L) compared to the CT group (60.89 ± 12.3 U/L and 49.25 ± 2.62 U/L), respectively. Additionally, in Aveloz-treated rats, we observed a significant increase ($p < 0.05$) in hepatocyte MPO activity (0.0004927 ± 0.000011 a.u.) compared to CT animals (0.001188 ± 0.000018 a.u.). Conclusion: This is the first study that evaluate the short-term effects of Euphorbia tirucalli ingestion on the liver. Our initial results show that Aveloz intake can cause liver dysfunction and increase hepatocyte inflammatory activity. These findings underscore the importance of further studies to investigate the actual effects of this plant on various physiological organs and systems. Support: National Council for Scientific and Technological Development (CNPq), Coordination for the Improvement of Higher Education Personnel (CAPES) e Espírito Santo Research Support Foundation (FAPES). Protocol: CEUA-UFES nº 01/2022</p>

Title	Water deprivation poses a catabolic challenge to systemic and skeletal muscle protein metabolism in mice
Authors	JOÃO DA CRUZ-FILHO, DANIELY MESSIAS COSTA, TATIANE OLIVEIRA SANTOS, RAQUEL PRADO SILVA, HEVELY CATHARINE ANJOS-SANTOS, NAIMA JAMILE DOS SANTOS MARCIANO, ROGER RODRÍGUEZ-GÚZMAN, ANA BEATRIZ HENRIQUE-SANTOS, DANIEL BADAUÊ-PASSOS JR., ANDRÉ SOUZA MECAWI, DANILO LUSTRINO
Affiliations	Department of Physiology, UFS, Department of Biophysics, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Dehydration (DH) is detrimental and originates from the deficit in total body water, usually as a result of low water intake. Even though it is not frequently faced as it should be, DH predisposes to development of chronic diseases, as well as to age-associated muscle mass loss. Nevertheless, little is known about the effect of DH on systemic energy and skeletal muscle protein metabolism. Objective: Thus, we aimed to investigate the metabolic adaptations provoked by 36-hour water deprivation (WD) model in mice. Methods: C57BL/6 male mice aged 8-12 weeks were used. They were submitted to a 36-h WD or pair-feed regimen, and their motor skills, biochemical, and metabolic parameters were analysed. Results: WD-induced DH was confirmed by hypernatremia (+5.9%; $p < 0.05$) and increased activity from the oxytocinergic and vasopressinergic secreting neurons from supraoptic and paraventricular hypothalamic nuclei. The mice also suffered from body mass loss (-15%; $p < 0.05$), hyporexia (-13%; $p < 0.05$) and had diminished liver mass (-15.5%; $p < 0.01$), hypoglycaemia (-23.8%; $p < 0.01$) and hypercholesterolemia (+20.1%; $p < 0.01$). Respiratory exchange ratio was reduced at night (-5%; $p < 0.01$). The relative mass of the soleus muscle (SOL) remained unaltered ($p = 0.55$), but its cross-sectional area (+10.12%; $p < 0.01$) and water content (+5.58%; $p < 0.05$) were surprisingly increased. Moreover, SOL had increased total (+48%; $p < 0.05$) and proteasomal (+106%; $p < 0.01$) proteolysis, with no alteration on MuRF-1 expression, but reduced Akt phosphorylation. Extensor digitorum longus (EDL) muscle, on the other hand, did not alter its proteolysis ($p = 0.59$) and the expression of the water-channel AQP4 did not altered neither on SOL nor EDL. Conclusion: Our results demonstrate DH poses a pro-catabolic profile in overall metabolism, compromising proper homeostasis. Nevertheless, different types of muscle fibre seem to respond differently to the 36-h WD challenge and may even have adapted during the time-period analysed. Support: CAPES (88887.669692/2022-00; 88881.691153/2022-01), FAPESP (19/27581-0) Protocol: CEUA/UFS nº 4492070222</p>

Title	Inefficient mitophagy as a potential cause of the accumulation of damaged mitochondria in the cardiac tissue of hypothyroid fed and fasted rats
Authors	JULIANA SANTOS ROMÃO, JESSIKA GEISEBEL OLIVEIRA NETO, CHERLEY BORBA VIEIRA DE ANDRADE, JORGE JOSÉ DE CARVALHO, CARMEN CABANELAS PAZOS-MOURA, KAREN DE JESUS OLIVEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, UFF, Instituto de Biofísica Carlos Chagas Filho, UFRJ, Departamento de Histologia e Embriologia, UERJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Hypothyroidism is a widely prevalent endocrine disorder and a cardiovascular risk factor. Thyroid hormones (TH) are pivotal regulators of heart function; still, the precise mechanisms by which hypothyroidism leads to heart dysfunction require further elucidation. TH exert a profound influence on mitochondria, the powerhouse of the cells. Previously, we demonstrated that hypothyroidism modulated mitochondrial dynamics in the heart and significantly blunted fasting-induced mitochondrial fusion. Hypothyroidism also increased mitochondrial damage and potentialized the damage induced by fasting. Mitophagy play a key role in the elimination of injured mitochondria. However, whether hypothyroidism impact mitophagy in the heart is not clear in the literature. Objective: Investigate the influence of a hypothyroid state on mitophagy in the heart of rats under fed and fasting conditions. Methods: Male Wistar rats (n=36) at the age of 9–11 weeks and weighing approximately 300 g were divided into four groups: euthyroid (Eu-fed), euthyroid fasted (Eu-fasted), hypothyroid (Hypo-fed), and hypothyroid fasted (Hypo-fasted). Hypothyroidism was induced with methimazole (0.03%) diluted in drinking water, provided for 3 weeks. Fasting was conducted by withdrawing the food 48h before the end of the treatment. The left cardiac ventricles and serum were collected for analysis. Total and free T4 (FT4) were quantified by ELISA. mRNA and protein expression were analyzed by qPCR and Western blot, respectively. Data were analyzed by Two-way ANOVA, followed by Holm Sidak's hoc test. Differences were considered significant at $p \leq 0.05$. Results: Hypothyroidism was confirmed by undetectable levels of total and FT4. Compared to the Eu-fed group, the Eu-fasted group had significantly reduced T4 (Eu-fasted: 18.9 ± 2.0 ng/mL vs Eu-fed: 38.8 ± 2.3 ng/mL; $p < 0.0001$) and FT4 levels (Eu-fasted: 1.04 ± 0.09 ng/dL vs Eu-fed: 1.57 ± 0.03 ng/dL; $p < 0.0001$). Regarding mitophagy pathways, although the mRNA levels of Parkin did not differ between groups, total Parkin protein levels notably increased in the hypothyroid rats regardless of nutritional status (thyroid status effect $p < 0.0001$). However, no differences were found in PINK1 and p-Parkin levels among groups. These data suggest that the PINK/Parkin pathway is not being activated in the heart in hypothyroidism, which may contribute to the accumulation of injured mitochondria observed in these rats. Bnip3l and Map1lc3b expression, genes related to mitophagy and autophagy, respectively, raised in the Eu-fasted compared to the Eu-fed group ($p = 0.001$ and $p < 0.0001$, respectively), and this effect was inhibited in the Hypo-fasted group. Therefore, hypothyroidism may interfere with BNIP3 pathway and autophagy during fasting, possibly suppressing them. Fundc1 levels were similar among groups. Nonetheless, Bnip3 levels increased in both Eu-fasted ($p < 0.0001$ vs Eu-fed) and Hypo-fed groups ($p = 0.0015$ vs Eu-fed), and this effect was intensified in the Hypo-fasted rats ($p = 0.0015$ vs Eu-fasted; $p < 0.0001$ vs Hypo-fed). Bnip3 expression may represent an attempt to counteract the accumulation of damaged mitochondria. However, this effect appears insufficient, since there is still an elevated number of damaged mitochondria despite the increased expression of Bnip3. Conclusion: The accumulation of damaged mitochondria in the heart of hypothyroid rats might be a consequence of inefficient mitophagy. Support: CAPES, FAPERJ and CNPq Protocol: CEUA/UFF nº 2488110221</p>

Title	Melanopsin, a novel player in mammalian thermoregulation
Authors	GIOVANNA ZANETTI, DANIELA DANTAS DAVID, JOSÉ ARAÚJO SOUTO-NETO, CRISTHIAN SUA-CESPEDES, GUILHERME GOMES, MARIA NATHÁLIA MORAES, ANA MARIA DE LAURO CASTRUCCI
Affiliations	Predikta, Predikta, Department of Physiology, University of São Paulo, Department of Biological Sciences, Federal University of São Paulo
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Undoing the view that opsins are only photoreceptor molecules, it is now known that they are present far beyond the retina, in mammalian peripheral tissues that respond to temperature stimuli. Melanopsin (OPN4) is classically known for its role in synchronizing the central circadian clock to light-dark cycles. Clock genes control circannual and daily thermogenic activity in brown adipose tissue (BAT). The most potent activator of BAT thermogenesis is the sympathetic nervous system and the activation of β-adrenoceptors in response to cold exposure, leading to uncoupling protein 1 (UCP1) activation. Upon UCP1 increase, the brown adipocytes can convert chemical energy into heat. In addition to sympathetic activation of thermogenesis, cardiac natriuretic peptides (NPs) have been shown to play a role in UCP1 activation.</p> <p>Objective: To investigate the metabolic changes triggered by cold in the absence of melanopsin. And if such events fluctuate throughout the day. Methods: The metabolic rate of male mice of genotypes B6;129 (WT) and <i>Opn4</i>^{-/-} aged 3 to 4 months (n= 4) was determined at 30°C, 22°C and 10°C and thermographic images were taken at 30°C and 22°C. Another group of the same genotypes (n= 4-8) was acclimated for 2 weeks at 30°C, under light/dark cycle 12:12, (800 lux LED lamps). Then, the animals were single-housed (food and water ad libitum) and separated into 2 groups: 1) control at 30°C for 2 weeks; 2) group at 22°C for 2 weeks. After, the animals were euthanized every 4 h, over 24 h and blood and BAT were collected to determine serum NP concentrations and gene expression respectively. The data were plotted as the mean \pm SEM. Differences were considered significant at p<0.05. Results: <i>Opn4</i>^{-/-} animals exhibited a greater increase in their metabolism than WT animals (n=4) (WT 28,5 g and <i>Opn4</i>^{-/-} 25,5 g), in order to guarantee thermoregulation facing the same cold challenge. Thermography data showed that <i>Opn4</i>^{-/-} animals had a higher temperature in the BAT and inguinal region when compared to WT at 22°C (n=5-6 per group), which suggests greater heat production. qPCR analyses showed that <i>Ucp1</i> transcripts were markedly elevated in both genotypes at 22°C compared to 30°C; on the other hand, the differences in <i>Per2</i>, <i>Bmal1</i>, and <i>Rev-erba</i> gene expression demonstrated that OPN4 participates in the regulation of the BAT clock (n= 3-4). The serum NP concentrations (n= 3-4) showed that OPN4 is essential for the NP pathway rhythmicity, and thus for the regulation of thermogenesis in BAT. Conclusion: In our pioneering research, we demonstrated that melanopsin is a component of the thermoreception signaling pathway and responsible for influencing the thermogenic response in BAT and for the local regulation of clock genes. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES 88882.377368/2019-01 JASN, 88887.615662/2021-00 GZ), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 167833/2023-5 GZ, 161118/2021-6 CSC, 305032/2023-2 to AMLC) and Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP grants 2017/24615-5 and 2018/14728-0 AMLC, 2017/26651-9 MNM; scholarships 2021/01659-2 GZ, 2022/04584-6 CSC, 2018/23043-0 DDD). Protocol: 350/2019, Institute of Biosci</p>

Title	THE ACUTE EFFECT OF TEMPERATURE ON WHITE ADIPOSE TISSUE DIFFERENTIATED 3T3-L1 CELLS: MODULATION OF THE BIOLOGICAL CLOCK
Authors	MIRIANE AVELINO DA SILVA, GIOVANNA ZANETTI, ANA MARIA DE LAURO CASTRUCCI
Affiliations	DEPARTMENT OF PHYSIOLOGY, UNIVERSITY OF SÃO PAULO
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Mammals have developed a circadian central clock located in the suprachiasmatic nucleus (SCN) in the hypothalamus that responds to the environmental light-dark cycle. Clocks similar to the one located in the SCN are found in peripheral tissues such as the kidney, liver, and adipose tissue. White adipose tissue (WAT) is the main energy reservoir; it stores triglycerides (TGs) in unilocular lipid droplets and secretes a large number of hormones and cytokines that regulate metabolism. Objective: To evaluate the acute effect of temperature on the expression of the clock genes <i>Per1</i> and <i>Bmal1</i>, natriuretic peptide receptors (<i>Nprs</i>) and <i>Ucp1</i> in 3T3-L1 cells differentiated in white adipose tissue. Methods: Low-temperature pulse stimulation: Differentiated 3T3-L1 cells were seeded at a density of 105 cells/well in 6-well plates with 3 mL of experimental medium and kept in the dark (DD) at 37°C with 5% CO₂ for 24 h. At the beginning of the 2nd day, the experimental medium was changed twice at an interval of 2 hours to synchronize the cell population (n=3-8). On the third day, the cells were divided into two groups: 1) group stimulated for 1 hour at 34°C, and 2) control group maintained at 37°C. Immediately, 2 and 6 hours after the end of the stimulus, total RNA was extracted, the reverse transcriptase reaction was performed, followed by quantitative PCR for gene expression analysis. Results: The expression of <i>Per1</i> and <i>Bmal1</i> in cells at 37°C showed no variation in their transcripts at the three times analyzed (0 h, 2 h and 6 h). After the 1 h pulse at 34°C, a change in <i>Per1</i> expression was observed with a marked increase at the 0 h time point (p<0.0001). On the other hand, the temperature pulse appears to have no effect on <i>Bmal1</i> expression. For the natriuretic peptide receptors <i>Npr1</i>, <i>Npr2</i> and <i>Npr3</i> and for the <i>Ucp1</i> gene, no significant differences were found between control cells and treated cells at the time points evaluated. Conclusion: 3T3-L1 cells differentiated into white adipose tissue responded immediately after the temperature pulse with an increase in <i>Per1</i> transcripts, indicating that low temperature regulates the expression of this gene. On the other hand, the low temperature stimulus had no effect on the <i>Bmal1</i>, <i>Npr1</i>, <i>Npr2</i> and <i>Npr3</i> receptors and <i>Ucp1</i>. More studies are needed to better understand how differentiated cells sense low temperatures and which signaling pathway modulates the clock in this tissue. Support: CNPq (305032/2023-2 to AMLC and 167833/2023-5 to GZ), FAPESP (2022/06190-5 and 2023/12676-0 to MAS; 2017/24615-5 to AMLC; 2021/01659-2 to GZ). Protocol: N.A.</p>

Title	Hypothyroidism disrupts glucose homeostasis in the heart of male rats.
Authors	NATHÁLIA PEREIRA DE FARIAS DA SILVA, JULIANA SANTOS ROMÃO, KAREN DE JESUS OLIVEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, Universidade Federal Fluminense
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The heart has a high energy demand, consequently its function depends on efficient energy production. Although lipids are the primary source of energy for the heart, glucose metabolism also has a vital role in maintaining heart homeostasis and a well-balanced use of these substrates is necessary. The regulation of energy metabolism in the heart by thyroid hormones is well recognized; however, the impact of hypothyroidism on cardiac glucose homeostasis remains not well defined. Objective: This study aims to investigate the effects of hypothyroidism on cardiac glucose metabolism of male rats. Methods: Male Wistar rats, aged 9-11 weeks and weighing approximately 300g, were divided into two groups (n=9, each): Euthyroid (Eu) and Hypothyroid (H). Hypothyroidism was induced by administering 0.03% Methimazole in drinking water for 21 days. Glycemia was analyzed using a glucometer. The left cardiac ventricles were harvested and frozen for Western blot and RT-qPCR analyses. Serum was collected for T4 level measurement using ELISA. Glycogen content was analyzed using a commercial kit. Data were analyzed by T-test or Mann-Whitney, with differences considered significant at $p \leq 0.05$. Results: Hypothyroid rats presented total and free T4 levels below the detection limit. Glycemia was reduced in the hypothyroid group (H: 93.6 ± 2.3 mg/dL vs Eu: 104.3 ± 2.1 mg/dL; $p=0.0031$). Molecular analysis revealed decreased protein expression of p-Akt ($p=0.02$) and reduced mRNA expression of Glut1, Glut4, Hk, and Gys1 ($p=0.0053$, $p=0.0008$, $p=0.0157$, and $p<0.0001$, respectively) in hypothyroid animals, suggesting a potential state of insulin resistance and diminished glucose uptake in the heart during hypothyroidism. Interestingly, the glycogen content in the cardiac ventricles was increased in the H group (H: 0.1241 ± 0.0111 $\mu\text{g}/\mu\text{L}$ vs Eu: 0.0551 ± 0.0051 $\mu\text{g}/\mu\text{L}$; $p=0.0001$). Moreover, in H group there was a trend towards increased protein expression of p-GSK3 ($p=0.0679$), a regulator of glycogen synthase activation, possibly compensating the reduced Gys1 mRNA expression. Additionally, Gabarap mRNA expression, involved in glycophagy, was reduced in H group ($p<0.0001$), suggesting reduced mobilization of glycogen, which may contribute to the increased glucose storage found in the hypothyroid heart. Conclusion: Hypothyroidism disrupts the expression of genes related to glucose uptake and glycogen mobilization in the heart of rats, possibly leading to metabolic changes that could contribute to cardiac dysfunction. Support: CAPES, FAPERJ and CNPq. Protocol: CEUA/UFF nº 2488110221.</p>

Title	Hypothyroidism modulates the expression of genes related to mitochondrial dynamics and mitophagy in the testis of adult rats
Authors	LORENA CRISTINA DE SOUZA E SOUZA, JULIANA SANTOS ROMÃO, KAREN DE JESUS OLIVEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, UFF
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Thyroid hormones play a crucial role in testicular development, function, spermatogenesis, and hormonal secretion. In cases of hypothyroidism, reproductive dysfunction is commonly observed. Mitochondria are vital components in male reproduction, essential for testosterone biosynthesis, cell differentiation, and spermatogenesis in the testis. Mitochondria continuously undergo changes in their number and morphology through the process of fusion and fission processes, a homeostatic mechanism known as mitochondrial dynamics. Mitochondrial dynamics involve fusion, where two or more mitochondria join to form a larger one, and fission, where a part of a damaged mitochondria is cut off to generate smaller ones, which are then eliminated by mitophagy. An imbalance in mitochondrial dynamics is linked to various pathological conditions. However, whether defects in mitochondrial dynamics in the testis are observed in hypothyroidism remains unknown. Objective: Analyze the expression of mitochondrial dynamics and mitophagy-related genes in the testis of hypothyroid rats. Methods: Male Wistar rats (n=18) were divided into two groups: euthyroid and hypothyroid. Hypothyroidism was induced with methimazole (0.03%) diluted in drinking water, provided for 3 weeks. Testis were weighed and frozen at -80°C for analysis. mRNA expression of the mitochondrial dynamics-related genes (fusion, fission, and mitophagy) was analyzed by qPCR. Total and free T4 were quantified by ELISA. All protocols were approved by CEUA/UFF #2488110221. Results: Hypothyroid rats exhibit undetectable levels of total and free T4. All genes analyzed involved in mitochondrial fission process were increased in the hypothyroid group (Dnm1l, p=0.0079; Mff, p=0.0164; Fis1, p=0.0201). Regarding mitochondrial fusion, an increase in Opa1 (p=0.0311) and Mfn1 (p=0.0021) expression was also found, while Mfn2 showed no statistical difference. In addition, hypothyroidism induced lower expression of Bnip3l (p=0.0002) and Bnip3 (p=0.0002), higher expression of Park2 (p<0.0001), and no changes in the Map1lc3b expression (p=0.1815). Conclusion: The increased expression of both fusion and fission-related genes observed in the hypothyroidism suggests an adaptive response to keep mitochondrial homeostasis. The damaged mitochondria resulting from fission, which are likely to undergo mitophagy, seem to follow the Park2 pathway, as the Bnip and Bnip3l pathways appear to be reduced in hypothyroid animals. Support: CAPES, FAPERJ, and CNPq Protocol: CEUA/UFF #2488110221</p>

Title	Role of the TRPV1 channel in the development of obesity induced by high-fat diet in mice (<i>Mus musculus</i>)
Authors	JULIA DOS SANTOS BRAULINO, ANA MARIA DE LAURO CASTRUCCI, CRISTHIAN DAVID SUA-CESPEDES
Affiliations	Department of Physiology, Institute of Biosciences, University of São Paulo, USP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The TRPV1 channel regulates white adipocyte browning and activates metabolic modulators, making it a potentially relevant target for metabolism studies. Obesity is characterized by the excessive accumulation of adipose tissue resulting from unbalanced energy expenditure and is associated with complications such as type 2 diabetes and the development of metabolic syndrome. Although the TRPV1 channel is widely investigated in metabolic research, the results in the literature are controversial due to different methodologies, especially the temperature at which the animals are kept, which is generally outside their thermoneutrality zone. Objective: We aimed to evaluate the role of the TRPV1 channel in the development of obesity induced by high-fat diet (HFD), using C57BL/6J (WT, n=6) and <i>Trpv1</i> knockout (KO, n=6) male mice aged 3 months, in thermoneutrality (30°C) or subjected to moderate cold (22°C). Methods: The animals were acclimated for 2 weeks at 30°C, under a 12:12h light-dark cycle (lights on at 7 h, 600 lux). During this period, the animals were fed chow diet (CD) consisting of 3.8 kcal/g and 50 g/kg fat (Nuvilab® CR-1 Irradiated, Quimtia S.A, SC, Brazil) and water ad libitum. After this period, the animals were single-housed and maintained for 8 weeks in thermoneutrality or 22°C. To induce obesity, all animals were fed a high-fat diet (HFD) consisting of 60% kcal and 348 g/kg fat (RH19572C, Rhoster Ind. e Com. Ltda., SP, Brazil). At week 7, we performed the glucose tolerance test (GTT), and at the end of the eight-week period, the animals were euthanized during the light phase (9 AM) and blood, hypothalamus, heart, liver, brown adipose tissue (BAT), white adipose tissue depots (iWAT, mWAT and pgWAT) and feces were collected (CEUA IB-USP 373/2021). Weight gain, food intake, determination of lipids in the blood, liver and feces, macroscopic analyses, and the expression of hypothalamic genes that regulate appetite were evaluated. Results: The protocol was effective in developing obesity in both genotypes and temperatures. No differences were found between groups for the weight and food consumption. In the KO animals, glucose metabolism was significantly slower at 22°C compared to KO control group (p=0.042). No differences for the fasting glucose levels or hepatic cholesterol and triglycerides between the genotypes were observed, but the mice subjected to cold showed higher levels of serum cholesterol and triglycerides compared to their controls at 30°C (p<0.05), regardless the genotype. Interestingly, <i>Trpv1</i>^{-/-} animals at 30°C eliminated more fat in the feces compared to the other groups (p=0.016). No differences for the mass of the organs were found. Increased expression of the hypothalamic leptin receptor was observed at 22°C in WT (p=0.048) and at 30°C in KO animals (p=0.003) compared to the WT mice at 30°C. The KO animals at 22°C showed reduced transcripts of the leptin receptor compared to KO animals at 30°C (p=0.044). The expression of hypothalamic ghrelin and its receptor showed no significant differences among the groups. Conclusion: Our results suggest that the absence of the TRPV1 channel does not affect weight gain in mice in thermoneutrality or at 22°C, but reveals a significant influence on obesity-related metabolic responses, especially in the moderate cold conditions present in animal vivaria. Support: CNPq (305032/2023-2 to AMLC, 131732/2024-2 to JSB, and 161118/2021-6 to CDSC), and FAPESP (2017/24615-5 to AMLC and 2022/04584-6 to CDSC) Protocol: CEUA IB-USP 373/2021</p>



Title	Three-dimensional human granulosa cells model characterization
Authors	ANDRÉ LUCAS LAGÔA DE FREITAS, VICTORIA REGINA SIQUEIRA MONTEIRO, TATHIANA PROENÇA PAMPOLHA, BIANCA MONTENEGRO DA CUNHA, TAISNARA INGRID GONÇALVES SILVA, MARLON LEMOS DIAS, LEANDRA SANTOS BAPTISTA, TÂNIA MARIA RUFFONI ORTIGA, FLAVIA FONSECA BLOISE
Affiliations	Programa de pós graduação em Fisiologia, UFRJ, Programa de Pós Graduação em Biotecnologia, INMETRO
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Granulosa cells (GC) regulate female gamete maturation, influenced by hypothalamic and pituitary hormones, guiding oocyte and GC differentiation. In addition, GC communicates via bidirectional signaling with the oocyte, and synthesizes steroid hormones (estrogen and progesterone), enzymes, and antioxidants that form the follicular fluid, contributing to oocyte maturation. GC forms a multilayer around the oocyte with gap junctions, facilitating the passage of metabolites and second messengers crucial for follicle development. Further, Two-dimensional in vitro models model lack cell-cell contact complexity. Thus, differences in cellular organization between in vivo and in vitro models can lead to misunderstandings of follicle physiology. Therefore, our work aims to characterize a three-dimensional cell culture model (spheroid) to study GC functional differences. Objective: The study aims to determine if the three-dimensional cell culture model better mirrors human granulosa physiology compared to traditional two-dimensional models. Methods: Human GC line COV434 was cultured in high-glucose DMEM with 10% fetal bovine serum (FBS) and 1% penicillin/streptomycin (P/S). Agarose hydrogels were created using a 9x9 silicone mold with 1% agarose solution. For the pilot proliferation assay, 5×10^5 or 8×10^5 cells were plated on the hydrogels to form the spheroids and cultured for 1, 7, 14, and 21 days. Spheroids were disrupted with trypsin, resuspended in DMEM with FBS and P/S, and counted with trypan blue in a Neubauer chamber. Cells were divided into 2D and 3D groups and incubated with $5 \mu\text{M}$ CellTrace CFSE dye. Both groups were cultured for 1, 4, and 7 days at 5×10^5 cells. The 2D group was plated on 6-well plates, and the 3D group on hydrogels. Cells were trypsinized, counted with trypan blue, and fixed in 4% paraformaldehyde. Analysis was done using BD FACS Canto II Flow cytometer, BD FACS Diva software, FlowJo™v10.8, and GraphPad Prism 9. Data were presented as mean \pm s.d. One-way ANOVA with Tukey's post hoc correction and Two-Way ANOVA with Sidak's correction were performed. Results: Cell numbers increased (except on day 1, due to plating) in both 5×10^5 (1 day=$2.4 \times 10^5 \pm 2.0 \times 10^5$; 7 days=$1.4 \times 10^6 \pm 8.4 \times 10^4$; 14 days=$2.3 \times 10^6 \pm 3.4 \times 10^5$; 21 days=$3.0 \times 10^6 \pm 5.4 \times 10^5$; $p=0.0037$) and 8×10^5 spheroids (1 day=$3.3 \times 10^5 \pm 1.2 \times 10^5$; 7 days=$1.9 \times 10^6 \pm 2.6 \times 10^5$; 14 days=$2.1 \times 10^6 \pm 3.8 \times 10^5$; 21 days=$3.4 \times 10^6 \pm 6.2 \times 10^5$; $p<0.0001$). Thus, COV434 cells adapt to the 3D model and remain proliferative. Viability in the 5×10^5 group (1 day=$97.0\% \pm 1\%$; 7 days=$95.0\% \pm 2.3\%$; 14 days=$91.0\% \pm 7.6\%$; 21 days=$68.8\% \pm 15\%$; $p=0.0128$) and the 8×10^5 group (1 day=$95.5\% \pm 3.3\%$; 7 days=$94.6\% \pm 1.5\%$; 14 days=$85.5\% \pm 11.2\%$; 21 days=$70.2\% \pm 15.2\%$; $p=0.0402$) was adequate until day 14, with better viability until day 7 (i.e.: $n=3$, One-Way ANOVA). Comparing 2D (1 day=$4.3 \times 10^5 \pm 3.2\%$; 4 days=$2.0 \times 10^6 \pm 3.0 \times 10^5$; 7 days=$3.5 \times 10^6 \pm 1.7 \times 10^6$) and 3D (1 day=$2.7 \times 10^5 \pm 7.4 \times 10^4$; 4 days=$6.6 \times 10^5 \pm 1.6 \times 10^5$; 7 days=$8.0 \times 10^5 \pm 9.6 \times 10^4$) cultures showed slower proliferation in 3D, resembling in vivo granulosa cell growth ($n=2$, Two-Way ANOVA). Conclusion: Granulosa demonstrated the capacity to organize itself in a three-dimensional shape, which resembles the ovarian follicle structure. 3D granulosa cells also presented the capacity to proliferate and remain viable. We will further evaluate proliferation by flow cytometry, cell death by immunohistochemistry, and folliculogenesis-related genes in 2D and 3D cultures by qPCR. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) Protocol: N.A.</p>



Title	MELANOPSIN (OPN4) AS A KEY PLAYER OF NATRIURETIC PEPTIDES PATHWAY IN MICE (<i>Mus musculus</i>)
Authors	LETÍCIA MENEZES VASCONCELOS, CRISTHIAN DAVID SUA-CESPEDES, LETÍCIA DE OLIVEIRA MARINHO, LIVIA THAIS FERREIRA LUZ PEDRO, ANA MARIA DE LAURO CASTRUCCI
Affiliations	Department of Physiology, Institute of Biosciences, University of São Paulo, USP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity is a multifactorial disease characterized by the excessive accumulation of fat. This condition is often associated with metabolic disorders and chronic diseases of the cardiovascular system. Classically, opsins are described as exclusive light sensors, but they are currently recognized as multifunctional sensors with the potential to sense temperature, light and metabolites. Melanopsin (OPN4) is a retinal photopigment that plays a role in the response to the light-dark cycle and has been shown to also play a role in the response to temperature. However, peripheral tissues considered “blind”, such as and the heart, also express melanopsin, being the heart the organ with the highest expression in the mouse. The heart is responsible for producing and secreting hormones known as natriuretic peptides (NPs) in response to cold stimuli and changes in blood pressure. In mammals, ANP and BNP stimulate thermogenesis in the brown adipose tissue (BAT). Objective: To evaluate whether melanopsin influences the natriuretic peptide pathway in mice with obesity induced by high-fat diet, under different temperature conditions. Methods: 32 male mice of the B6;129 (WT) and <i>Opn4</i>^{-/-} (B6;129 background) genotypes, 3 months old, were acclimated by 2 weeks in thermoneutrality (30°C) and fed chow diet (CD, 3.8 kcal/g and 50 g/kg fat) (Nuvilab® CR-1 Irradiated, Quimtia S.A, SC, Brazil) and water ad libitum. After the animals were single-housed, they were fed high-fat diet (HFD, 60% kcal and 348 g/kg fat) (RH19572C, Rhostron Ind. e Com. Ltda., SP, Brazil) and kept at 30°C or moderate cold (22°C) for 8 weeks. After this period, the animals were euthanized (CEUA-IBUSP 373/2021) and then BAT and blood were collected. Serum levels of ANP and BNP were quantified by ELISA following the manufacturer’s instructions (RayBio® Mouse/Rat ANP/BNP EIA Kit, GA, USA). The NP receptors <i>Npr1(a)</i>, <i>Npr2(b)</i>, <i>Npr3(c)</i> were analyzed, using <i>Rpl0</i> as the normalizing gene. The gene expression data were analyzed using the log method (2-$\Delta\Delta CT$). Results: HFD <i>Opn4</i>^{-/-} animals showed lower levels of ANP compared to HFD WT animals regardless the temperature (p=0.008 at 30°C) and (p=0.033 at 22°C), while BNP was lower only at 22°C (p=0.02). No differences in CD groups were observed. CD WT animals showed lower expression of <i>Npr1</i> (p=0.0007) and <i>Npr3</i> (p=0.0001) in BAT when maintained at 22°C compared to 30°C. When compared to CD WT, CD <i>Opn4</i>^{-/-} animals showed a reduction in <i>Npr2</i> (p=0.002) and <i>Npr3</i> (p=0.0001) transcripts at 30°C, as well as <i>Npr1</i> at both temperatures (p=0.0001 at 30°C) and (p=0.002 at 22°C). In the HFD group, <i>Opn4</i>^{-/-} animals showed a decrease in <i>Npr1</i> levels when kept at 30°C (p=0.009) compared to WT animals under the same conditions. Also, HFD WT animals in thermoneutrality showed a significant expression reduction for the three receptors when compared to the same group fed chow food (p<0.05). Conclusion: In WT mice fed a commercial diet, the cold stimulus decreased the expression of <i>Npr1</i> and <i>Npr3</i> in the brown adipose tissue. However, the implementation of a high-fat diet led to a loss of these responses. In addition, our data suggest that melanopsin is an important component of the thermosensing pathway, since its absence resulted in low levels of serum natriuretic peptides and their receptors in BAT, as well as a lack of response to cold stimuli. Support: CAPES (88887.940383/2024-00 to LMV), CNPq (305032/2023-2 to AMLC and 161118/2021-6 to CDSC), and FAPESP (2017/24615-5 to AMLC, 2022/04584-6 to CDSC) Protocol: CEUA-IBUSP 373/2021</p>

Title	LEPTIN RECEPTOR DELETION IN POMC NEURONS ABOLISHES FASTING-INDUCED ACTIVATION OF CRFPVN NEURONS IN MICE
Authors	ANA BEATRIZ MARÇAL, NATHALIA LOPES FERREIRA, ANA PAULA NEVES BRIANEZI, ANDRÉ SOUZA MECAWI, RODRIGO RORATO
Affiliations	Biofísica, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Fasting-induced metabolic stress increases the hypothalamic-pituitary-adrenal (HPA) axis activity. The paraventricular corticotropin-releasing factor neurons (CRFPVN) are critical for activating the HPA axis, and it has been suggested that projections from the Arcuate Nucleus (ARC) neurons expressing leptin receptors (Lepr) underlie the activation of CRFPVN neurons during fasting. Since Lepr is highly expressed in arcuate proopiomelanocortin neurons (POMC), we used Cre-LoxP technology to inactivate the Lepr in POMC cells and investigate the effects on the activity of CRFPVN neurons in response to fasting.</p> <p>Objective: Investigate the effect of Lepr deletion in POMC cells on the activity of CRFPVN neurons in response to fasting. Methods: Pomc-Cre mice were mated with Lepr^{flox/flox} mice. Control mice (WTLEPR) and mice with Lepr deletion in POMC (POMCLEPR) were single-housed (12 weeks-old), handled for one week, and assigned to the groups: fed+saline, 36h-fasted+saline, and 36h-fasted+leptin (n=5/group). Throughout the experimental protocol, animals received 4 i.p. injections of saline or leptin (0.5µg/kg) every 8 hours. After 36h of fasting, animals were anesthetized and perfused for brain collection for cFos/CRF double immunostaining. Results: As expected, we observed increased cFos expression in CRFPVN neurons of WTLEPR mice fasted for 36h (30.5±4.1) compared to WTLEPR-fed mice (5.1±1; p=0.009). Additionally, we observed decreased neuronal activity in CRFPVN neurons of WTLEPR mice fasted and treated with leptin (10.5±2.6), compared to WTLEPR-fasted mice (30.5±4.1; p=0.003). Interestingly, compared to WTLEPR mice, we did not observe an increase in cFos expression in CRFPVN neurons of POMCLEPR 36h-fasted mice (7.9±2.3). Also, POMCLEPR 36h-fasted and treated with leptin mice (13.2±2.5) showed no significant changes in cFos expression in CRFPVN neurons. Conclusion: The impaired activation of CRFPVN neurons in 36h-fasted POMCLEPR mice supports the substantial role of leptin signaling via POMC neurons in the neurocircuitry controlling the adaptive activation of the HPA in response to metabolic stress. Support: FAPESP Protocol: 1276210720</p>

Title	USING THE COMPARATIVE TOXICOGENOMICS DATABASE TO SELECT MOLECULAR TARGETS TO INVESTIGATE THE EFFECTS OF GLYPHOSATE EXPOSURE ON TYPE 2 DIABETES DEVELOPMENT
Authors	LUÃ HENRIQUE URRUTIGARAY, DIOVANA GELADI DE BATISTA, JULIA MATZENBACHER DOS SANTOS, VINICIUS CRUZAT, CAROLINE BRANDÃO QUINES, VITOR ANTUNES DE OLIVEIRA, THIAGO GOMES HECK
Affiliations	PPGAIS, UNIJUI, Programa de Pós Graduação em Modelagem Matemática e Computacional, UNIJUI, School of Nursing, University of Pittsburgh, Faculty of Health, Southern Cross University, Curso de Psicologia, UNIJUI
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Defective cell stress response (CSR) is associated with senescence (SEN) and oxidative stress (OS) processes in metabolic-related tissues as part of type 2 diabetes mellitus (T2DM) development. Environmental exposure to pollutants has been described as a factor capable of impairing CSR, resulting in the acceleration of T2DM development. However, it is not clear if the exposure to glyphosate (GLY) pesticides account to T2DM development by affecting CSR through OS and SEN pathways. Objective: To define targets genes in OS and SEN pathways for investigating the effects of GLY exposure on T2DM development. Methods: This research used the The Comparative Toxicogenomics Database (CTD, http://ctdbase.org/) genes that interact with GLY (mesh ID and PubChem n° 000097797), T2DM (MeSH ID= D003924; OMIM ID=125853) and CSR ontology (GO:0033554). The database harmonizes cross-species heterogeneous data for chemical exposures and their biological repercussions by manually curating and interrelating chemical, gene, phenotype, anatomy, disease, taxa, and exposure content from the published literature. Subsequently, common genes affected by these conditions were identified. The results were used to identify common genes related to OS and SEN. Thus, the direct chemical-phenotype interaction and the gene-disease association was examined between the listed genes in CTD by the computationally predicted tetramer. The search included GLY as the chemical that interacts with each gene product listed to trigger a phenotype that could be connected to different diseases. Lastly, we selected the gene that fit our research proposal. Results: 2,898 genes have been manually curated as interactions with GLY, 34,345 were found with T2DM, and 14,455 with CSR. Among them, 2,214 were common only to GLY and T2DM, 4 genes were common only to GLY and CSR, and 2,352 genes were common only to T2DM and CSR. Thus, 580 genes were common to all (named as Gly-T2DM-CSR gene set). Evaluating the interaction between these 580 genes, OS and SEN ontologies, 409 genes remained only in the Gly-T2DM-CSR set, while 1,454 only in OS and 102 only in the SEN set of genes. Also, 131 genes were common only to Gly-T2DM-CSR and OS, while 27 were common only to Gly-T2DM-CSR and SEN, and 17 were common only to OS and SEN. Only 13 genes were common to all Gly-T2DM-CSR-OS-SEN gene set as follows: ABL1, BECN1, BMAL1, CDKN2A, GCH1, MAP2K1, MAP2K4, MAPK8, MIF, SIRT1, TP53, TRP53 and ZEP277. Between these genes, SIRT1 (NAD-dependent protein deacetylase sirtuin-1) meets the criteria for investigating GLY exposure and T2DM development, as CTD listed it as a gene related to metabolic syndrome. SIRT1 is a protein that links transcriptional regulation directly to intracellular energetics and participates in the coordination of several cellular functions, including cell cycle, response to DNA damage, metabolism, apoptosis, and autophagy. Moreover, SIRT1 serves as a sensor of the cytosolic ratio of NAD⁺/NADH, which is altered by metabolic changes (Science. 16;305(5682):p390, 2004). Conclusion: This study reveals a potential for GLY exposure to disrupt CSR, OS, and SEN pathways, thereby contributing to the development of T2DM and indicate SIRT-1 as a target for further research about molecular pathways involved in GLY-induced T2DM. Support: CAPES, PPGAIS-UNIJUI, FAPERGS, CNPq, grants 307926/2022-2, and 405546/2023-8 to TGH). Protocol: não se aplica.</p>

Title	Hypothalamic brain areas directly connected to CRF PVN
Authors	ANA PAULA NEVES BRIANEZI, NATHALIA LOPES FERREIRA, ANA BEATRIZ DE ASSIS MARÇAL, ANDRÉ DE SOUZA MECAWI, RODRIGO CESAR RORATO
Affiliations	Biofísica, UNIFESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The activation of corticotrophin-releasing factor neuron (CRF PVN) is crucial to increase hypothalamic-pituitary-adrenal (HPA) axis activity in response to food deprivation. Studies demonstrated that a decrease in plasma leptin levels contributes to increase CRF PVN activity during fasting. Since the paraventricular nucleus (PVN) neurons do not express <i>Lepr</i>, we used a modified rabies virus to determine which hypothalamic brain areas expressing <i>Lepr</i>, are monosynaptically connected to CRF PVN neurons.</p> <p>Objective: Determine hypothalamic brain areas directly connected to CRF PVN neurons. Methods: We subjected <i>Crh-IRES-Cre</i> mice (10-12 weeks old, n=3) to stereotaxic surgery for the unilateral administration of a helper virus, AAV-hSyn- FLEX-TVA-P2A-eGFP-2A-oG, into the PVN. After 21 days, the same animal received a unilateral injection of a modified rabies virus [SADDG-mCherry (EnvA)]. Finally, 7 days later, the animals were perfused for brain collection. Samples were used to determined hypothalamic brain areas directly connected to CRF PVN neurons. In addition, we also performed immunostaining for POMC to determine if these neurons can communicate directly CRF PVN about changes in peripheral energy stores.</p> <p>Results: The surgery was validated by observing eGFP (helper virus) expression only in the PVN from <i>Crh-IRES-Cre</i> mice. As expected, the colocalization between eGFP and mCherry (rabies virus) were detect in the PVN. We observed consistent mCherry expression throughout the ARC, DMH, and VMH. The number of mCherry-expressing neurons in those areas was higher between -1,46 to -1.94mm from bregma. Interestingly, we also observed colocalization of POMC and mCherry throughout the ARC. Conclusion: Our qualitative study indicates that hypothalamic brain nuclei sensitive to changes in hormones and metabolites are directly connected to CRF PVN neurons. Additionally, ARC neurons expressing POMC can also provide direct information to CRF PVN and contribute to changes in the HPA axis activity during metabolic stress.</p> <p>Support: FAPESP and CNPq. Protocol: CEUA: 3627271022</p>

Title	Hypothyroidism differentially affects adiposity and lipid profile in a sex- and time-of-day dependent manner
Authors	BRUNO HENRIQUE GOMES, AYLÁ SECIO-SILVA, PAULO HENRIQUE EVANGELISTA-SILVA, LETÍCIA SELVATICI-TOLENTINO, TATIENNE NEDER FIGUEIRA-COSTA, RODRIGO ANTONIO PELICIARI-GARCIA, FRANCEMILSON GOULART-SILVA, PAULA BARGI-SOUZA
Affiliations	Ciências Biológicas, UNIFESP, UNIVERSIDADE FEDERAL DE SÃO PAULO, Nutrição, UFT, UNIVERSIDADE FEDERAL DO TOCANTINS, Fisiologia e Biofísica, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS, Fisiologia e Biofísica, USP, UNIVERSIDADE DE SÃO PAULO
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Thyroid hormones (THs), T3 and T4, play important roles in regulating metabolism, body temperature, and other physiological processes. Hypothyroidism, a condition characterized by lower THs concentration, leads to harmful metabolic changes and circadian clock desynchronization, as recently described for the suprachiasmatic nucleus of hypothalamus, anterior pituitary gland, heart and jejunum. These rhythmic disruptions might contribute to body weight (BW) alterations and changes in the daily lipid profile of affected individuals. However, whether the hypothyroid-induced metabolic changes are sex- and time-of-day dependent remain unknown. Objective: To evaluate the effects of hypothyroidism on body weight, adiposity and daily lipid profile of male (M) and female (F) adult mice. Methods: Male and female C57BL/6J mice, approximately 6 weeks old, were divided into control (C) and hypothyroid (H) groups. Hypothyroidism was induced by administration of methimazole (0.1%) and sodium perchlorate (1%) in drinking water for 45 days. Body weight (BW) was evaluated throughout whole experiment. Adiposity was assessed by evaluating the weight of mesenteric (Me), perigonadal (Pg), and retroperitoneal (Rt) fat deposits, and total fat percentage was calculated. The animals were anesthetized and euthanized by decapitation at Zeitgeber time (ZT) 4-8 (light phase) or 16-20 (dark phase) (ZT0: lights on, 7am). Blood was collected from the trunk immediately after decapitation, and the serum was obtained for measurements of total cholesterol, triglycerides (TG), HDL, LDL and total T4 serum concentration. The anterior pituitary gland was collected to measure the Tshb mRNA expression by RT-qPCR. Unpaired Student's t-test was used for the analyses of Tshb mRNA and total fat percentage. Two-way Analysis of Variance (ANOVA) followed by Bonferroni post-test was conducted for the analyses of adiposity (adipose depots and treatment main effects), total cholesterol, TG, HDL, LDL and total T4 serum concentrations (treatment and time main effects). Statistical analyses were performed using GraphPad Prism 9 software. Results: The hypothyroidism induction was confirmed by increased Tshb mRNA expression in anterior pituitary gland and decreased total T4 serum concentration. The control group showed a BW increase while H mice of both sexes exhibited weight stagnation associated with a lower total fat percentage in the H animals (M: $P < 0.0005$; F: $P < 0.01$; $n = 11-16$/group/sex). Male mice showed reduced Me and Pg adipose depots ($P < 0.0001$ for Me and Pg in males) while only Me was reduced in hypothyroid females ($P < 0.001$) ($n = 19-26$/group/sex). The H animals of both sexes showed increased cholesterolemia during light and dark phases ($P < 0.01$ for F in both phases and M during dark phase; $P < 0.05$ in M during light phase; $n = 5-10$/group). No statistically significant differences were depicted for TG serum concentration. Serum LDL concentration was increased in H mice of both sexes only during dark phase (F: $P < 0.001$, M: $P < 0.01$; $n = 7-12$/group). Finally, serum HDL concentration was increased only during the dark phase for hypothyroid females ($P < 0.01$; $n = 10-13$/group). Conclusion: These data suggest that hypothyroidism affects the adiposity in a sex dependent manner and the lipid profile according to the phase of the day. Together, these findings may explain, at least in part, the sex-dependent impairments in metabolic and body composition found in hypothyroidism. Support: CNPq (403972/2021-3), CAPES e FAPEMIG (APQ-00013-22) Protocol: Protocolo CEUA: 170/2021 e 349</p>

Title	Avaliação do perfil diário proteômico e fosfoproteômico do fígado de camundongos machos e fêmeas submetidos ao hipotireoidismo
Authors	ISABELA CARVALHO GUIMARÃES, LUCAS RODRIGUES RIBEIRO, MARCELLA NUNES MELLO-BRAGA, THIAGO VERANO-BRAGA, RODRIGO ANTONIO PELICIARI GARCIA, PAULA BARGI DE SOUZA
Affiliations	Fisiologia e Biofísica, UFMG, Ciências Biológicas, UNIFESP, Bioquímica e Imunologia, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O fígado é um órgão chave na regulação do metabolismo e alvo de ações transcricionais e pós-transcricionais dos hormônios tireoidianos (HTs), principalmente da triiodotironina (T3). Etapas como a sinalização intracelular, a síntese e a degradação de substratos energéticos no fígado são controladas pelo relógio biológico circadiano e moduladas por diversos hormônios. A ritmicidade circadiana é essencial para ajustar as demandas energéticas diárias do organismo. Nosso grupo recentemente demonstrou que o hipotireoidismo, caracterizado por baixa produção de HTs, está associado a alterações na expressão gênica dos componentes do relógio biológico. Em conjunto, nossa hipótese é que o hipotireoidismo altera o relógio biológico do fígado e, por consequência, o perfil diário de proteínas envolvidas na regulação diária do metabolismo energético. Objective: Nosso objetivo consiste em avaliar o perfil diário do proteoma e fosfoproteoma do fígado ao longo das 24 h em camundongos machos e fêmeas submetidos ao hipotireoidismo. Methods: Camundongos com 7 semanas de vida, machos e fêmeas, da linhagem C57BL/6 foram divididos em dois grupos: Eutireoideo (Controle) e Hipotireoideo (H). O hipotireoidismo foi induzido com tratamento de metimazol (0,1%) e perclorato de sódio (1%) dissolvidos na água por 45 dias. Os animais foram mantidos em um ciclo claro-escuro de 12:12 h (Zeitgeber Time (ZT) 0 = 07:00 h), com comida e água ad libitum. Ao final do experimento, os animais foram anestesiados por inalação de isoflurano e eutanasiados em intervalos de 4 h ao longo de um período de 24 h e o tecido hepático foi coletado e imediatamente congelado (n=5/ZT/grupo). O tecido foi homogenizado em 200 µL do tampão de lise, seguido de sonicação no gelo. Após, as amostras foram centrifugadas a 5.000 g por 10 min em temperatura ambiente (TA). O sobrenadante foi recuperado e o conteúdo total de proteínas foi mensurado no Nanodrop. A seguir, 50 µg de proteínas totais foram adicionados em tampão de trietil-amônio-bicarbonato (TEAB) num volume final de 100 µL. As amostras foram então tripsinizadas (1:50) a 37 °C por 16-18h. No dia seguinte, as amostras foram quantificadas no Qubit. Próximas etapas: As amostras serão marcadas com o sistema Tandem Mass Tag (TMT, ThermoFisher), enriquecidas com fosfopeptídeos, dessalinizadas e submetidas a espectrometria de massa de alta resolução. A identificação das proteínas diferencialmente expressas e vias de sinalização alteradas serão feitas com o uso das plataformas e softwares disponíveis (Perseus, UniProtKB, Gene Ontology, KEGG e PhosphoSitePlus). Results: Com este estudo, esperamos quantificar e identificar as possíveis proteínas e vias envolvidas na regulação circadiana do metabolismo hepático, identificar possíveis diferenças entre os sexos, além de caracterizar o efeito do hipotireoidismo na regulação diária da função e metabolismo hepático. Conclusion: Nossos resultados apresentam alto potencial para identificação de novos alvos e vias modulados por ações genômicas e/ou não genômicas dos HTs no metabolismo hepático, possibilitando novas intervenções farmacológicas para o tratamento da esteatose hepática não alcoólica associada ao hipotireoidismo. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG) (APQ-00013-22) e Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPQ) (403972/2021-3) Protocol: CEUA: 170/2021 CEUA: 349/2023</p>

Title	Analysis of the effects of probiotic supplementation as a preventive therapy for cognitive decline in Wistar rats during periostropause
Authors	JÚLIA ZANUTO DOURADINHO, LÍVIA VILAS BOAS RUAS TEIXEIRA, THAINÁ DAGUANE ESPERANÇA, BEATRIZ PROCÓPIO STRINGHETTA-VILLAR, ISABELLA RIBEIRO PRADELA, LUANA GALANTE DOURADINHO, DÉBORA PRAZIAS CAVALCANTE, RENAN JOSÉ BARZOTTI, LARISSA VICTORINO SAMPAIO, ANTONIO HERNANDES CHAVES NETO, RITA CÁSSIA MENAGATI DORNELLES
Affiliations	Departamento de Ciências Básicas, Laboratório de Fisiologia Endócrina e Envelhecimento, Universidade Estadual Paulista "Júlio de Mesquita Filho" (UNESP)
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The phase of female reproductive senescence, perimenopause, is accompanied by an irregular menstrual cycle, reduced secretion of ovarian hormones, altering the redox state, and may lead to behavioral changes. Similar to the human, rodent shares common features of the perimenopausal transition, including decline in follicles, irregular cycling, irregular fertility, steroid hormone fluctuations, and insensitivity to estrogen, characterized as periostropause. Currently, the beneficial potential of probiotic therapy is gaining increasing scientific interest due to its ability to modulate the intestinal microbiota and intervene in oxidative and behavioral stress, the latter being influenced by axis-intestine-brain communication. Objective: To investigate the effects of probiotic supplementation with VSL#3 as a strategy to minimize oxidative deficits as well as evaluate the effect on memory modulation in female rodents during the periostropause phase.</p> <p>Methods: After confirming the persistent diestrus cycle, seventeen 21-month-old Wistar rats were randomly assigned to either the saline group (NaCl; 0.5 mL/day) or the probiotic group (VSL#3; 12.86 billion live bacteria/kg/day; diluted to 0.5 mL/kg/day/saline). The treatments were administered via gavage for 42 days (CEUA nº 1028-2023). To analyze exploratory and locomotor activities, anxiety behavior, and memory, female rats were evaluated using the open field test (OF) and object recognition test (OR) before treatment (at 21 months) and after treatment (at 23 months). Blood and hippocampal samples from the experimental rats were collected for redox state analysis. Data are expressed as mean ± SEM. The significance level for rejecting the null hypothesis was set at $p < 0.05$. Results: In the 23-month-old female rats, those in the probiotic group spent significantly more time exploring the object than those in the saline group ($p=0.042$). Additionally, long-term memory tests showed an interaction between the intervention and age ($p=0.028$). Post hoc analysis revealed that the VSL#3 supplemented group performed better than the saline group of the same age ($p=0.044$). In the open field test, both the saline ($p=0.009$) and probiotic ($p=0.02$) groups spent less time in the center. However, the thigmotaxis rate was higher in the 23-month-old saline group rats (0.0006). Analysis of the hippocampal redox state in rats supplemented with VSL#3 showed improved redox balance, with higher antioxidant capacity ($p=0.0216$) and lower oxidant capacity ($p=0.0076$). In plasma, the probiotic group exhibited a lower total oxidizing capacity ($p=0.0051$). Conclusion: The study provides data that probiotic therapy is effective in improving explicit long-term memory, showing that significant changes occur in the biomechanics and biochemistry of the brain of naturally aged female rats. However, we did not observe an improvement in the anxiolytic profile in the treated group, showing that probiotic supplementation in this window was not satisfactory. Furthermore, it was observed that probiotic supplementation was able to modulate the redox state by increasing the total antioxidant capacity in the hippocampus of the rats, while the untreated group had a higher concentration of cellular hydroperoxides, showing an increase in total oxidative capacity, possibly due to the influence of cellular senescence. Support: - Protocol: CEUA nº 1028-2023</p>

Title	Assessment of health risk markers in women post Sars-CoV2 infection with Type 2 Diabetes Mellitus and Hypertension assisted in the SUS-Macaé/RJ.
Authors	INGRID BERANGER DA COSTA PEREIRA, KELSE TIBAU DE ALBUQUERQUE
Affiliations	Programa de Pós Graduação Multicêntrico em Ciências Fisiológicas, UFRJ Macaé
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Some patients recovered from covid-19 can present indications and symptoms related to the systemic manifestations caused by the infection and several biomarkers are associated with health problems. As the post-infection population keeps increasing and affected over time by variants, it is essential to analyze possible plasma modifications that may elucidate the pathophysiological changes, especially in patients with diabetes and hypertension. (Nalbandian, A., Sehgal, K., Gupta, A. et al. Post-acute COVID-19 syndrome. Nature Medicine 27, 601–615, 2021). Objective: To assess vascular, inflammatory and glycemic plasma markers, in the late period post- Sars-CoV2 infection in diabetic and hypertensive women assisted at SUS-Macaé/RJ. Methods: The study was cross-sectional and realized between August 2023 and March 2024 in the patients assisted at the Center for Reception and Post-Covid-19 recovery and Dona Alba Medical Specialties Center in Macaé/RJ. The patients were female, with DM2 or HT, aged between 18 and 59 years old and affected by Sars-CoV2 infection in the period from January 2021 and January 2022, after the first dose of the vaccine and report of post-infection symptoms, or with no history of Covid-19 in the period assessed. A nurse professional collected the blood to analyze: insulin, glucose, fructosamine, total cholesterol, HDL-cholesterol, LDL-cholesterol, triacylglycerol, D-dimer, ferritin, interleukin-6, alanine and aspartate aminotransferase. The following division was made for comparison between the groups: group 1 (DM2 without covid), group 2 (DM2 with covid), group 3 (HT without covid) and group 4 (HT with covid). For statistical evaluation between groups, the Levene's test and Shapiro-Wilk test were used, being significant for p-values < 0.05. Results: A total of 42 patients was assessed, and in the groups 1 (n=8) and 2 (n=10) a statistically significant association was found with glucose (p=0,03), with group 2 having more inadequacy. In the group 3 (n=12) and 4 (n=12) a statistically significant association was found with HDL-cholesterol (p=0,008), with group 4 having more inadequacy. Conclusion: The group with Sars-CoV2 infection presented more inadequacy in the biochemical parameters compared with the control groups, which possible mean a negative health outcome in the patients. A multidisciplinary intervention may be necessary for post-covid health recovery. Support: Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (FAPERJ) Protocol: 70512223.6.0000.5699</p>

Title	Evaluation of KNDy neurons response to suckling stimulus in lactating rats.
Authors	MATHEUS VIANA, ISABELE BEATRIZ PEREIRA ALVEZ, EVELYN CRISTINE DOS SANTOS ÁLVARES, RAPHAEL ESCORSIM SZAWKA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: In mammals, lactation can be characterized as a physiological hyperprolactinemic state. During this period both hypothalamic gonadotrophin releasing hormone (GnRH) and pituitary luteinizing hormone (LH) secretion decrease, resulting in a loss of gonadal function also known as lactation-induced infertility. Since most of the GnRH neurons do not express PRL receptor, the PRL-mediated inhibition of GnRH frequency and amplitude is plausibly established through PRL-sensitive afferents, such as kisspeptin neurons from the arcuate nucleus of the hypothalamus (ARC), which strongly stimulates GnRH secretion and also modulate PRL release. Indeed, lactation-induced infertility is characterized by reduced kisspeptin expression in the ARC and suppressed LH secretion. ARC kisspeptin neurons co-express neurokinin B (NKB) and dynorphin A (DynA), which work as autocrine regulators at the KNDy cell body respectively promoting stimulatory and inhibitory signals. Even though the suckling exerted by the pups on the dam's nipple is the strongest stimulus responsible for the PRL secretion and an inhibitory signaling to the reproductive axis, the mechanism by which suckling exerts these effects are not well known. Here, we further analyzed the response of KNDy neurons to the suckling stimulus in the lactating rat. Objective: This study aimed to investigate whether KNDy neurons are activated by suckling in lactating rats as well as to determine the impact of suckling on kisspeptin and NKB expression in the ARC. Methods: Lactating dams were separated from their pups for 5 h and further assigned to the following groups: rats that did not have their pups returned (LAC, n=9), pups returned with restricted access to suckling (LAC+P, n=7) and pups returned with no restriction to suckling (LAC+S, n=9). Virgin rats on diestrus were used as non-lactating controls (N-LAC, n=7). The brains were immunohistochemically processed for c-Fos and NKB, and c-Fos and kisspeptin double labelings. LH and prolactin were measured by ELISA in the blood collected through cardiac puncture before transcardiac perfusion. Protocols were approved by the Ethics Committee on the Use of Experimental Animals of the Universidade Federal de Minas Gerais (338/2019) Results: PRL levels significantly increased in LAC+S ($P < 0.05$), whereas pup separation was able to return PRL secretion in LAC and LAC+P rats to N-LAC levels. LAC+S animals showed markedly reduced LH levels compared to N-LAC ($P < 0.001$) and LAC ($P < 0.05$). LH was also decreased in the LAC+P group compared to N-LAC ($P < 0.01$). ARC ($P < 0.001$) and PVN ($P < 0.05$) single-label c-Fos expression was higher in all lactating dams than on N-LAC rats, with no difference among LAC, LAC+P and LAC+S rats. The number of kisspeptin-immunoreactive (ir) neurons in the ARC was equally reduced in all lactating animals compared to N-LAC ($P < 0.001$). On the other hand, the number of NKB-ir neurons in the ARC did not differ between lactating and N-LAC rats and was significantly increased in LAC+S rats compared to LAC and LAC+P ($P < 0.05$). Moreover, c-Fos expression in either Kiss-ir or NKB-ir neurons did not change in any lactating group. Conclusion: Our results show KNDy neurons are not activated by suckling. Associated with the suppression of LH secretion, kisspeptin neuropeptide expression in the ARC is reduced during lactation, whereas suckling paradoxically elevates NKB expression in the ARC. These findings provide new information on the modulation of KNDy neurons by suckling during lactation. Support: CNPq and CAPES Protocol: 338/2019</p>



Title	Dose supra fisiológica de cipionato de testosterona promove dano oxidativo e aumenta marcadores de proliferação e apoptose celular nas glândulas submandibulares de ratos Wistar
Authors	LARISSA VICTORINO SAMPAIO, ARIELI RAYMUNDO VAZÃO, RAYARA NOGUEIRA DE FREITAS, RENAN JOSÉ BARZOTTI, GUILHERME EDUARDO ROCHA SILVA, LIVIA DA SILVA PRADO TORRES, ALLICE DOS SANTOS CRUZ VERAS, GIOVANA RAMPAZZO TEIXEIRA, ANA CLÁUDIA DE MELO STEVANATO NAKAMUNE, ANTONIO HERNANDES CHAVES NETO
Affiliations	Educação Física, UNESP, Ciências Básicas, UNESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O uso abusivo e indiscriminado de esteroides anabolizantes androgênicos (EAA), tornou-se um sério problema de saúde mundial, sendo descritos inúmeros prejuízos a função de órgãos como coração, fígado e rins. Além disso, resultados prévios do nosso grupo demonstram que a administração de dose supra fisiológica de cipionato de testosterona, um EAA amplamente comercializado no Brasil, promoveu distúrbios na secreção de proteína total, amilase e eletrólitos salivares em ratos. Todavia, os mecanismos envolvidos na disfunção salivar induzida por EAA ainda não foram esclarecidos. Objective: Diante disso, o objetivo desse trabalho foi analisar o efeito da administração de dose supra fisiológica de cipionato de testosterona no estado redox, na histomorfometria e em marcadores de proliferação e apoptose celular nas glândulas submandibulares de ratos Wistar. Methods: Vinte ratos Wistar (<i>Rattus norvegicus albinus</i>), 12 semanas de idade, 300-400g, foram distribuídos aleatoriamente em dois grupos experimentais (n=10): grupo controle (C) e grupo cipionato de testosterona (CT). O CT (Deposteron®, EMS Sigma Pharma LTDA, Brasil) na dose de 20 mg/kg foi injetado por via intramuscular, semanalmente, por 6 semanas. Após o período experimental, os animais foram pesados, sedados com cloridrato de xilazina (10 mg/kg, IM) e cloridrato de cetamina (75 mg/kg, IM), eutanasiados via punção cardíaca e as glândulas submandibulares foram removidas, limpas e pesadas. As glândulas do lado direito foram armazenadas a -80 °C para realização do homogenato tecidual e análise do estado redox dos seguintes parâmetros: capacidade oxidante total (COT), peroxidação lipídica (TBARS), proteína carbonilada (PC), capacidade antioxidante total (CAT), ácido úrico (AU), glutathiona reduzida (GSH), superóxido dismutase (SOD), catalase e glutathiona peroxidase (GPx). As glândulas do lado esquerdo foram fixadas em solução de Bouin para o processamento histológico, no qual os cortes foram corados com hematoxilina & eosina para realização da análise histomorfométricas por meio da quantificação da área de ácinos, ductos, túbulos convolutos granulares e tecido conjuntivo. Além disso, nos cortes foi conduzido a imuno marcação para o antígeno nuclear de células em proliferação (PCNA) e caspase-3, marcadores de proliferação e apoptose celular, respectivamente. Os resultados paramétricos foram analisados pelo teste Student t não-pareado ($p < 0,05$). Results: O estresse oxidativo associado com CT foi caracterizado pelo aumento da COT ($p < 0,001$), TBARs ($p < 0,01$) e PC ($p < 0,05$). A análise da capacidade antioxidante não-enzimática evidenciou maior concentração de GSH ($p < 0,001$) no grupo CT, enquanto CAT e AU foram semelhantes entre os grupos. O desequilíbrio da defesa antioxidante enzimática induzido pelo CT foi caracterizado pelo aumento das atividades da SOD ($p < 0,01$), catalase ($p < 0,05$) e redução da GPx ($p < 0,05$). O CT promoveu aumento da área de túbulos convolutos granulares ($p < 0,01$) e redução da área acinar ($p < 0,05$), porém não alterou a área de ductos e tecido conjuntivo. Da mesma forma, houve aumento na imuno marcação de PCNA ($p < 0,001$) e caspase-3 ($p < 0,01$) no grupo CT. Conclusion: Portanto, concluímos que o tratamento com dose supra fisiológica de CT promove dano oxidativo e alterações morfológicas, além de estimular proliferação e apoptose celular nas glândulas submandibulares de ratos Wistar, o que pode ser um fator de risco para a disfunção das glândulas salivares. Support: CAPES, FAPESP (processo 2022/11245-3), Edital 8/2023 – PIBIC Ensino Médio Nº 8803. Protocol: CEUA FOA/UNESP nº 0373-2022.</p>

Title	Maternal ZIKV causes placental oxidative damage by upregulating mRNA levels of oxidants and antioxidants enzymes
Authors	VERÔNICA MÜLLER DE OLIVEIRA NASCIMENTO, IRIS SOARES ANDRADE, CHERLEY BORBA VIEIRA DE ANDRADE, RAKEL KELLY SILVA ALVES, ALESSANDRA CRISTINA CHAGAS VALIM, LARISSA SIMÕES DIAS, KLAUS NOVAES FONTES, LUCIANA BARROS DE ARRUDA, SHARTON VINÍCIUS ANTUNES COELHO, ENRRICO BLOISE, RODRIGO SOARES FORTUNATO, TÂNIA MARIA RUFFONI ORTIGA
Affiliations	Programa de Pós Graduação em Ciências Biológicas, Fisiologia, UFRJ, Departamento de Virologia, UFRJ, Departamento de Morfologia, UFMG, Programa de Pós Graduação em Endocrinologia, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: In 2015, a sudden increase of microcephalic newborns emerged in Brazil (SCHULER-FACCINI et al., 2015). Later, Zika virus (ZIKV) vertical transmission was associated with a wide spectrum of congenital abnormalities, namely the Congenital Zika Syndrome (CZS) (DE CARVALHO et al., 2017). Fetal outcome may be impacted even when ZIKV vertical transmission is absent, probably via ZIKV placental infection (ANDRADE et al., 2021). In this connection, in vitro studies have demonstrated that ZIKV may infect and cause oxidative stress in trophoblast cells (CERVANTES et al., 2023). We hypothesized that ZIKV infection in mid-pregnancy will cause placental oxidative stress in mice. Objective: To investigate whether ZIKV infection in pregnant dams will trigger placental oxidative stress. Methods: At gestational day (GD)12.5, pregnant mice (C57BL/6; 8-12 weeks old) (CEUA: 036/16, A7/20-036/16) were infected i.v. with ZIKV-BRPE243 (5x10⁷ PFU; Z group; n=22) or Mock (supernatant of noninfected C6/36 cells; M group; n=28). At GD18.5, c-section was performed and placentas were weighted, sorted by sex [Female Mock (FM), Female ZIKV (FZ), Male Mock (MM) and Male ZIKV (MZ)], fixed in 4% paraformaldehyde for histological analyses or frozen at -80°C for biomolecular analysis. We evaluated placental nitrotyrosine residues by immunohistochemistry (n=5 fetuses, each from a different dam), mitochondria and granular endoplasmic reticulum ultrastructures by transmission electron microscopy (n=5) and Nox1, Cybb (NOX2), Sod1, Sod2, Sod3, Gpx1, Gpx3, Cat and Cdkn2a mRNA levels by qPCR (n=9). Data were represented as mean±SEM, analyzed by Student's t test and significant differences between groups were considered when p<0.05. Results: Maternal ZIKV infection increased nitrotyrosine residues in the placental labyrinth zone of female (FM: 16.16±0.64 %; FZ: 25.03±0.62 %; p<0.0001) and male (MM: 21.38±0.17 %; MZ: 24.64±0.17 %; p<0.0001) fetuses, as well as in the placental junctional zone of female (FM: 11.43±1.25 %; FZ: 17.19±1.86 %; p=0.0167) and male (MM: 14.07±0.48 %; MZ: 16.96±0.18 %; p=0.0002) fetuses. Moreover, we found degenerated mitochondria and granular endoplasmic reticulum with dilated cisterns in placentas of both FZ and MZ groups. ZIKV increased the placental mRNA levels of the oxidant enzyme Nox1 in female (FM: 1±0.11; FZ: 1.29±0.07; p=0.0221) and male (MM: 1±0.09; MZ: 1.28±0.14; p=0.0535) fetuses, while increasing Cybb mRNA levels only in the female placenta (FM: 1±0.22; FZ: 1.52±0.14; p=0.0304). In addition, mRNA levels of the the antioxidant enzyme Sod2 were increased only in the female placenta (FM: 1±0.09; FZ: 1.37±0.14; p=0.0259), while Sod3 mRNA levels were increased in placentas of both female (FM: 1±0.17; FZ: 1.71±0.21; p=0.0084) and male (MM: 1±0.22; MZ: 1.70±0.36; p=0.0573) fetuses. Gpx1 (FM: 1±0.08; FZ: 1.45±0.11; p=0.0022) and Gpx3 (FM: 1±0.10, FZ: 1.43±0.12, p=0.0072) mRNA levels were increased by ZIKV infection only in the female placenta. Placental Sod1, Cat and Cdkn2a mRNA levels were not affected by infection in both sexes. Conclusion: Together, our data showed that maternal ZIKV infection caused oxidative damage and upregulated the mRNA levels of oxidants and antioxidants enzymes in the murine placenta of both female and male fetuses, indicating that oxidative stress was triggered by the virus at some point throughout gestation and may be involved in the pathogenesis of CZS. Support: CAPES, CNPq, FAPERJ Protocol: 036/16 e A7/20-036/16</p>

Title	LOWER LIVER GLYCOGENOLYTIC ACTIVITY OF ISOPROTERENOL IS DUE TO DEGRADATION OF ITS SECOND MESSENGER IN YOUNG GOTO-KAKIZAKI RATS.
Authors	FRANCIELE PASQUINI DALL' AQUA, OTÁVIO VINÍCIUS CUSTÓDIO JORGE, MARIA FERNANDA SIQUEIRA, LUNNA BOSQUETTI UEMURA, MANOEL OSVALDO ESTEVAM FÁVARO, GIOVANNA PAIS GALVÃO ESTEVES, ROBERTO BARBOSA BAZOTTE, ROBERTO BARBOSA BAZOTTE, RUI CURI, RUI CURI, GISELE LOPES BERTOLINI, PRISCILA CASSOLLA
Affiliations	Physiological Sciences, UEL, Post Graduate Program in Physiological Sciences, UEM, Interdisciplinary Post Graduate Program in Health Sciences, UNICSUL, Butantan Institute, USP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The Goto-Kakizaki (GK) rat is a model of non-obese insulin resistance, which spontaneously develops type 2 diabetes mellitus with a chronology like that in humans. Objective: The main of this work was to evaluate liver responsiveness to isoproterenol, a beta-adrenergic agonist, and the response to the second messenger of the beta-adrenergic pathway, cyclic adenosine monophosphate (cAMP) and its phosphodiesterase-resistant synthetic analogue, 6-dibutyryl cAMP (6-db cAMP). Methods: To this end, three days after confirmation of insulin resistance at the end of the 8th week of age by the insulin tolerance test (ITT), the animals were submitted to in situ liver perfusion, through which an infusion was made at isoproterenol concentrations of 10 μM, 20 μM or 40 μM for the evaluation of the dose-response curve of beta-adrenergic agonist on glucose production, glycolysis and glycogenolysis in GK and control rats (C), or 3 mM cAMP or 3 mM 6-db cAMP. Statistical analysis was performed using unpaired Student's t-test and one-way ANOVA followed by Tukey's test and $p < 0.05$ was adopted. Results: The ITT confirmed insulin resistance in the GK group ($p = 0.0041$). The hepatic response to isoproterenol was lower in GK animals at all concentrations for glucose production [10 μM, GK area under curve (AUC) 0.383 ± 1.974 ($n = 8$), C AUC 9.309 ± 3.277 ($n = 6$), $p = 0.0299$; 20 μM, GK AUC 0.346 ± 1.754 ($n = 11$), C AUC 12.390 ± 4.350 ($n = 10$), $p = 0.0224$, and 40 μM, GK AUC 0.201 ± 2.147 ($n = 11$), C AUC 12.210 ± 1.277 ($n = 10$), $p = 0.0003$] and for glycogenolysis [10 μM, GK AUC 0.655 ± 2.308 C AUC 11.160 ± 3.856, $p = 0.0295$; 20 μM, GK AUC 5.705 ± 0.7124, C AUC 15.020 ± 3.593, $p = 0.0153$; and 40 μM, GK AUC 6.198 ± 1.299, C AUC 15.790 ± 1.660, $p = 0.0003$], but there was less glycolysis only at the highest concentration [10 μM, GK AUC 1.863 ± 0.440, C AUC 3.796 ± 1.157, $p = 0.1083$; 20 μM, GK AUC 2.435 ± 0.443; C AUC 3.940 ± 0.8006, $p = 0.1081$; and 40 μM, GK AUC 2.219 ± 0.673, C AUC 4.389 ± 0.665, $p = 0.0355$]. Although GK rat livers did not respond to cAMP infusion in glucose production [GK AUC-23.630 ± 10.220 ($n = 4$), C AUC 9.470 ± 4.522 ($n = 4$), $p = 0.0084$] and glycogenolysis [GK AUC-30.190 ± 10.930; C AUC 24.690 ± 4.235, $p = 0.0034$], there was greater glucose production [GK AUC 79.260 ± 8.423 ($n = 3$), C AUC 20.000 ± 5.202 ($n = 5$), $p = 0.0014$], and glycogenolysis [GK AUC 76.870 ± 9.675, C AUC 18.860 ± 4.001, $p = 0.0016$] in GK rats from 6-db cAMP. Conclusion: Therefore, isoproterenol did not stimulate glycogenolysis and liver glucose release in fed GK animals, probably due to the higher rate of degradation of the second messenger of the beta-adrenergic pathway, cAMP. Support: FAPESP nº 2018/09868-7; Government of the State of Paraná, Paraná Science and Technology Council, and State Secretariat for Science, Technology, and Higher Education (SETI) (budget allocation # 4560.19.571.06.6153; e-protocol 21.234.745-0). Protocol: (CEUA/UEL) nº 019.2023</p>



Title	MATERNAL OBESITY INCREASES ENDOCANNABINOID SIGNALING AND TRIGLYCERIDE CONTENT IN THE LIVER OF WEANLING RAT OFFSPRING.
Authors	LARISSA DE BRITO FASSARELLA, THAMIRIS CHAGAS DIAS, JULIANA PENA GONÇALVES, CAMILA CALVIÑO MORAES, CAROLINA DOS SANTOS FERREIRA, ALEXANDRE GUEDES TORRES, TATIANA EL BACHA PORTO, CARMEN CABANELAS PAZOS DE MOURA, ISIS HARA TREVENZOLI
Affiliations	Instituto de Biofísica Carlos Chagas Filho, UFRJ, Instituto de Nutrição Josué de Castro, UFRJ, Instituto de Química, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Nutritional, environmental, or hormonal insults early in life modulate biological systems and increase the risk of lifelong metabolic diseases such as obesity and metabolic dysfunction-associated steatotic liver disease (MASLD). Both obesity and MASLD have been associated with increased activity of the endocannabinoid system (ECS). The ECS is composed of the lipid endocannabinoids anandamide (AEA) and 2-arachidonoylglycerol (2-AG), which bind to CB1 and CB2 receptors and are metabolized by fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL) enzymes. Objective: In this study, we investigated the effect of maternal perinatal obesogenic diet on ECS components in the liver of male and female offspring at weaning. Methods: All procedures were approved by the CEUA/CCS/UFRJ (protocol 129/21). Female Wistar rats, 60 days old, were fed a standard diet (CT; 9% kcal lipids) or an obesogenic diet (OD; 40% kcal lipids + 9.5% kcal sucrose) for 9 weeks before mating and during pregnancy and lactation. The liver of offspring of both sexes was collected at weaning for analysis of endocannabinoid signaling by western blotting and HPLC-MS and for fatty acid content by GC-FID. Liver TG content was quantified by a commercial kit based on an enzymatic-fluorimetric method. Data were analyzed by two-way ANOVA followed by Sidak post-hoc test. Pearson correlations were performed between liver 2-AG and leptinemia and polyunsaturated fatty acid (PUFA) liver content, considering the total animal sample stratified by offspring sex. Results: Maternal OD increased body weight at weaning (+6.6%, $p < 0.05$), visceral adiposity (male: +153.6%, $p < 0.05$; female: +226%, $p < 0.05$) and subcutaneous adiposity (male: +101.5%, $p < 0.05$; female: +110.9%, $p < 0.05$) in both sexes. OD offspring presented increased liver weight (male: +17%, $p < 0.05$; female: +17.8%, $p < 0.05$), liver TG content (+172%, $p < 0.05$) and hypertriglyceridemia (+68.3%, $p < 0.05$), compared with CT offspring. Maternal consumption of OD increased the content of 2-AG (male: +53%, $p < 0.05$; female: +152.6%, $p < 0.05$), the total content of saturated and monounsaturated fatty acids in the liver of male and female offspring (SFA: male: +30%, $p < 0.05$; female: +41%, $p < 0.05$; MUFA: male: +208%, $p < 0.05$; female: +283%, $p < 0.05$) and also the total polyunsaturated fatty acid content (PUFA: +12.5%, $p < 0.05$), regardless of sex. Maternal obesity reduced the n-3 PUFA content (male: -19%, $p < 0.05$; female: -17%, $p < 0.05$) and increased the n-6 PUFA content in females (+22%, $p < 0.05$), as well as increased the n-6/n-3 ratio in both sexes of the offspring at weaning (male: +42%, $p < 0.05$; female: +46.5%, $p < 0.05$). The hepatic content of 2-AG positively correlated with the n-6 content only in female offspring (female: $r = 0.5967$; $p = 0.0147$) and with the n-6/n-3 ratio in both sexes (male: $r = 0.6288$; $p = 0.0091$; female: $r = 0.8565$; $p < 0.0001$). On the other hand, the content of 2-AG showed a negative correlation with the n-3 content, regardless of sex (male: $r = -0.5435$; $p = 0.0295$; female: $r = -0.6494$; $p = 0.0065$). Conclusion: Perinatal maternal obesogenic diet induces early hepatic steatosis and increases hepatic 2-AG content in the offspring at weaning, regardless of sex. Hepatic 2-AG content showed a strong positive correlation with the n-6/n-3 ratio and a negative correlation with n-3 PUFA content. Together, these results suggest that maternal nutrition at critical stages of development can modulate the offspring's ECS, predisposing them to or preventing the onset of metabolic diseases. Support: Faperj, Cnpq Protocol: 129/21</p>



Title	Efeitos da co-exposição aos contaminantes ambientais tributilestanho, cádmio e mercúrio no sistema reprodutivo de ratas.
Authors	FLÁVIA CAROLINE FARIAS DOS SANTOS, JONES BERNARDES GRACELI
Affiliations	Morfologia, UFES
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A poluição dos oceanos está disseminada, constituindo-se em uma mistura complexa de metais pesados, plásticos, produtos químicos manufaturados, petróleo, resíduos industriais, pesticidas, fertilizantes entre outros. Quanto à água para consumo, no estado do Espírito Santo–ES, após o desastre de Mariana–MG em 2015, a água da CESAN apresentou níveis de metais pesados acima dos limites de segurança estabelecidos pelo Ministério da Saúde em diversos pontos do ES. Soma-se a isso a bioacumulação dos contaminantes, cádmio (Cd), mercúrio (Hg) e tributilestanho (TBT), que leva à exposição simultânea da população a estes contaminantes via ingestão de animais contaminados. Sabe-se que, individualmente, estes três contaminantes são capazes de promover toxicidade no sistema reprodutor feminino. Porém, as consequências da exposição a esta mistura de TBT+Cd+Hg para o organismo animal ainda não foram relatadas. Objective: Investigar se a co-exposição aos contaminantes tributilestanho (TBT), cádmio (Cd) e mercúrio (Hg) causaria alterações reprodutivas em ratas. Methods: Ratas Wistar (<i>Rattus norvegicus albinus</i>) adultas (n=10, 8-12 semanas com 230-250g) foram co-expostas aos contaminantes TBT (100ng/kg/dia), Hg (4,6 mg/kg, dose inicial e 0,07 mg/kg/dia, doses de manutenção) e Cd (100 mg/L). Os animais foram tratados por 15 dias. Todos os protocolos foram aprovados pelo CEUA-UFES (04/2023). Foi avaliado o peso do ovário e do útero, o ciclo estral, a histomorfometria do ovário e do útero e os níveis hormonais. Os dados foram representados como média \pm E.P.M. As comparações entre os grupos foram realizadas por meio de testes t de Student e teste de Mann-Whitney para dados gaussianos e não gaussianos, respectivamente. O valor de $p < 0,05$ foi considerado estatisticamente significativo. Results: Após a exposição à mistura TBT+Hg+Cd (MIX) não foi observada alteração de peso do ovário e do útero ($p > 0,05$, n=5). Na análise do ciclo estral, foram observadas irregularidades nos grupos expostos aos contaminantes, porém sem significância estatística ($p > 0,05$, n=5). Na morfologia ovariana, foi observado aumento do número de folículos pré-antrais ($p < 0,05$ CON: $0,91 \pm 0,10$ e MIX: $1,37 \pm 0,19$ n.^o/mm², n=5) e diminuição da quantidade de corpo lúteo ($p < 0,05$ CON: $1,366 \pm 0,049$ e MIX: $1,162 \pm 0,073$ n.^o/mm², n=5). Ademais, a razão entre a quantidade de folículos pré-antrais e antrais foi maior após a exposição aos contaminantes ($p < 0,05$ CON: $0,71 \pm 0,11$ e MIX: $1,38 \pm 0,23$ n.^o/mm², n=5). Outras alterações na morfologia ovariana foram encontradas, como presença de células inflamatórias, gotículas lipídicas e hiperemia no corpo lúteo. Com a avaliação hormonal, observamos aumento dos níveis séricos de FSH ($p < 0,05$ CON: $6,02 \pm 0,33$ e MIX: $11,08 \pm 1,34$ μg/ mL, n=5) e uma tendência ao aumento nos níveis de estrogênio ($p = 0,08$ CON: $18,7 \pm 5,4$ e MIX: $31,8 \pm 3,2$ pg/ mL, n=5). Na morfologia uterina foi observado aumento da área do útero ($p < 0,05$ CON: $2,88 \pm 0,08$ e MIX: $3,63 \pm 0,23$ mm², n=5) e do miométrio total ($p < 0,05$ CON: $0,233 \pm 0,008$ e MIX: $0,306 \pm 0,011$ mm, n=5). Além disso, também foi observado diminuição do número de glândulas ($p < 0,05$ CON: $24,3 \pm 2,2$ e MIX: $16,4 \pm 1,4$ n.^o/mm², n=5). Em uma análise qualitativa, foi observado hiperplasia e presença de granulomas nas glândulas uterinas. Conclusion: Com estes dados preliminares, constata-se que os contaminantes quando são administrados simultaneamente prejudicam o sistema reprodutivo de ratas e possivelmente a fertilidade, o que será avaliado posteriormente. Support: FAPES [#19/2022-TO 981/2022; #N^o 03/2021, TO: 486/2021] CNPQ [# 307224/2021-0]. LHT. Protocol: CEUA-UFES (04/2023)</p>

Title	Norepinephrine activity in the preoptic area and arcuate nucleus in the hot-flash model of ovariectomized rats
Authors	TUNDE FEMI ABRAHAM, KAOMA STEPHANI DA COSTA SILVA, RAPHAEL ESCORSIM SZAWKA
Affiliations	Fisiologia e Biofísica, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Estradiol (E2) deficiency disrupts normal thermoregulatory responses in the preoptic area (POA), which clinically manifest as the vasomotor symptom of hot flash (HF). Previous studies suggest a role for norepinephrine (NE) in HF, as pharmacological increases in NE can trigger HF in postmenopausal women, and this can be attenuated by the α2-adrenergic agonist clonidine. Additionally, a neuronal population in the arcuate nucleus (ARC), which co-expresses kisspeptin, neurokinin B, and dynorphin (KNDy), facilitates cutaneous vasodilation and HF in the absence of E2. We have recently demonstrated that NE terminals contact KNDy neurons in rats, potentially playing a role in the genesis of HF. Objective: To evaluate NE activity in the POA and ARC in the hot-flash model of ovariectomized rats. Methods: Two month-old female Wistar rats (CEUA Nº.262/2020) weighing 250-300 g. Rats were ovariectomized (OVX) or sham operated and subsequently, a temperature datalogger was implanted intra-peritoneally for measurement of abdominal temperature (Tabd). Tail skin temperature (Tskin) was measured with a sub-cutaneous thermo-sensor implanted at 2 cm from the base of the tail. Temperature recordings were performed at intervals of five minutes for one hour under controlled room temperature (24 ± 0.5 °C). Rats were assigned into 3 groups: sham-operated on diestrus day (Diestrus, n=8), OVX treated with oil (OVX, n=8), and OVX treated with E2 (OVX+E2, n=8). Fifteen days after ovariectomy, Tskin and Tabd were measured. At the end of the experiment, the animals were decapitated, their brains were removed and immediately frozen to perform microdissections of the POA and ARC. The microdissections were measured for NE and 3-methoxy-4-hydroxy-phenylglycol (MHPG) concentrations by high-performance liquid chromatography with electrochemical detection (HPLC-ED). Results: Ovariectomy reduced the uterine weight ($P < 0.001$) compared with diestrus, and this was prevented by the E2 treatment in OVX+E2 rats. Tskin and the heat loss index significantly increased in OVX rats when compared with diestrus ($P < 0.001$). These effects were completely prevented by E2 in OVX+E2 rats. However, no significant difference was observed in the Tabd between groups. NE concentrations in the ARC were higher in OVX+E2 rats compared with diestrus and OVX rats ($P < 0.05$), whereas no significant difference between the groups was observed for NE concentrations in the POA. A significant increase ($P < 0.05$) was also observed in MHPG concentrations in the ARC of OVX+E2 rats compared with the other groups, but not in the POA. The MHPG/NE ratio did not differ between groups in either the POA or ARC. Conclusion: Our study demonstrates that E2 treatment in OVX rats increases NE concentrations and release in the ARC, as revealed by MHPG levels, which is associated with the reduction in skin heat dissipation. Whether the NE inputs to KNDy neurons are directly or indirectly involved in heat dissipation remains to be determined. Further investigation is required to explore the role played by NE in the ARC and POA in the modulation of HF. Support: FAPEMIG, CNPQ Protocol: CEUA Nº.262/2020</p>

Title	Inhibitory Role of KNDy Neurons in the Estrogenic Regulation of Gonadotropin Secretion in Female Rodents
Authors	ANA CLARA CAMPIDELI-SANTANA, KAOMA STEPHANI DA COSTA SILVA, ROBERTA ARAUJO-LOPES, LUMA MOREIRA ANTUNES, LIQUE M. COOLEN, MICHAEL N. LEHMAN, RAPHAEL ESCORSIM SZAWKA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Department of Biological Sciences, Kent State University
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Neurons in the arcuate nucleus (ARC) of the hypothalamus that coexpress kisspeptin, neurokinin-B, and dynorphin (KNDy) play a crucial role in the control of gonadotropin-releasing hormone (GnRH) neurons and, thus, on luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion. According to the KNDy hypothesis, neurokinin-B stimulates kisspeptin while dynorphin signaling inhibits kisspeptin, resulting in the generation of GnRH/LH pulses. However, the neuroendocrine mechanisms involved in the estrogenic regulation of the KNDy neuron to control LH and FSH secretion are not fully understood. Objective: Our first objective was to perform a longitudinal evaluation of female rats in which KNDy neurons were ablated to determine the integrated role of this neuronal population in the control of pulsatile LH and basal FSH secretion under different estrogenic conditions. We then characterized the expression of the kappa (Oprk1)-, mu (Oprm1)-, and delta (Oprd1)-opioid receptors in kisspeptin neurons of the ARC (ARC-Kiss1) and anteroventral periventricular nucleus (AVPV-Kiss1), and in GnRH (Gnrh1) neurons of female mice and rats under different estrogenic conditions. Methods: Adult female rats underwent a neurochemical ablation of KNDy neurons via intra-ARC stereotaxic injections of neurokinin-3 receptor agonist conjugated with saporin (NK3-SAP) or blank saporin (Control). Female mice and rats with low (diestrus) and high (proestrus) endogenous estradiol (E2) levels were perfused and brains were analyzed by RNAscope in situ hybridization. Results: Diestrus NK3-SAP rats with 74% loss of KNDy neurons displayed increased frequency, amplitude, and baseline levels of LH pulses and higher basal FSH secretion. After ovariectomy, parameters of LH and FSH secretion were increased but did not differ between NK3-SAP and Control ovariectomized (OVX) rats. In a second cohort of NK3-SAP rats with 64% KNDy neuron loss, OVX rats treated with E2 (OVX+E2) displayed reduced LH pulsatile secretion and, in this condition, the NK3-SAP lesion again increased LH pulse frequency but not pulse amplitude or baseline levels. Thus, the partial loss of KNDy neurons facilitates LH and FSH secretion in the presence of E2, suggesting that the dynorphin signaling might be responsible for the inhibitory role of KNDy neurons on the gonadotrophin output. Regarding the opioid receptors, in both mice and rats, there was a high expression of Oprk1 in ARC-Kiss1 neurons, which was reduced on proestrus compared to diestrus. On the other hand, Oprd1 expression in ARC-Kiss1 neurons increased on proestrus, while the Oprm1 expression in Kiss1 neurons was differently modulated by estrous cycle depending on the rostro-caudal ARC region and species. The AVPV-Kiss1 neurons displayed a high degree of co-expression of Oprd1, Oprm1, and Oprk1, unchanged across the cycle. All opioid receptors were found in Gnrh1 neurons, and the co-expression of Oprk1 was higher on proestrus than on diestrus. Conclusion: The submaximal loss of KNDy neurons accelerates and amplifies LH pulses and FSH secretion. This inhibitory effect of KNDy neurons depends on the presence of E2 and is possibly mediated by dynorphin. Accordingly, Oprk1, Oprm1, and Oprd1 are abundantly expressed in the GnRH network. Oprk1 expression in ARC-Kiss1 and GnRH neurons is modulated by E2 and possibly involved in the mechanism of negative-feedback to restrain gonadotrophin secretion. Support: FAPEMIG, CNPq, CAPES, Pro-reitoria de Pesquisa-UFMG, and Brain Health Research Institute (BHRI) Protocol: 272/2020</p>



Title	Modulação do perfil metabólico de linfócitos de ratos diabéticos não obesos (Goto-kakizaki) pela suplementação com ácidos graxos ômega-3
Authors	HENRIQUE DE SOUZA FALCÃO, MARIA JANAINA LEITE DE ARAÚJO, TIAGO BERTOLA LOBATO, ELVIRAH SAMANTHA DE SOUSA SANTOS, ANA CAROLINA GOMES PEREIRA, ILANA SOUZA CORREA, JOÃO CARLOS DE OLIVEIRA BORGES, LAUREANE NUNES MASI, MARIA ELIZABETH PEREIRA PASSOS, GABRIELA MANDÚ GIMENEZ, SANDRO MASSAO HIRABARA, TÂNIA CRISTINA PITHON-CURI, RUI CURI, RENATA GORJÃO
Affiliations	Ciências da Saúde, UNICSUL
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O Diabetes Mellitus tipo 2 (DM2) está frequentemente ligado à síndrome metabólica e obesidade, mas a incidência em indivíduos magros também é elevada. Estudos mostram que ácidos graxos ômega-3 podem modular a ativação de linfócitos, mas as vias metabólicas afetadas são desconhecidas. Caracterizar essas vias é crucial para entender o efeito dos AGs na função e polarização das células T.</p> <p>Objective: Este estudo teve como objetivo investigar os efeitos da suplementação com AGs ômega-3 na modulação de vias metabólicas envolvidas com a diferenciação de linfócitos em ratos diabéticos não obesos (Goto-Kakizaki). Methods: Foram utilizados animais GK (n=16) e Wistar (n=16) divididos em: 1) suplementados com 2 g/kg de óleo de peixe rico em n-3 (EPA 540 mg/g e DHA 100 mg/g), 3 vezes por semana, da 8ª à 16ª semana de vida (WT n-3 e GK-n-3); 2) ratos que receberam a mesma quantidade de água (WT-CT e GK-CT). Posteriormente, foram realizados os testes de tolerância à glicose (GTT) e à insulina (ITT) (n= 13). Após a eutanásia, os linfócitos dos linfonodos mesentéricos foram isolados para análises de captação de glicose por citometria de fluxo em linfócitos estimulados com PMA/ionomicina por 12 horas (n= 5). Em seguida realizamos a avaliação da expressão gênica de enzimas hexoquinase, fosfofrutoquinase, glicose-6-fosfato-desidrogenase, citrato Sintase, acil-Coa desidrogenase e fator de transcrição HIF1-alfa por PCR em tempo real (n= 10). Posteriormente, avaliamos a cinética enzimática de hexoquinase, fosfofrutoquinase, citrato sintase, piruvato quinase e lactato desidrogenase (n = 10). Results: Em relação ao GTT, observamos uma maior área sobre curva para os animais GK controle (30776 ± 27) comparado com os animais WT-CT (12914 ± 1003) e GK n-3 (23327 ± 1279). O teste de kITT demonstrou um menor decaimento no grupo GK controle (-0,0042 ± 0,0009 %/min) comparado com os grupos WT controle (0,011 ± 0,006), e GK n-3 (0,0040 ± 0,00120). Foi observada uma maior captação de glicose nos animais GK-CT (8332 ± 396 para média de fluorescência) em relação aos animais suplementados com n-3 (5710 ± 543). Observamos uma maior expressão gênica de citrato sintase no grupo GK controle em relação aos grupos GK n3 e WT n3 (GK CT: 1,4 ± 0,3 e GK n-3: 0,7 ± 0,4). Os linfócitos do grupo GK controle apresentaram maior expressão gênica de HIF-1 alfa em relação aos grupos GK n-3 e WT controle (WT CT: 0,8 ± 0,2, WT n-3: 0,9 ± 0,2, GK CT: 3,8 ± 0,3 e GK n-3: 2,1 ± 0,3). A enzima acil-Coa desidrogenase foi menos expressa nos linfócitos dos ratos GK controle em relação aos animais WT-CT (WT CT: 0,6 ± 0,2 e GK CT: 0,25 ± 0,1). Também foi observada uma maior expressão gênica de fosfofrutoquinase nos animais WT n3 em relação aos animais controle e GK, e uma maior expressão da mesma enzima em animais GK controle, em relação aos animais GK n3 (WT n-3: 2,5 ± 0,3, WT CT: 1,2 ± 0,2, GK CT: 1,9 ± 0,2 e GK n-3: 0,5 ± 0,1). A atividade de citrato sintase foi maior no grupo GK controle em relação aos grupos GK n3 e WT controle (GK CT: 79,48 ± 11,21 e GK n-3: 2554 ± 9,44 nmol/min/mg de proteína). A atividade de fosfofrutoquinase foi maior no grupo GK controle em relação ao grupo WT-CT (GK CT: 18,52 ± 5,55 e WT CT: 0,09 ± 2,00 nmol/min/mg de proteína). Conclusion: Esses resultados sugerem que a suplementação com n-3 pode exercer efeitos benéficos na regulação metabólica e imunológica em ratos diabéticos não obesos, oferecendo novas perspectivas para futuras intervenções terapêuticas no tratamento do DM2. Support: FAPESP, CNPq, CAPES Protocol: 010-2020</p>



Title	Análise funcional e histomorfométrica das glândulas salivares de ratos Wistar submetidos ao jejum intermitente
Authors	RENAN JOSE BARZOTTI, LARISSA VICTORINO SAMPAIO, JOSÉ VITOR FURUYA DE LIMA, ELIAN BERTOLDO DE LISBOA, RAYARA NOGUEIRA DE FREITAS, GUILHERME EDUARDO ROCHA SILVA, ANA CLAUDIA DE MELO STEVANATO NAKAMUNE, ANTONIO HERNANDES CHAVES NETO
Affiliations	Ciências Básicas, UNESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O Jejum Intermitente (JI) é uma estratégia alimentar baseada na restrição de períodos alimentares que tem ganhado muita popularidade devido à sua eficácia na redução de peso corporal. Além disso, estudos experimentais têm demonstrado que além de reduzir o peso, também pode melhorar o controle glicêmico e as dislipidemias, reduzir a progressão e severidade de doenças cardiovasculares, e ter efeitos neuroprotetores durante a senescência. No entanto, os cérebros de ratos jovens submetidos ao JI de curto prazo apresentaram aumento do dano oxidativo aos lipídios e proteínas, acompanhado de redução na defesa antioxidante enzimática. Já as glândulas salivares têm demonstrado sensibilidade entre a função e estado redox diante de padrões alimentares e nutricionais. Objective: O objetivo deste estudo foi analisar o efeito do JI na histomorfometria e função das glândulas salivares. Methods: Para tanto, 20 ratos Wistar machos, com 12 semanas de idade e pesando de 350 a 450 gramas, foram estratificados por peso corpóreo e aleatoriamente divididos em 2 grupos (n = 10 ratos / grupo): o grupo Ad Libitum (AL) teve acesso contínuo a água e ração durante todo o tratamento, enquanto o grupo JI teve acesso contínuo a água, mas foram privados de alimentação por 24 horas em dias alternados pelo período de 12 semanas. Os pesos corporais, consumo de água e ração foram registrados ao longo do tratamento para cálculo de eficiência alimentar. Ao fim do experimento, os animais foram anestesiados, tiveram a salivação induzida por pilocarpina, e a saliva coletada por 10 minutos, cronometrados a partir da queda da primeira gota. Em seguida, foram eutanasiados por exsanguinação, e as glândulas salivares foram então excisadas, limpas, pesadas e fixadas em formol 10% tamponado para processamento histológico. Para a análise histomorfométrica, as glândulas foram incluídas em paraplast®, cortadas em seções de 5 µm, coradas com hematoxilina e eosina, e a quantificação das áreas de ductos, ácinos e tecidos conjuntivo foi realizada com aumento de 40x. Para a análise funcional, foram determinados o fluxo salivar, pH e capacidade tamponante, concentração de eletrólitos (cálcio, fosfato, sódio, cloreto e potássio), atividade da amilase salivar e estado redox da saliva (capacidade antioxidante total e dano oxidativo aos lipídeos e as proteínas. Os resultados foram normalizados pelo teste de Shapiro Wilk, comparados pelo teste t de Student não-pareado e foi considerado como estatisticamente significativo o valor de $p < 0,05$. Results: O JI diminuiu o ganho de peso ($p < 0,0001$), peso final ($p < 0,0001$), consumo de ração ($p = 0,00008$) e eficiência alimentar ($p < 0,0001$). Além disso, houve redução no peso absoluto da glândula submandibular ($p = 0,0233$) e aumento no peso relativo da glândula parótida ($p = 0,0099$) no grupo JI. No entanto, não foram observadas diferenças estatisticamente significantes na histomorfometria das glândulas, assim como no fluxo, composição bioquímica e estado redox da saliva. Conclusion: Apesar das alterações no peso das glândulas, os parâmetros estruturais e funcionais não demonstraram diferenças entre os grupos, sugerindo que o JI não causa alterações morfofuncionais nas glândulas salivares. Support: CAPES – Código de Financiamento 001 / Edital 8/2023 – PIBIC Ensino Médio Nº 8859 Protocol: CEUA FOA/UNESP nº 257-2023</p>

Title	INJEÇÃO DA PROTEÍNA S DO SARS-CoV-2 ALTERA O CICLO ESTRAL EM CAMUNDONGAS
Authors	LARISSA SIMÕES DIAS, VERÔNICA MÜLLER DE OLIVEIRA NASCIMENTO, RAKEL KELLY SILVA ALVES, HANAILLY RIBEIRO GOMES, ALESSANDRA CRISTINA CHAGAS VALLIM, EMANUELLE V. DE LIMA, JULIA HELENA ROSAURO CLARKE, TÂNIA MARIA RUFFONI ORTIGA
Affiliations	Programa de Pós Graduação em Endocrinologia (Medicina), UFRJ, Instituto de Biofísica Carlos Chagas Filho, UFRJ, Instituto de Ciências Biomédicas, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: No ano de 2020, emergiu uma pandemia decorrente da propagação do novo coronavírus da Síndrome Respiratória Aguda Grave 2 (SARS-CoV-2), desencadeando a doença conhecida como COVID-19 (LU, R. et al., 2020). Apesar de ser, principalmente, associada a problemas cardiorrespiratórios, observou-se que gestantes também são suscetíveis a consequências adversas, incluindo aumento do risco de parto prematuro e morte fetal (GUROL-URGANCI, Ipek et al., 2021). Logo, uma série de estudos clínicos tem sido conduzida com o intuito de esclarecer o impacto da COVID-19 sobre o curso gestacional e pós parto. Entretanto, existem poucos estudos sobre os efeitos da proteína Spike na reprodução feminina e estudos com modelo animal. Objective: O objetivo do nosso estudo foi analisar o ciclo estral das camundongas após a injeção da proteína Spike (S) do SARS-CoV-2. Methods: Foram utilizadas camundongas da linhagem Swiss (CEUA: 083/21) com idades de 5 (G1) e 3 meses (G2). Para testar se o insulto com a proteína S poderia alterar o ciclo estral, realizamos a citologia vaginal diariamente, ao longo de 55 dias consecutivos. Inicialmente, o ciclo estral das camundongas foi monitorado por um período de 16 dias. No 17º dia, os animais foram subdivididos em dois subgrupos: Grupo Spike (GS1: n=3; GS2: n=4) e Grupo Controle (GC1: n=3; GC2: n=4), aos quais foi administrada, respectivamente, a primeira injeção da proteína S purificada e da solução salina (10 µL, via subcutânea). O acompanhamento do ciclo prosseguiu por mais 14 dias. No 31º dia, uma segunda injeção da proteína S e da solução salina foi administrada, seguida de mais 24 dias de monitoramento do ciclo estral. Foram realizadas análises qualitativas, a fim de demonstrar o ciclo estral completo das camundongas e também realizamos análises quantitativas, buscando analisar a regularidade, duração e quantidade dos ciclos estrais das camundongas. Results: Os resultados foram analisados por meio do teste Two-Way ANOVA. Os dados são representados como média±SEM e as diferenças entre os grupos foram consideradas significativas quando $p < 0,05$. Vimos que, inicialmente, as camundongas do G1 e do G2 apresentaram ciclos estrais regulares (4-5 dias). Porém, após a administração da 1ª dose da proteína S, tornaram-se irregulares (6-7 dias). Após a 2ª dose da proteína S, a irregularidade aumentou e foi caracterizada pela interrupção dos ciclos estrais por até 9 dias consecutivos e a permanência nas fases luteais. Também observamos que a duração dos ciclos estrais das camundongas infectadas pela proteína S foi aumentada tanto no GS1 (GC1: $4,1 \pm 0,4$ dias; GS1: $6,27 \pm 0,42$ dias; $p = 0,0008$) como no GS2 (GC2: $5 \pm 0,3$ dias; GS2: $6,3 \pm 0,53$ dias; $p = 0,0089$). Porém, ao analisarmos a quantidade de dias que as camundongas permaneceram em cada fase do ciclo estral, vimos que apenas as camundongas infectadas do GS2 permaneceram mais tempo no metaestro e no diestro em comparação às controles (GC2: $28,7 \pm 3,6$ dias; GS2: $36,25 \pm 1,5$ dias, $p = 0,0004$). A quantidade de dias das demais fases não foi alterada. Além disso, a injeção da proteína S ocasionou redução no número total de ciclos estrais, tanto no GS1 (GC1: 14 ± 1 dias; GS1: $8,6 \pm 1,15$ dias; $p = 0,0003$) quanto no GS2 (GC2: $12 \pm 0,8$ dias; GS2: $8,7 \pm 0,9$ dias; $p = 0,0037$). Conclusion: Logo, os dados obtidos sugerem que o insulto pela proteína S do SARS-CoV-2 induziu irregularidades no ciclo estral das camundongas, caracterizadas pela permanência nas fases luteais, prolongamento da duração e diminuição da quantidade de ciclos estrais. Também observamos que a idade das camundongas infectadas não afetou os resultados. Support: FAPERJ, CNPQ e CAPES Protocol: 083/21</p>

Title	Prolactin attenuates anxiety-like behavior and stress-induced activation of the paraventricular nucleus of the hypothalamus in male rats
Authors	EVELYN CRISTINE DOS SANTOS ALVARES, PATRICIA C. HENRIQUES, LEONARDO DE OLIVEIRA GUARNIERI, KAOMA S. C. SILVA, MATHEUS VIANA, ROBERTA ARAÚJO-LOPES, MÁRCIO FLÁVIO DUTRA MORAES, RAPHAEL ESCORSIM SZAWKA-
Affiliations	Fisiologia e Biofísica, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Besides its involvement in lactation, prolactin (PRL) modulates anxiety and stress responses in females, but it is unknown whether PRL plays a similar role in males. Objective: To characterize PRL anxiolytic and anti-stress actions in male rats and investigate the neuroendocrine mechanisms involved. Methods: To determine the dose-response of PRL anxiolytic effect, Wistar male rats received intracerebroventricular (i.c.v.) injections of different doses of ovine PRL (oPRL, 0.05-3.0 µg/µL; n=6-8 rats/dose), vehicle (Veh, n=8), or diazepam (n=6) and were investigated in the elevated plus maze (EPM) and novelty-suppressed feeding tests. To map the brain regions responding to PRL, male rats received an i.c.v. injection of Veh (Veh, n=6) or oPRL at 0.5 µg/µL (PRL-0.5, n=4; anxiolytic dose) or 3.0 µg/µL (PRL-3, n=7; non-anxiolytic dose) and were transcardially perfused after 30 minutes. The brains were processed for double-label immunohistochemistry (IHC) to phosphorylated STAT5 (pSTAT5), a marker of PRL receptor (PRL-R) activation, and oxytocin (OT). We then investigated the effect of PRL on the neuronal activation of the paraventricular nucleus of the hypothalamus (PVN) in response to stress. Male rats received two i.c.v. injections 10 minutes apart of Veh, Veh and oPRL (0.5 µg/µL), or the PRL-R antagonist S179D-PRL and oPRL (Ant+oPRL). Ten minutes later, rats underwent restraint stress for 40 minutes (Stress, n=6-8 animals/group) or were left undisturbed (Control, n=6-8 animals/group). The brains were processed for double-label IHC to the marker of neuronal activity, c-Fos, and OT in the PVN. Results: I.c.v. oPRL at the doses of 0.5 and 1.0 µg/µL increased the percentage of entries in the open arms of the EPM (p<0,001) and reduced the latency to feeding (p<0.05), and these anxiolytic effects were comparable to those of the anxiolytic drug diazepam. Conversely, the high dose of 3.0-µg/µL oPRL did not change these parameters when compared to Veh, thus being considered as a non-anxiolytic dose. oPRL was found to induce massive STAT5p expression in the preoptic area, arcuate nucleus, and PVN of male rats. Nevertheless, the PVN was the only brain region in which rats treated with the anxiolytic PRL-0.5 displayed a higher pSTAT5 expression than those receiving the non-anxiolytic PRL-3 (p<0.01). The same difference between PRL-0.5 and PRL-3 was found in pSTAT5 coexpression in OT neurons of the PVN (p<0.05). These findings suggested the PVN as a neuroendocrine target for the PRL anxiolytic effects. Regarding PRL modulation of the PVN, oPRL alone or combined with the PRL-R antagonist did not change c-Fos or OT expression in the PVN of Control rats. Stress, in turn, increased the single-label expression of c-Fos in the PVN of Veh rats (p<0.001) and this effect was blocked by oPRL (p<0.001). Likewise, stress increased the percentage of OT-neurons expressing c-Fos in the PVN of Veh rats (p<0.05), which was also blocked in oPRL-treated rats (p<0,05). The S179D-PRL treatment in Ant+oPRL-Stress rats partially neutralized the oPRL effects. Conclusion: We demonstrate that central PRL has a dose-dependent anxiolytic effect in male rats. The activation of PRL-R in the PVN correlates with the anxiolytic dose of oPRL, with lower responsivity to higher doses. Moreover, PRL negatively modulates global and OT-neuron activation in the PVN in response to restraint stress. Thus, our findings reveal that PRL has anxiolytic and anti-stress effects in male rats, probably conveyed through its action on the PVN. Support: CNPq, FAPEMIG, CAPES Protocol: 338/2019</p>

Title	LH AND FSH SECRETION IN MALE AND FEMALE RATS DETERMINED BY HIGHLY SENSITIVE ELISA
Authors	ANDRÉ FERNANDES GOMES, ROBERTA ARAÚJO LOPES, ANA CLARA CAMPIDELI SANTANA, MARIANA DE SOUZA SANTOS, SORAIA MACARI, RAPHAEL ESCORSIM SZAWKA
Affiliations	Fisiologia e Biofísica, UFMG, Departamento de Odontologia Restauradora, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Serum levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH) are commonly assessed in the diagnosis of reproductive function disorders. Therefore, accurate methodologies are required for hormonal measurement in both animals and humans. Objective: Development of a novel highly sensitive FSH ELISA and, using tail-tip blood sampling combined with the ELISA assays, longitudinal evaluation of LH and FSH secretion in male and female rats under different hormonal conditions. Methods: Male and female Wistar rats aged 3 months and weighing approximately 250g were used. The animals were provided from the Centro de Bioterismo do Instituto de Ciências Biológicas da Universidade Federal de Minas Gerais (CEBIO/UFMG). The castration surgeries, orchiectomy (ORX) and ovariectomy (OVX), were carried out to simulate situations of high levels of LH and FSH. Simulated surgeries (SHAM), were performed as controls. The blood samples were collected from the tail-tip with a 1-hour interval between collections. In experiment 1, we validated the ultrasensitive ELISA technique for LH and FSH by performing the parallelism test. Experiments 2, 3 and 4 were carried out in a cross-over experimental model, in which each animal was a control of itself in the different hormonal conditions evaluated. Results: The parallelism test revealed that the addition of rat plasma does not cause a non-specific interaction in the ELISAs for LH and FSH. The first result showed that the ELISA method detected an increase in LH and FSH secretion in OVX rats compared to those in diestrus (SHAM). In ORX animals (n=6), the ELISAs detected a significant increase in LH and FSH secretion compared with the previous gonad-intact condition ($p < 0.01$ for LH and $p < 0.001$ for FSH). Following the subsequent treatment with testosterone (ORX+T), LH levels returned to gonad-intact values ($p < 0.01$), whereas FSH secretion was significantly reduced but partially restored to basal levels ($p < 0.05$ compared with Intact and ORX+T). During the rat estrous cycle, LH and FSH displayed low basal levels during diestrus (D; n=7), and the preovulatory surges of both hormones were detected on the afternoon of proestrus (P; n=6). On estrus (E; n=6), FSH levels were still declining throughout the day, while LH secretion had returned to basal levels. After OVX, LH and FSH levels were similarly increased compared with diestrus ($p < 0.01$ for LH and $p < 0.001$ for FSH). Following the estradiol treatment (OVX+E2), LH and FSH levels were reduced during the morning period, with a greater suppression of FSH secretion. In the afternoon, E2 induced a sharp LH surge between 17 and 18 h, whereas the FSH surge was found as a gradual increase from 17 to 19 h. Conclusion: These data provide a recharacterization of LH and FSH secretion in the rats determined by ELISA in the tail-tip blood of longitudinally investigated animals. Support: CNPQ, CAPES, FAPEMIG. Protocol: CEUA Nº 216/2022</p>

Title	Estradiol and kisspeptin treatments prevent but do not recover bone loss caused by ovariectomy in rats
Authors	MARIANA DE SOUZA SANTOS, ROBERTA ARAÚJO LOPES, ISABELE BEATRIZ PEREIRA ALVES, DAVID R. GRATTAN, SORAIA MACARI, RAPHAEL ESCORSIM SZAWKA
Affiliations	Fisiologia e Biofísica, UFMG, Department of Anatomy, University of Otago, Departamento de Odontologia Restauradora, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The drastic decrease in estrogen levels caused by ovarian failure after menopause is responsible for causing an imbalance in bone homeostasis, favoring reabsorption and resulting in bone diseases such as osteoporosis. Kisspeptin binds to Kiss1 receptor (Kiss1r) to stimulate gonadotropin-releasing hormone (GnRH) release and, consequently, the secretion of gonadotrophins and gonadal steroids. However, kisspeptin may have actions in peripheral tissues. Previous studies have demonstrated the possibility of direct actions of kisspeptin on bone cells in vitro. Objective: The aim of the present study was to determine the effects of systemic treatments with kisspeptin-10 (Kp-10) or estradiol (E2) in preventing or recovering the bone loss caused by the lack of E2 after ovariectomy. Methods: Three-month-old female Wistar rats (n = 6, CEUA: 229/2020) weighing approximately 250g were underwent surgery to perform either a simulated surgery (Sham) or ovariectomy (OVX). Sham and OVX rats were treated with saline, E2, or Kp-10 for thirty days starting on the first day (experiment 1) or the thirty day (experiment 2) after surgery to investigate the prevention or recovery of bone loss, respectively. The weight of the uterus was used to evaluate the success of the ovariectomy. The femurs of these rats were analyzed for the bone phenotype by micro-computed tomography (microCT). Results: E2 or Kp-10 treatment initiated on the day after ovariectomy was equally effective in preventing the reduction in bone volume, bone volume fraction, trabecular number, and trabecular separation ($p < 0.05$). The decrease in bone mineral density, in turn, was blocked by E2 ($p < 0.001$) and only partially contained by Kp-10 ($p < 0.01$). E2 but not Kp-10 prevented the decrease in uterine weight, demonstrating no estrogenic effect for the Kp-10 treatment in OVX rats ($p < 0.01$). Moreover, bone parameters in Sham rats were not affected by E2 or Kp-10 treatments. On the other hand, neither E2 nor Kp-10 was able to recover the femoral bone loss when treatments started thirty days after ovariectomy, with the bone effects of estrogen deficiency already present, as previously determined. Conclusion: Our findings demonstrate that systemic treatment with Kp-10 prevents bone loss in OVX rats with comparable effectiveness to the E2 replacement for most parameters of bone microarchitecture, whereas neither Kp-10 nor E2 can recover the loss of femoral bone after one month of estrogen withdrawal. Support: CNPq, CAPES, FAPEMIG Protocol: 229/2020</p>

Title	POSSÍVEIS EFEITOS DA VITAMINA D NO DESENVOLVIMENTO FOLICULAR EM MODELO MURINO – RESULTADOS PRELIMINARES
Authors	HANAILLY RIBEIRO GOMES, LAURA MARIA BORGES NAVARRO, MARCELA ALVES CALLIL, LARISSA S. DIAS, FLAVIA BLOISE, TANIA MARIA ORTIGA-CARVALHO
Affiliations	Fisiologia, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A vitamina D desempenha um importante papel no sistema reprodutor feminino. Concentrações inadequadas dessa vitamina podem estar associadas a fatores de infertilidade, como a anovulação crônica, endometriose e até o câncer de mama. Mulheres de 30 anos apresentam maiores níveis de calcitriol possuem maiores taxas de fecundidade e menor probabilidade de perdas gestacionais. Contudo, estudos sobre a influência da vitamina D na gestação e maturação oocitária ainda são escassos. Objective: Estudar a relação entre as diferentes variações no consumo alimentar de vitamina D na maturação oocitária murina. Methods: Os procedimentos com os animais foram previamente aprovados (n° A20/22-153-16, CEUA/UFRJ). Foram utilizadas fêmeas C57Bl6 de 8 a 10 semanas de idade. Estas foram divididas em 3 grupos (n=5 em cada) com diferentes dietas contendo unidades (UI) diferentes de vitamina D: grupo controle (CTR, 1000UI), grupo suplementado (SUP, 10000UI) e o grupo deficiente (DEF, 0UI). As dietas foram fornecidas durante 31 dias. No 32° dia, as fêmeas foram eutanasiadas para coleta dos ovários. Técnicas de imunohistoquímica foram realizadas usando-se o marcador proliferação nuclear Ki-67 e a técnica de coloração Hematoxilina e eosina para avaliação do número de camadas em cada fase folicular. A contagem dos folículos foi determinada de acordo com o método de Pedersen & Peters (1968) que determina a classe do folículo com base no tamanho, morfologia e número de camadas de células da granulosa. Os folículos podem ser classificados de acordo com suas estruturas foliculares, características e seu grau de maturação, em primário, secundário, pré-antral, antral e maduro. Os resultados do Ki-67 foram submetidos a análises estatísticas por meio do teste One-Way ANOVA, e as diferença entre os grupos foram consideradas significativas quando $p < 0,05$. A contagem das camadas foi feita manualmente. Results: Nos folículos primários a distribuição número de camadas das células da granulosa é similar entre os grupos. Em relação a proliferação celular não observamos diferença entre os grupos (CTR $0,14 \pm 0,03$; SUP $0,18 \pm 0,07$; DEF $0,12 \pm 0,07$; $p = 0,19$). No folículo secundário é possível observar que há um maior número de folículos com maior número de camadas nos grupos SUP e DEF quando comparado com o CTR, entretanto, foi observado que o grupo DEF apresenta um maior número de folículos com mais camadas em relação aos outros grupo. Não houve diferença na proliferação celular (CTR $0,17 \pm 0,08$; SUP $0,19 \pm 0,09$; DEF $0,12 \pm 0,08$; $p = 0,19$). Nos folículos pré-antral, antral e maduro, foram observados um número maior de folículos com mais camadas no grupo SUP em relação aos grupos CTR e DEF. Os resultados da proliferação celular nos folículos pré-antrais, foi observado uma diferença entre o grupo DEF e SUP (SUP $0,27 \pm 0,17$; DEF $0,13 \pm 0,9$; $p = 0,045^*$), mas quando comparados com o grupo CTR ($0,16 \pm 0,09$) não há diferença significativa entre os grupos. Nos folículos antral (CTR $0,13 \pm 0,09$; SUP $0,32 \pm 0,19$; DEF $0,16 \pm 0,10$; $p = 0,06$) e maduro (CTR $0,38 \pm 0,28$; SUP $0,28 \pm 0,19$; DEF $0,16 \pm 0,03$; $p = 0,45$) não observamos diferenças na proliferação celular entre os grupos. Conclusion: Nossos dados sugerem que diferentes doses de vitamina D são capazes de aumentar o número de folículos com maior número de camadas, entretanto, em relação ao aumento da proliferação celular só foi observado nos folículos pré-antrais. Support: CAPES, Cnpq e FAPERJ Protocol: A20/22-153-16</p>

Title	Gluconeogenesis from pyruvate contributes to hyperglycemia in non-obese diabetic gk rats probably due greater capacity of the liver gluconeogenic pathway
Authors	OTÁVIO VINÍCIUS CUSTÓDIO JORGE, FRANCIELE PASQUINI DALL AQUA, MARIA FERNANDA SIQUEIRA, LUNNA UEMURA BOSQUETTI, MANOEL OSVALDO ESTEVAM FÁVARO, GIOVANNA PAIS GALVÃO ESTEVES, ROBERTO BARBOSA BAZOTTE, RUI CURI, GISELE LOPES BERTOLINI, PRISCILA CASSOLLA
Affiliations	Department of Physiological Sciences, UEL, Department of Pharmacy, UEM, Interdisciplinary Post Graduate Program in Health Sciences, UNICSUL
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The liver is crucial for maintaining glucose homeostasis, since it can produce and store glucose. Diabetes mellitus (DM) is a disorder characterized by chronic hyperglycemia and alterations in the metabolism of carbohydrates, lipids and proteins, due to defects in the production, secretion and/or action of insulin, where the hepatic metabolism of glucose may be altered. Type 2 DM (DM2) is caused by insulin resistance (in sensitive organs), followed by loss of its action and secretion and is commonly associated with obesity. However, there are groups of individuals with DM2 who have a low body mass index. The Goto-Kakizaki (GK) rat is an animal model of insulin resistance without obesity, which develops DM2 spontaneously with a chronology very similar to that of humans. Objective: Considering the possible hepatic contribution to hyperglycemia in the GK rat, this study aimed to evaluate the liver gluconeogenic pathway from the pyruvate precursor in these animals. Methods: The insulin tolerance test (ITT) using insulin lispro was carried out on GK (n = 7) and Wistar rats (control group, n = 5) in the 8th week of life, and the pyruvate tolerance test (PTT) at the beginning of the 9th week of age. After 3 days of recovery, the groups were submitted to the in situ liver perfusion technique, in which increasing concentrations of pyruvate (1.5 mM, 3.0 mM, 5.0 mM, 7.5 mM, and 9.0 mM) were infused to assess the dose-response curve of in situ liver gluconeogenesis. The experimental protocols were approved by the Animal Use Ethics Committee (CEUA/UEL) of the State University of Londrina (Protocol No. 019.2023). Statistical analysis of parametric data was carried out using the unpaired Students t-test, two-way ANOVA followed by the Bonferroni test or the Sidak test, or one-way ANOVA followed by the Tukey test, and for non-parametric data, the Mann-Whitney test. The significance level adopted was 5%. Results: The decay constant (kITT) of glycemia was used to confirm insulin resistance in the experimental model (AUC of GK 0.2700 ± 0.4782, AUC of C 2.530 ± 0.4783, p = 0.0102). The GK rats showed hyperglycemia (p<0.05) and greater in vivo gluconeogenesis from pyruvate at all times evaluated (AUC of GK 3669 ± 265.1, AUC of C 1256 ± 103.7, p < 0.0001). The contribution of the liver was demonstrated by the dose-response curve to this precursor in the perfusion technique. Although sensitivity to the precursor and hepatic responsiveness to pyruvate for the concentration considered saturating for control rats (5 mM) were similar between young GK and control rats, glucose releasing was elevated for the 9 mM concentration (AUC of GK 9.973 ± 1.296, AUC of C 6.272 ± 0.6541, p = 0.0194), indicating greater hepatic capacity for glucose production. Conclusion: Thus, liver gluconeogenesis from pyruvate appears to contribute to the moderate hyperglycemia observed in the young phase of this animal model of insulin resistance, and this pathway could be a target for future interventions to mitigate the complications of chronic hyperglycemia in lean diabetics. Support: FAPESP nº 2018/09868-7; Government of the State of Paraná, Paraná Council for Science and Technology, and State Secretariat for Science, Technology, and Higher Education (SETI) (budget allocation # 4560.19.571.06.6153; protocol 21.234.745-0). Protocol: CEUA/UEL Protocol nº 019.2023</p>

Title	TEMPORAL CHARACTERIZATION OF TRABECULAR BONE LOSS AFTER OVARECTOMY IN RATS
Authors	ISABELE BEATRIZ PEREIRA ALVES, MARIANA DE SOUZA SANTOS, ROBERTA ARAÚJO LOPES, SORAIA MACARI, RAPHAEL ESCORSIM SZAWKA
Affiliations	Fisiologia e Biofísica, UFMG, Odontologia Restauradora, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The reduction of estrogen levels after menopause leads to the development of osteoporosis in women. Bone loss is faster in the initial years after menopause, before stabilizing at a slower rate of bone resorption. Ovariectomy is a commonly used rodent model of postmenopausal osteoporosis. However, the temporal profile of bone loss in this model is still unclear. Objective: Here, we aimed to characterize the temporal profile of bone loss after ovariectomy in rats. Methods: Adult Wistar rats underwent bilateral ovariectomy or Sham surgery (n = 6/group). The weight of the uterus was used as a control to ensure the success of the ovariectomy. The femurs were evaluated by microcomputed tomography (μCT) at 15 days, 1, 2, and 6 months after surgeries. Analysis of variance (ANOVA) was used to compare group means and p values less than 0.05 ($p < 0.05$) were considered statistically significant. Results: The uterine weight was equally reduced in ovariectomized (OVX) rats compared with Sham at all evaluated time points, indicating low levels of estradiol. The Femur length did not differ among groups. After 15 days of ovariectomy, rats displayed a significant but partial reduction in bone mineral density (BMD) compared to Sham animals ($p < 0,05$), indicating that this period was insufficient to develop a full bone loss. A consistent reduction in BMD, bone volume, bone volume/total volume, trabecular number, and an increase in trabecular separation were observed at 1 month after ovariectomy ($p < 0,05$). Except by the trabecular separation, further increased in 6-month OVX rats ($p < 0,05$), the severity of bone loss in all the parameters measured did not change from 1 to 6 months of ovariectomy. Conclusion: These findings demonstrate that the great majority of trabecular bone loss occurs early, within the first month after ovariectomy in the rat, which seems to represent the bone response to the rapid decrease in estradiol levels. Support: CNPq Protocol: CEUA: 229/2020</p>



Title	Investigação da ação do estradiol sobre a diferenciação adipogênica e expressão dos receptores do sistema endocanabinoide in vitro
Authors	JULIANA PENA GONÇALVES, MARIANA MACEDO DE ALMEIDA, ISIS HARA TREVENZOLI
Affiliations	Pós graduação em Ciências Biológicas (Fisiologia), UFRJ, Departamento de Farmacologia, UFJF
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Na obesidade há um acúmulo excessivo de gordura corporal, na forma de tecido adiposo branco (TAB). Indivíduos obesos apresentam superativação do sistema endocanabinóide (SEC), composto pelos ligantes canabinoides endógenos, seus receptores de membrana (CB1 e CB2) e enzimas que fazem síntese e degradação dos ligantes. A sinalização via CB1 em adipócitos brancos aumenta a lipogênese e o acúmulo de triglicerídeos, e diminui a lipólise, favorecendo o acúmulo de gordura. Em modelo de obesidade em ratos (induzido por dieta hiperlipídica materna) demonstramos aumento de peso corporal, hipertrofia de adipócitos e aumento do receptor CB1 no TAB das fêmeas, associado com redução sérica de estradiol. Em modelo de ovariectomia de ratas adultas, observamos aumento de CB1 no TAB, sugerindo que a redução dos níveis circulantes de estradiol pode aumentar a sinalização local de CB1. No entanto, o crosstalk entre este hormônio e o SEC, bem como seus efeitos diretos sobre os adipócitos, é algo que ainda permanece a ser investigado. Objective: Nosso objetivo é determinar o efeito direto do estradiol sobre a adipogênese e sobre a expressão dos componentes do SEC. Methods: Primeiramente, avaliamos o efeito de diferentes concentrações de estradiol (10-5M, 10-7M, 10-9M e 10-11M) sobre a diferenciação adipogênica da linhagem de pré-adipócitos 3T3-L1. Para mimetizar um ambiente mais obesogênico, durante o processo de diferenciação adicionamos às culturas o ácido palmítico. A análise da diferenciação adipogênica foi realizada pela marcação das células com o corante fluorescente de lipídios neutros BODIPY, que evidencia as gotículas lipídicas que se formaram no citoplasma após o estímulo à diferenciação sob diferentes condições. Esta análise foi feita por fotomicrografia de fluorescência, com quantificação do percentual de área marcada. Results: Em relação aos efeitos da adição de estradiol sobre a diferenciação, os resultados indicam um aumento no acúmulo lipídico nas culturas, em resposta as maiores concentrações do hormônio. O aumento do acúmulo lipídico foi estatisticamente significativo nas concentrações 10-5M e 10-9M, em comparação com o controle (apenas veículo e sem estradiol)(medianas: controle= 100 ±27,20; 10-5M estradiol= 206,2 ±207,4; 10-9M estradiol= 153,3 ±354,0, n=5). Resultados preliminares mostram que a presença de ácido palmítico estimulou o acúmulo lipídico pelos adipócitos. No entanto, a presença de maiores concentrações de estradiol reduziu o efeito do ácido palmítico e resultou em um menor acúmulo lipídico. Conclusion: Portanto, o efeito do estradiol sobre a capacidade adipogênica pode diferir, a depender das condições basais (controle ou sobrecarga de ácidos graxos). Como perspectiva, avaliaremos a sinalização do SEC durante a diferenciação adipogênica in vitro sob diferentes concentrações de estradiol e ácido palmítico. Nossos achados podem fornecer as bases moleculares para novas terapias anti-obesidade diferenciais entre os sexos. Support: FAPERJ, CNPq Protocol: N.A.</p>



Title	Dieta obesogênica durante a gestação e a lactação altera a concentração de endocanabinoides circulantes em ratas de forma tempo dependente.
Authors	LETÍCIA ALABURDA DE ARAUJO, LARISSA DE BRITO FASSARELLA, LUCAS SANTOS BARBOSA DE LIMA, CAMILA CALVIÑO MORAES, ISIS HARA TREVENZOLI
Affiliations	IBCCF, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O sistema endocanabinoide (SEC) é composto por receptores canabinoides, diversas enzimas metabolizadoras e canabinoides endógenos lipídicos como a anandamida (AEA), 2-araquidonoilglicerol (2-AG), palmitoiletanolamida (PEA) e a oleoiletanolamida (OEA). O SEC tem função importante em eventos reprodutivos como a implantação do blastocisto, placentação e parto, com aumento progressivo do seu tônus durante a gestação. Na lactação, o SEC dos neonatos promove o início da amamentação, o neurodesenvolvimento, a adipogênese e a termorregulação, mas os impactos de uma possível transferência materna de endocanabinoides para a prole são pouco conhecidos. No entanto, sabe-se que condições pró-inflamatórias associam-se a alterações do SEC com desfechos negativos da gestação como pré-eclâmpsia e aborto prematuro. Neste estudo, testamos a hipótese que o consumo de uma dieta obesogênica pró-inflamatória no período pré-gestacional, na gestação e na lactação em ratas aumentaria os níveis de endocanabinoides circulantes de acordo com o período reprodutivo. Objective: Avaliar os níveis séricos dos endocanabinoides AEA, 2-AG, OEA e PEA de ratas ao final da gestação e ao final da lactação e possíveis alterações induzidas pelo consumo de dieta obesogênica. Methods: Os procedimentos com animais foram aprovados pelo CEUA/CCS/UFRJ (147/21). Ratas Wistar com 60 dias de idade foram submetidas à dieta controle (10% de calorias provenientes de lipídios) ou dieta hiperlipídica obesogênica (40% de lipídios e 9,5% de sacarose) durante 9 semanas pré-acasalamento, gestação e lactação. Níveis séricos de AEA, 2-AG, OEA e PEA maternos foram dosados em um subgrupo de ratas submetidas à cesárea ao final da gestação (dia gestacional 20; a termo) e em um segundo subgrupo no final da lactação, 21 dias após parto natural. Os lipídios foram extraídos e purificados das amostras de soro utilizando cartuchos de cromatografia SPE para a quantificação do endocanabinoides por cromatografia líquida de ultra alta eficiência acoplada à espectrometria de massas (UPLC/MS/MS). Os resultados foram analisados através do two-way ANOVA seguido do pós-teste Tukey, considerando a dieta materna e o período reprodutivo como fatores principais. Diferenças foram consideradas significativas quando $p < 0.05$. Results: As concentrações séricas de AEA, 2-AG, PEA e OEA foram maiores na gestação em comparação com a lactação ($p < 0,05$), independente da dieta. A dieta obesogênica aumentou a adiposidade visceral em ratas progenitoras ($p < 0,05$) e reduziu a concentração de 2-AG ao final da gestação ($p < 0,0001$), enquanto aumentou a concentração de OEA na lactação ($p < 0,01$), sem efeitos sobre os demais endocanabinoides. Conclusion: Os níveis séricos de endocanabinoides lipídicos podem ser modulados por uma dieta materna inadequada, uma vez que são moléculas provenientes do ácido araquidônico (ômega 6). Além disso, os endocanabinoides são influenciados pelos diferentes momentos do ciclo reprodutivo, como o pré-parto e o pós-lactação, com possíveis impactos no desenvolvimento inicial da prole. Support: Faperj, Cnpq Protocol: 147/21</p>



Title	Vitamin D deficiency delays brown adipose tissue atrophy without affecting the thermoregulatory changes in lactating rats
Authors	MATHEUS LEONARDO MORO, ALINE ZANATTA SCHAVINSKI, JOÃO BATISTA CAMARGO NETO, GABRIEL HUNZICKER SKIBA, ISIS DO CARMO KETTELHUT, LUIZ CARLOS CARVALHO NAVEGANTES
Affiliations	Fisiologia, Universidade de São Paulo, Bioquímica e imunologia, Universidade de São Paulo
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Previous studies suggest that calcitriol suppresses brown adipose tissue (BAT) thermogenesis. However, the role of this hormone in BAT atrophy induced by lactation is unknown. Objective: This study aimed to investigate the role of calcitriol on physiological BAT atrophy during lactation. Methods: Five-week-old female Wistar rats were fed either a vitamin D-deficient diet (0 IU vit.D3/kg) or a vitamin D-sufficient diet (1000 IU vit.D3/kg). After six weeks, vitamin D-sufficient (CT) and deficient (VD) rats were either bred with age-matched males or remained virgin until the end of the experiment. On postnatal day 2, both virgin (V) and lactating (L) rats had their interscapular and dorsal regions shaved, and a telemetric temperature sensor (SubCue, AB, Canada) was placed inside the peritoneal cavity. The BAT thermogenic index (BTI) was calculated using infrared thermography by subtracting dorsal skin temperature (DST) from interscapular skin temperature (IST). The rats were euthanized at weaning and seven days postweaning for blood and BAT collection. Data were expressed as mean±SEM(n=3-18), and statistical analysis was performed using two-way ANOVA or Mann-Whitney test (*p<0.05) (CEUA: 1241/2023). Results: Vitamin D deficiency was confirmed before breeding (6,5±0,5 vs. 32±1,3 ng/mL in CT animals), and the offspring's weight gain during lactation was assessed to ensure that breastfeeding occurred similarly between the groups (25,6±3,5 vs. 25,6±6,4 g in CT). On the 14th day of lactation (lactation peak), control dams (L-CT) increased core body temperature (38,8±0,3 vs. 37,4±0,3 °C in V-CT) and reduced the BTI (1,1±0,1 vs. 1,7±0,2 in V-CT) as compared to the virgin group. These changes were associated with a reduction in BAT mass (207±4,6 vs. 339±26 mg in V-CT) and the BAT UCP-1 protein content (0,42±0,1 vs. 1±0,1 AU in V-CT) at weaning. Although L-CT BAT mass did not return to V-CT values seven days postweaning (200±30,5 vs. 339±26 mg in V-CT), both core body temperature (37,8±0,3 vs. 37±0,2 °C in V-CT) and the BTI (1,8±0,1 vs. 1,4±0,2 in V-CT) were reestablished entirely at this point. The vitamin D deficiency neither affects the lactation-induced core body temperature increase (38,4±0,2 vs. 37,3±0,1 °C in V-VD) nor the BTI changes at lactation peak (1±0,2 vs. 1,9±0,2 in V-VD). At weaning, even though BAT UCP-1 protein content was reduced in L-VD (1,3±0,2 vs. 0,5±0,1), the BAT mass was not affected (310±35,8 vs. 355±19,6 mg in V-VD). Seven days postweaning, the BAT mass was reduced in these animals (246±20,2 vs. 355±19,6 mg in V-VD), but both BTI (1,54±0,1 vs. 1,55±0,3 in V-VD) and core body temperature (37,4±0,1 vs. 37,6±0,3 °C in V-VD) returned to V-VD values. Conclusion: Vitamin D deficiency delays BAT atrophy during lactation, but other physiological adaptations during this period may offset the functional outcomes. Support: CAPES, CNPQ, FAPESP Protocol: 1241/2023</p>

Title	Oral glucose intolerance in obese-hypothalamic male rats may associate to SGLT-1 and Glut12 overexpression and disturbance of the purinergic control in the intestine
Authors	BRUNA SCHUMAKER SIQUEIRA, MARINA HELENA FORLIN, ELIZANGELA STEIN, FÁTIMA FERREIRINHA, PAULO CORREIA-DE-SÁ, SABRINA GRASSIOLLI
Affiliations	Laboratório de Farmacologia e Neurobiologia, U.Porto, Laboratório de Fisiologia Endócrina e Metabolismo, UNIOESTE
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity is associated to glucose intolerance and increased risk of type 2 diabetes (T2D). The glucose absorption rate is increased in T2D, thus contributing to glucose intolerance. Glucose absorption in the intestine occurs via transepithelial transport, which is operated by the type 1 sodium-glucose cotransporter (SGLT-1) located at the apical membrane of enterocytes with subsequent diffusion across the basolateral membrane through type 2 glucose transporters (Glut2). Overexpression of Glut12 in the intestine may also participate in glucose intolerance, hyperinsulinemia and inflammation. ATP-sensitive ionotropic purinoceptors, like P2X7 and P2X4, have been associated with intestinal Glut2 internalization and enteric inflammation, respectively. Hypothalamic obese rats present glucose homeostasis imbalance, yet intestinal glucose transporters and purinoceptors have not been studied in this context. Objective: Here, we investigated the relationship between oral glucose intolerance and the density/distribution of both glucose transporters and ionotropic purinoceptors in the ileum of hypothalamic obese rats. Methods: Male Wistar rats were divided into control (CT, n=6) and hypothalamic obese (Hyp-Ob; n=6) animals, which were induced via administration of high doses of monosodium L-glutamate (MSG; 4g/kg) during first post-natal days. An oral glucose tolerance test (OGTT, 2g/kg) was carried out 148 days after induction, by calculating the area under the curve (AUC) and the time to reach the peak (minutes). Isolated pancreatic islets were challenged “in vitro” with glucose (5.6 and 16.7mM). Two days after the glucose tolerance test, the animals were sacrificed; body weight (BW) and naso-anal length (NAL) were used to calculate the Lee Index (LI). The white adipose tissue (WAT) from retroperitoneal (r) and inguinal (i) depots were excised and weighed, the ileum was collected for immunostaining with specific antibodies against P2X7, P2X4, SGLT-1, Glut-2 and Glut12), and used for confocal microscopy observation. The serum was used to measure triglycerides (TG), fasting blood glucose (FBG) and insulin (FBI), which were used to calculate insulin resistance (IR) by triglyceride and glucose index (TyG) and Quantitative Insulin Sensitivity Check Index (QUICKI) for insulin sensitivity. Results: The BW and NAL was reduced by 23% and 13%, respectively, in Hyp-Ob rats resulting in a higher LI (9.7%) and adiposity WAT-r (34%), WAT-i (143%) in relation to CT animals. The Hyp-Ob rats also display higher FBI (630%) and TG (72%) leading to greater IR (TyG; 72%) and lower insulin sensitivity (QUICKI; 14%). High glucose (16.7mM)-induced insulin secretion was 228% higher in the pancreatic islets of Hyp-Ob vs. CT rats. During OGTT, Hyp-Ob also show a delay (216%) in the time to peak compared to CT animals. The apical membrane of Hyp-Ob enterocytes overexpressed the SGLT-1 transporter. Hyp-Ob animals also possess higher levels of Glut12 associated with reduced amounts of Glut-2 and P2X4 compared to CT rats. The myenteric plexus of Hyp-Ob rats exhibit higher levels of P2X7 and SGLT-1 compared to the CT group. Conclusion: Hyp-Ob animals present altered oral tolerance to glucose associated with hyperinsulinemia, insulin hypersecretion and IR. Overexpression of SGLT-1 and Glut12 may explain these alterations, while surplus amounts of P2X4 and P2X7 receptors may be associate to internalization and elimination of Glut-2 in the intestine. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES. The LFN/MedInUP-ICBAS-UP team is supported by FCT project grants (UIDB/04308/2020 and UIDP/04308/2020). Protocol: CEUA nº38-19 de 27/09/2019.</p>

Title	Effects of early exposure to polystyrene microplastics on metabolic parameters in zebrafish: impacts on the development of obesity and type II diabetes mellitus in adulthood
Authors	BERNARDO LANNES MONTEIRO FONTES, CINTIA RODRIGUES PINHEIRO, MARINALDO PACÍFICO CAVALCANTE NETO
Affiliations	Laboratório Integrado de Ciências Morfofuncionais, UFRJ, UNIVERSIDADE FEDERAL DO RIO DE JANEIRO
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Plastic is a material used in different sectors of society. The increase in its use is due to population and industrial growth, and its inadequate disposal results in the pollution of different biomes and organisms. Among its types, polystyrene (PS) stands out as one of the most widely used plastics. Factors such as increased temperature and friction stimulate degradation, generating microplastics (MPs) (<5mm). The accumulation of MPs in the environment has caused impacts on ecosystems, as they can accumulate in the food chain, affecting several organisms. Concentrations of MPs in packaging may be low, but constant exposure can lead to various health risks and can act as endocrine disruptors (EDs). Furthermore, the phenomenon of metabolic programming modulates critical phases of development, promoting morphological, metabolic and functional adjustments, which determine a greater predisposition to pathological states in adult life. Thus, this exposure to MPs at critical stages of development may predispose adults to the development of chronic diseases of metabolic origin such as obesity and type II diabetes mellitus (DM2). Disturbances in the insulin signaling pathway, mainly in IR receptors, are striking manifestations in DM2. In this context, DEs, like MPs, have been associated with imbalances in this signaling, possibly leading to the development of DM2. Therefore, it is essential to understand the repercussions of exposure to MPs in the early stages on health in adult life. Objective: To evaluate the effects of exposure to PS-MPs, from fertilization to the 27th day of the larval stage, on endocrine and metabolic parameters, associated with obesity and DM2, both at the end of exposure and in adulthood (152 days of life) in zebrafish. Methods: Zebrafish eggs will be randomly distributed into three experimental groups: PS-MPs group- 100 µg/l, PS-MPs group- 1000 µg/l and control. The embryos, at 2 hpf, will be exposed until the 27th day of the larval stage to PS-MPs with fluorescence at concentrations of 100 µg/l or 1000 µg/l. Subsequently, after the 27th day, this exposure to MPs will cease and the animals will develop until 5 months (152 days of life, without MPs). As for the analyses, for the accumulation of PS-MPs, 10 animals per group and age will be used to evaluate the accumulation of PS-MPs in fish with 48 hpf, 72 hpf, 27 dpf and 152 dpf. In the glycemic analysis, the oral glucose tolerance test will be used. Insulin dosage will be assessed using commercial enzyme immunoassay for zebrafish. For body fat, it will be done with lipophilic fluorescent dyes. The gene expression of IR, IRS-1 and IRS-2 in the liver of adults will be assessed by RT-PCR. For larvae, an analysis of the protein content of IR, IRS-1, IRS-2 will be carried out by immunohistochemistry. Dunnett, Kruskal-Wallis and Dunns tests will be used to analyze the data. Results: We assumed the accumulation of PS-MPs in animals and the alteration of markers related to obesity and DM2. Conclusion: Evidence the impact of exposure to MPs in early life on pathophysiological changes with age. Such a study will contribute to advancing knowledge of the physiological mechanisms of these conditions, especially in the study of the effects of environmental contaminants on health. Support: CNPq Protocol: 01200001568201387 Protocolo 00</p>

Title	Evaluation of daily oscillations of kidney function in male and female hypothyroid rats
Authors	DERRICK KRETLI SOUZA, LETÍCIA SELVATICI TOLENTINO, BRUNO HENRIQUE GOMES, ANA FLÁVIA PEIXOTO-DIAS, LAURA BARROSO FERREIRA DE OLIVEIRA, ARTHUR FORNAZARI IOST, ERIKA LIA BRUNETTO, DIOGO DE BARROS PERUCHETTI, RODRIGO ANTONIO PELICIARI-GARCIA, PAULA BARGI DE SOUZA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Thyroid hormones (THs) play a crucial role in renal growth and development, directly influencing tubular metabolism. In humans, the hypofunction of the thyroid gland is associated with reduced glomerular filtration rate and renal hemodynamic alterations. In parallel, we have shown that THs modulate the circadian rhythmicity of clock genes and target transcripts in a tissue-dependent manner, as depicted in the heart and anterior pituitary. However, the effects of THs on the daily oscillations of kidney function have not been investigated yet. Objective: This study aimed to characterize the effect of hypothyroidism on the daily regulation of renal function in both male and female mice. Methods: Male and female Wistar rats were equally divided into Control (C: euthyroid) and Hypothyroid (Tx) groups. Hypothyroidism was induced by thyroidectomy under deep anesthesia followed by methimazole (0.03%) and CaCl₂ (4.5 mM) supplementation in drinking water for 21 days. Next, the animals were placed in metabolic cages, and after 48 h adaptation, the total volume of urine was collected, and the water intake and urinary volumes were measured up to 48 h, every 6 h. Urinary creatinine, glucosuria, and proteinuria were measured, and normalized by total urinary volume and body weight. At the end of the experiment, the animals were euthanized under deep anesthesia; the anterior pituitary gland was collected for Tshb mRNA expression analysis by RT-PCR. Temporal oscillations were analyzed through one-way ANOVA and 24 h cosine adjustment of the data. Overall, statistical significance was considered when P<0.05. All protocols were approved by CEUA-UFMG 47/2020. Results: The increase of Tshb mRNA in anterior pituitary and reduction of heart/body weight ratio confirmed the hypothyroidism induction in both sexes. Urinary creatinine, glucosuria and proteinuria exhibited a well-defined circadian rhythmicity in the C group, independently of sex. Advance in the proteinuria's acrophase, and increases in glucosuria's mesor and amplitude were also observed in female Tx rats, while males exhibited a slightly reduction of proteinuria over the 24h. Conclusion: Our data showed that hypothyroidism impairs the daily pattern of kidney function and possibly the energy metabolism in a sex dependent manner, with females being more affected. Additionally, the kidney circadian clock seems to be another target for THs, highlighting their tissue-specific actions. Support: CNPq, Conselho Nacional de Desenvolvimento Científico e Tecnológico, FAPEMIG, PRPQ, Pró-Reitoria de Pesquisa Protocol: CEUA-UFMG 47/2020</p>

Title	NOVA PROPOSTA DE MODELO DE INDUÇÃO DE DIABETES EM RATOS POR COMBINAÇÃO DE DIETA RICA EM LIPÍDIOS E ADMINISTRAÇÃO DE ESTREPTOZOTOCINA
Authors	AMANDA SUELLENN DA SILVA SANTOS OLIVEIRA, JOYCE LOPES MACEDO, ANA KAROLINNE DA SILVA BRITO, LAIS LIMA DE CASTRO ABREU, ADRIANA MARIA VIANA NUNES, ANA VICTÓRIA DA SILVA MENDES, GUSTAVO VIANA CASTRO, CLIDENOR SELES DA SILVA JUNIOR, SAMUEL DE SOUSA PEREIRA ARAÚJO, JOÃO PAULO JACOB SABINO, DANIEL DIAS RUFINO ARCANJO, MARIA DO CARMO DE CARVALHO E MARTINS
Affiliations	Departamento de Biofísica e Fisiologia, Universidade Federal do Piauí, UFPI
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O modelo animal que faz utilização de uma dieta rica em gordura (DRG) combinada com administração de estreptozotocina (STZ) é usado para produzir forma de doença com características semelhantes àquelas observadas no diabetes tipo 2 em humanos. Entretanto, existe uma grande variação no método quanto às doses de STZ, tempos de indução e composição da ração utilizada. Esta revisão se propõe a investigar as características dos protocolos de indução de diabetes mellitus tipo 2 utilizando dieta hiperlipídica e baixa dose de estreptozotocina em ratos Wistar. Objective: Desenvolver um protocolo experimental de indução de diabetes com características semelhantes àquelas do diabetes tipo 2 em humanos utilizando dieta hiperlipídica combinada com baixa dose de estreptozotocina em ratos Wistar. Methods: Rattus norvegicus machos (peso corporal: 180 a 200g) foram aleatoriamente divididos em grupo controle (ração comercial) e grupo dieta hiperlipídica e normoproteica (DHLNP) (58,6 %-ração comercial, 14,6 %-banha, albumina 6,6%, e 20%-açúcar). Estreptozotocina (STZ; 20 ou 30 mg/kg diluída em tampão citrato pH 4,5) ou veículo (grupo controle) foram administrados no 36º dia, por via intraperitoneal, após jejum de 12 horas. A confirmação do diabetes ocorreu 72 horas após injeção de STZ por meio de medida de glicemia capilar de jejum (12 horas de jejum). Foi utilizado como critério para determinar presença de diabetes valores de glicemia de jejum iguais ou superiores a 250 mg/dL. Após 28 dias de acompanhamento, amostras de sangue e tecidos foram coletadas para análises. Os resultados foram representados como média \pm erro padrão da média. Para comparações múltiplas entre os grupos, utilizou-se o Teste t e/ou Análise de Variância (ANOVA) seguida do pós-teste de Tukey. Foi utilizado o programa estatístico GraphPad Prism 8.0.1 (Graph Pad Software, Inc., San Diego, CA, EUA), sendo o nível de significância estabelecido em $p < 0,05$. Results: No grupo que recebeu dose de STZ de 30 mg/kg todos os animais tiveram diagnóstico confirmado de diabetes, enquanto o grupo que recebeu a dose de 20 mg/kg, apenas 50 % dos animais apresentavam valores de glicemia ≥ 250 mg/dL 72 h após administração de STZ. No grupo DHLNP+STZ 30 mg/kg houve aumento do HOMA-IR (CN: $2,22 \pm 0,72$; DHLNP+STZ 30: $32,56 \pm 15,58$), redução do HOMA-B (CN: $89,68 \pm 27,76$; DHLNP+STZ 30: $32,56 \pm 15,58$) e QUICK (CN: $0,34 \pm 0,01$; DHLNP+STZ 30: $0,26 \pm 0,01$). Ademais, os achados histopatológicos indicaram uma redução significativa da área das ilhotas pancreáticas (CN: $155.097.690 \pm 29.690.390$ (μm); DHLNP+STZ 30: $59.135.140 \pm 4.715.169$ (μm)) e foi identificada presença de inflamação nos animais diabéticos quando comparados ao grupo controle. As médias de variação de ganho de peso corporal ao final do experimento nos grupos controle e DHLNP-STZ 30 mg/Kg foram, respectivamente, de $42,14 \pm 3,97$ e $9,85 \pm 14,49$ g, não houve alterações no peso relativo da gordura visceral entre os grupos experimentais. Conclusion: O modelo proposto com dieta hiperlipídica combinada com estreptozotocina em dose de 30 mg/Kg foi eficiente para induzir diabetes com características de diabetes tipo 2, o que foi evidenciado pelo aumento da glicemia de jejum, da resistência à insulina e aumento da adiposidade. Support: Fundação de Amparo à Pesquisa do Estado do Piauí, FAPEPI; Programa Pesquisa para o SUS – PPSUS – CHAMADA FAPEPI/SESAPI/MS-Decit/CNPq Nº 004/2020. Protocol: Comissão de Ética no Uso de An</p>

Title	Efeitos tóxicos causados pela exposição a mistura de contaminantes tributilestanho e cádmio no eixo reprodutivo de ratas Wistar
Authors	AMANDA DOS SANTOS NUNES, JONES BERNARDES GRACELI
Affiliations	Pós Graduação de Ciências Fisiológicas, UFES
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A poluição de metais pesados tem aumentado, expondo ainda mais a população e o meio ambiente, representando uma preocupação mundial. Estudos têm demonstrado a relação entre a exposição destes contaminantes com o desenvolvimento de fisiopatologias. No Espírito Santo, há um aumento na contaminação da água para consumo devido à poluição dos oceanos, causada pela prática portuária e industrial. Além disso, a região enfrenta altos níveis de contaminação do solo. A CESAN constatou níveis elevados de metais pesados acima dos limites de segurança estabelecidos pelo Ministério da Saúde. No Espírito Santo, os contaminantes cádmio (Cd) e tributilestanho (TBT) são encontrados com abundância em solos e águas, favorecendo uma exposição simultânea da população via ingestão de animais contaminados. Hoje em dia, existem vários estudos destes contaminantes isolados, que evidenciam consequências capazes de promover toxicidade em órgãos reprodutivos. Contudo, ainda não há evidências na exposição simultânea de TBT+Cd . Objective: Investigar os possíveis efeitos tóxicos da exposição aos contaminantes combinados tributilestanho e cádmio no eixo reprodutivo de ratas Wistar. Methods: Foram utilizadas ratas wistar adultas (8-10 semanas com n=10/grupo). Todos os protocolos foram aprovados pelo CEUA-UFES (04/2023). Foram utilizadas 19 ratas no total. As ratas foram pesadas e divididas aleatoriamente em grupos: a) controle (CON; n=9) tratados com solução veículo (Etanol 0.1%, 0,1 mL/300 g ,via gavagem). (b) (TBT+Cd n=10) tratados com 100µg/Kg/dia ,via gavagem e Cd 100mg/L em água ingerida. O tratamento durou 15 dias. Foi avaliado o ciclo estral diariamente . Para análise da morfometria do útero e ovário, foram realizados cortes histológicos e corados com Hematoxilina- Eosina (H&E). Para avaliação da densidade de colágeno foi realizado coloração Picro Sirios. Results: Após a exposição aos contaminantes da mistura (TBT+Cd) não foi observado alteração de peso corporal, e observou diminuição do peso do ovário, e aumento do peso uterino no grupo tratado ($p>0,05$ vs CON, n=10). Na análise do ciclo estral foram observadas irregularidades no grupo exposto aos contaminantes, com diminuição da fase no proestro e diminuição da duração do ciclo total ($p>0,05$ vs CON, n=10). Nas dosagens hormonais, foram observados diminuição do estradiol e testosterona no grupo tratado ($p>0,05$ vs CON, n=10). Na morfologia ovariana foi observada diminuição na quantidade de folículos primordiais, folículos primários, folículos pré-antrais e antrais, tendo diminuição na reserva ovariana, e diminuição do corpo lúteo ($p<0,05$vs CON, n=10). Na morfologia uterina, foi observado aumento da área do útero do grupo mistura, em contrapartida teve redução da área do endométrio e aumento do miométrio externo e interno ($p<0,05$ vs CON, n=5). Não foi observado diferença estatística na quantidade de glândulas, e foi observado aumento da espessura do epitélio luminal do grupo tratado ($p<0,05$ vs CON, n=5). Na análise histológica com PicroSirius Red, foi observado diminuição de deposição de colágeno no ovário e aumento no útero ($p<0,05$ vs CON, n=5). Todos os dados são expressos como média \pm SEM. Conclusion: Os resultados mostram impactos significativos nas alterações estruturais e funcionais do útero e ovário, indicando piora no sistema reprodutivo de ratas. Esses achados ressaltam a importância da regulamentação e monitoramento desses poluentes ambientais, favorecendo novos estudos posteriormente. Support: FAPES Protocol: CEUA-UFES (04/2023).</p>

Title	ROLE OF INTERLEUKIN 6 IN THE ACTIVATION OF THE UBIQUITIN-PROTEASOME SYSTEM IN OXIDATIVE MUSCLES OF DENERVATED MICE
Authors	LETICIA CIRELLI RUIZ, NEUSA MARIA ZANON, HENRIQUE JORGE NOVAES MORGAN, ÍSIS DO CARMO KETTELHUT, LUIZ CARLOS CARVALHO NAVEGANTES
Affiliations	Physiology, USP, Biochemistry & Immunology, USP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Muscle atrophy is characterized by the loss of muscle mass due to a predominance of protein degradation pathways. Interleukin 6 (IL-6) is a molecule with pleiotropic functions and was identified as a myokine that participates in the induction of protein catabolism in inflammatory situations. However, its contribution to the activation of the ubiquitin-proteasome proteolytic system (UPS) in non-inflammatory models such as peripheral nerve injury has not yet been well elucidated. Objective: The present study aims to investigate the role of muscle IL-6 in activating the UPS system in oxidative muscles of denervated mice</p> <p>Methods: Male C57Bl/6 wild-type (WT) and IL-6 KO mice (~25g and 12 weeks of age) were subjected to bilateral sciatic nerve section (atrophic denervation) and euthanized after 3 days. Their soleus muscles were weighed and incubated with the tendons fixed on appropriate supports for 2h and the activity of the UPS system was determined by the difference in tyrosine release in medium with or without the proteasome inhibitor (MG-132). IL-6 and TNF-α were quantified in plasma and gastrocnemius muscle by ELISA. Values were expressed as mean\pmSEM (n=6) and statistical analyzes were performed using the t-student test or two-way ANOVA (*p<0.05) (CEUA: 065-2021). Results: Atrophic denervation did not generate a systemic inflammatory condition in the animals, as it selectively increased the plasma concentration of IL-6 (28.09\pm5.32 vs. 7.05\pm4.34 pg/ml control group) and did not was able to induce the production of TNF-α (not detectable). It was found that denervation also selectively increased muscle IL-6 content (31.46\pm2.67 vs. 19.04\pm1.13 pg/mg control group) and this effect was completely abolished in IL- KO animals. 6. As expected, denervated muscles from WT animals lost mass and showed greater proteolytic activity of the UPS system (0.16\pm0.01 vs. 0.05\pm0.01 mmol tyrosine/mg WT sham group). However, this proteolytic activity was significantly lower in denervated muscles of IL-6 KO animals (0.09\pm0.02 vs. 0.06\pm0.01 mmol tyrosine/mg IL-6 sham KO group) when compared to the WT group. In innervated animals, UPS activity was similar in muscles from WT and IL-6 KO animals. Conclusion: The data obtained in this study suggest that muscle IL-6 participates in the activation of the UPS system in oxidative skeletal muscle (soleus) of mice, after the loss of motor innervation. Support: CAPES and CNPQ. Protocol: 065-2021</p>

Title	EFFECTS OF ALTERNATE-DAY FASTING AND TIME-RESTRICTED FEEDING ON ADIPOSITY AND BEHAVIOR IN MIDDLE-AGED FEMALE RATS
Authors	WELERSON ROBERTO DOS REIS, BRUNA LETÍCIA ENDL BILIBIO, LUCAS MACHADO SULZBACHER, JÚLIA FURSEL PACHECO, ANNA KAROLINA KRETSCHMANN FLORENCIO DE SOUZA BAGETTI, MIRNA STELA LUDWIG, THIAGO GOMES HECK
Affiliations	Curso de Medicina, UNIJUÍ, Programa de Pós Graduação em Atenção Integral à Saúde, UNIJUÍ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity is a multifactorial condition that is associated with metabolic and behavioral changes, which can be exacerbated in female aging (Best Pract Res Clin Obstet Gynaecol, 29p:548-553, 2015). This is because obesity facilitates neuroendocrine changes and triggers immune-inflammatory processes that can culminate in diseases such as diabetes, cardiovascular diseases, anxiety, and depression (Menopause, 23p:488-493, 2016). Thus, calorie restriction by intermittent fasting (IF) can promote weight loss and contribute to reducing adiposity (J Acad Nutr Diet, 115p:1203, 2015), and alternate-day fasting (ADF) and time-restricted feeding (TRF) are the most popular of the IF protocols. Objective: We investigated if ADF and TRF can modify body weight, adiposity and behavior in obese middle-aged female rats. Methods: Female Wistar rats (n=23), aged 15 months, were fed either a standard (11% fat) or high-fat diet (58% fat) for 8 weeks. They were then divided for an additional 8 weeks to receive IF interventions 5 d/wk, spanning from week 9 to 16, composing 4 groups: Control (C, standard diet, n=5), HFD (n=5), HFD+ADF (24-hour fasting, n=8), and HFD+TRF (14-hour daily fasting, n=5). The ADF protocol consisted of 24-h fasting followed by free access to the HFD on a subsequent day. The TRF protocol consisted of a daily fasting period of 14 h followed by free access to the HFD for 10 h. Except for weekends. The weights of the animals were measured weekly and at the end of the study, an Open Field Test (OFT) was applied. Total time in movement and time spent in the periphery of the apparatus were assessed to evaluate animal behavior. Data of bodyweight and white adipose tissue (WAT) are presented as mean \pm s.d., while behavior data is presented as median (interquartile range). Comparisons between groups for bodyweight, WAT data were performed by one-way analysis of variance (ANOVA) followed by Tukey and Newman-Keuls post hoc test respectively. Behavior was analyzed using Kruskal-Wallis test followed by Dunn's post hoc test. Considering a significance $P < 0.05$. Results: Only the HFD group presented a higher body weight compared to the control group at the end of the study [Bodyweight (g): C=298\pm20; HFD=387\pm60*; HFD+TRF=337\pm20; HFD+ADF=348\pm32; *P=0.101 vs. C, F(3, 19) = 4.998]. HFD consumption increased adiposity in all HFD groups, and neither IF intervention modified the adiposity of the animals [WAT (%tissue weight/final body weight): C=2.5\pm0.9; HFD=9.4\pm1.8*; HFD+TRF=8.0\pm1.2*; HFD+ADF=8.0\pm1.8*; *P < 0.0001 vs. C; F 3,19 = 21.44]. Also, there were no alterations in mobility time in the open field test [Mobility time (sec): C=61.8(17.7-122.6); HFD=58(19.5-94,5); HFD+TRF=23.7(13.2-38.2); HFD+ADF=68.6(27.8-81.1); P=0.389, F(3, 18)=1,062]. However, HFD showed higher time spent in the periphery compared to the control group, whereas the HFD+ADF group showed a lower time spent in the periphery compared to HFD group [periphery time (sec): C=260(243.4-291.4)*; HFD=297(296.4-298.5); HFD+TRF=297.5(285.2-298.5); HFD+ADF= 273(252.3-291.2)*; *P= 0.0365 vs. HFD]. Conclusion: IF may have benefits as a non-pharmacological strategy for obesity treatment by attenuating weight gain and anxiety-like behavior. Support: CAPES, PPGAIS-UNIJUÍ, FAPERGS, CNPq, grants 307926/2022-2, and 405546/2023-8 to TGH). Protocol: CEUA 013/2018</p>



Title	Assessment of the functional impact of IL-17 exposure on human granulosa cells
Authors	MARIANNA RIBEIRO CABRAL, ANDRÉ LUCAS LAGÔA DE FREITAS, MAYCK MEDEIROS AMARAL DA SILVA, JULIANA BORGES VIEIRA, JOHNATAS DUTRA SILVA, SABRINA SODRÉ DE SOUZA SERRA, MONIQUE MARTINS MELO, PEDRO LEME SILVA, FLAVIA FONSECA BLOISE, FERNANDA FERREIRA CRUZ
Affiliations	Medicina Regenerativa, Instituto de Biofísica Carlos Chagas Filho, UFRJ, Fisiologia e Biofísica Celular, Instituto de Biofísica Carlos Chagas Filho, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Asthma is one of the most common chronic lung diseases among women of reproductive age. Among its immune responses, the Th17-mediated inflammation and its main cytokine IL-17 are involved in the neutrophilic phenotype, usually associated with systemic inflammation and severe asthma. Serum IL-17 values >20 pg/ml are observed in severe compared to mild/moderate asthma and is an independent predictor of asthma severity. Previous studies have highlighted a possible link between asthma and infertility. Asthmatic women were associated with an increased time to pregnancy, as well as a greater need for fertility treatment compared to women without asthma. It has been hypothesized that systemic inflammation present in asthma could affect the reproductive organs, impact the reproductive cycle's phases, and alter ovarian follicular dynamics. Granulosa cells form the cell layer closest to the oocyte, providing physical support, growth factors, and essential hormones to maintain proper follicular development. Objective: Therefore, the present work aims to investigate the functional impacts of IL-17 exposure on granulosa cells, regarding cell viability and proliferation. Methods: To examine this, we cultured human granulosa-like tumor cell line COV434 in Dulbecco's Modified Eagle Medium (DMEM) high glucose, supplemented with 10% fetal bovine serum (FBS) and 1% penicillin/streptomycin (P/S). The cells were cultured in a humidified atmosphere with 5% CO₂ at 37°C. Results: Initially, we evaluated the responsiveness of COV434 cells to asthma-related inflammatory mediators by qPCR, and we analyzed the IL-17 receptors mRNA expression (IL-17RA: 0.1236 ± 0.0220; IL-17RC: 0.1036±0.0333; IL-4R: 0.0668 ±0.0251; IL-5RA: non-detected; IL-12Rβ2: non-detected). Currently, we are evaluating the effect of different concentrations of IL-17 (10, 100, and 1000 pg/ml) and different exposure times (24, 48, and 72 hours) on COV434's proliferation and viability by flow cytometry using carboxyfluorescein diacetate succinimidyl ester (CFSE) and AnnexinV-FITC/Propidium iodide, respectively. Conclusion: Thus, assessing the functional impacts of IL-17 on granulosa cells will allow us to ascertain the direct or indirect involvement of this asthma-related inflammatory mediator in female infertility. From this, it would be possible to start seeking safe and effective alternatives to improve fertility in asthmatic women. This project has financial support from the Coordination for the Improvement of Higher Education Personnel (CAPES), the National Council for Scientific and Technological Development (CNPq) and Carlos Chagas Filho Foundation for Research Support in the State of Rio de Janeiro (FAPERJ). Support: Coordination for the Improvement of Higher Education Personnel (CAPES), the National Council for Scientific and Technological Development (CNPq) and Carlos Chagas Filho Foundation for Research Support in the State of Rio de Janeiro (FAPERJ). Protocol: N.A.</p>

Title	MUTAÇÃO NA PROTEÍNA GPNMB INDUZ AUMENTO DE MASSA GORDA E REDUÇÃO NA EXPRESSÃO HEPÁTICA DE GENES ASSOCIADOS AO METABOLISMO LIPÍDICO E DE CARBOIDRATOS EM CAMUNDONGOS SUBMETIDOS A DIETA HIPERLIPÍDICA E FRUTOSE
Authors	ELIZ MARIA DE OLIVEIRA FURTADO, JULIANO JEFFERSON DA SILVA, ANA FLÁVIA TOSTES, PIETRA SOUSA BARSANELE, JOSÉ CIPOLLA NETO, DANUSA SOARES DIAS, MARISTELA DE OLIVEIRA POLETINI, LEONARDO VINÍCIUS MONTEIRO DE ASSIS, MARIA NATHÁLIA DE MORAES
Affiliations	Departamento de Ciências Biológicas, UNIFESP, Departamento de Fisiologia e Biofísica, USP, Departamento de Ciências Biológicas, USP, Center in Brain, Behavior and Metabolism, University of Lubeck, Departamento de Fisiologia e Biofísica, UFMG, Departamento de Educação Física, UFMG
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Alterações no estilo de vida, como sedentarismo e consumo de dietas ricas em gordura, contribuem para distúrbios metabólicos, como resistência à insulina e diabetes mellitus tipo 2 (DM2), que podem levar a danos hepáticos. Em casos de DM2 e esteatohepatite não alcoólica, observa-se alta expressão da proteína GPNMB, uma glicoproteína transmembrana correlacionada positivamente com um maior índice de massa corporal (IMC) em roedores e humanos. Desta forma, altas concentrações de GPNMB podem ser consideradas um marcador de alteração metabólica e/ou um fator de risco para distúrbios metabólicos.</p> <p>Objective: Neste estudo, propomos investigar o papel da proteína GPNMB no desenvolvimento de alterações metabólicas em camundongos controle e portadores da mutação na proteína GPNMB, submetidos a uma dieta hiperlipídica (HFD) combinada com uma solução oral de frutose a 30% em água (FRUT). Camundongos machos de 3 meses de idade da linhagem DBA/2J (que expressam a forma mutante da proteína, GP-) e camundongos controle (GP+) foram submetidos a HFD (48,4% de lipídios, 30,1% de carboidratos e 21,5% de proteínas) associada a FRUT por 12 semanas, tendo seu peso corporal e consumo alimentar avaliados ao longo do tratamento. Methods: Após 8 e 12 semanas de HFD+FRUT, foi realizado um teste de tolerância à glicose (GTT), avaliação da composição corporal, ensaio de calorimetria indireta (em 30°C e 10°C) e análise da expressão de genes relacionados ao metabolismo de carboidratos e lipídios no fígado (CEUA nº 7699101023). Results: Identificamos que os animais GP- apresentam maior ganho de massa gorda da 8ª à 12ª semana de HFD+FRUT (16,5±0,93 e 17,0±0,53) em comparação aos camundongos GP+ em 12 semanas de HFD+FRUT (10,7±0,59). No GTT, observamos que animais GP- apresentam maior tempo de metabolização da glicose plasmática, comprovado pela área sobre a curva (AUC) quando comparado aos animais GP+. Adicionalmente, a 10°C, identificamos que os animais GP- apresentaram um RER (taxa de troca respiratória) de 0,69, enquanto os GP+ apresentaram um RER de 0,81, indicando que animais GP- têm menor oxidação de carboidratos e aumento na oxidação de lipídios. Além disso, animais GP- submetidos a 12 semanas de HFD+FRUT apresentam a menor expressão de <i>Glut2</i> e <i>Gys2</i> no fígado, sugerindo uma redução na captação de glicose pelas células hepáticas, o que pode explicar os resultados obtidos no teste de tolerância à glicose e uma possível diminuição no armazenamento de glicogênio. Ademias a alteração nos genes <i>Ppar</i>, <i>alfa</i> e <i>gama</i>, sugere uma mudança no metabolismo lipídico, o que pode contribuir para o aumento da gordura corporal. Conclusion: Esses resultados indicam que os animais GP- apresentam regulação negativa dos processos metabólicos avaliados, o que pode ter implicações importantes na homeostase energética e no metabolismo de carboidratos e lipídios. Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (2023/08461-9) Protocol: 7699101023</p>

Title	NORADRENERGIC BUNDLES REGULATE HEPATIC FUEL DISPOSAL BY COORDINATING AUTOPHAGY DURING ACUTE COLD STRESS
Authors	HENRIQUE JORGE NOVAES MORGAN, ALINE ZANATTA SCHAVINSKI, ANA PAULA ASSIS, ANA ELISA CALEIRO SEIXAS AZZOLINI, LAYANNE CABRAL DA CUNHA ARAUJO, JOÃO PAULO GABRIEL CAMPOREZ, LUCIANE CARLA ALBERICI, ISIS DO CARMO KETTELHUT, LUIZ CARLOS CARVALHO NAVEGANTES
Affiliations	Departamento de Fisiologia, USP, Departamento de Bioquímica e Imunologia, USP, Departamento de Ciências BioMoleculares, USP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Autophagy, one of the main cellular degradation processes, is essential to maintain gluconeogenesis and ketogenesis in the liver. When directed towards the degradation of lipids, we call it lipophagy. Its dysregulation is involved in several hepatic pathologies such as steatosis. Even though the well described action of pancreatic hormones in regulating autophagy, the role of sympathetic nervous system remains unclear. Objective: We aimed to investigate the role of the hepatic noradrenergic system in lipophagy and its influence on gluconeogenesis and ketogenesis during acute cold stress. Methods: For this, neonate male mice were sympathectomized (6OHDA; 100mg.kg-1.dia-1) and 10 weeks later were exposed to cold (4°C) for 3-6h, a model of hepatic noradrenergic activation. For autophagy studies, leupeptin (ip; 40mg.Kg-1) was used previously to stress protocol to block autophagosome degradation. The Oroboros system was used to measure the β-oxidation in the liver in the presence of palmitoyl-carnitine. Western blot and Rt-qPCR were used to analyze the content and phosphorylation levels of proteins and gene expression, respectively. Tritiated water was used to label the synthesized lipids. The Folch method was used to measure hepatic lipid content. The results are expressed as means \pm SEM (n=3-5/group) and were submitted to appropriate statistical analysis considering the level of significance of $p < 0.05$. Results: Cold increased the autophagy flux (2-fold), blood glucose (214.2 ± 6.9 vs 135.8 ± 7.2mg/dL RT), ketone body (1.7 ± 0.1 vs 1.0 ± 0.1mmol RT) and hepatic noradrenaline (70%), effects that were abolished or attenuated in 6OHDA mice. Plasma levels of glucagon, corticosterone and fatty acids were increased (50%) while insulinemia was reduced in saline and 6OHDA mice exposed to cold (20%). In innervated mice, cold also increased protein and genes of gluconeogenesis (G6Pase and PEPCK), ketogenesis (CPT1a and ACAA2) and autophagic (LC3 and ULK1), these effects were attenuated or abolished in 6OHDA mice. The leupeptin-induced blockage of autophagy in cold-exposed mice inhibited the hyperglycaemia and attenuated the increase in ketone body plasma levels. Cold induced a lipid accumulation in the liver (2-fold) that was even higher in 6OHDA mice (2.5-fold). The leupeptin-induced blockage of autophagy in cold-exposed mice increased the lipid accumulation in the same levels as occurs in 6OHDA mice. Cold stimulated hepatic lipogenesis but not “de novo” fatty acid synthesis. Hepatic beta-oxidation was unchanged during cold but reduced in 6OHDA. Liver immunofluorescence of LC3 and bodipy revealed an increase of co-localization during cold, indicating lipophagy, that was attenuated by 6OHDA. Conclusion: Data suggest cold-inducible sympathoexcitation leads to the activation of lipophagy, which participates in the regulation of hepatic gluconeogenesis and ketogenesis. Support: Fapesp 2021/05848-4. Protocol: CEUA 065-2021.</p>



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Title	Avaliação da homeostase glicêmica e sensibilidade insulínica em modelo experimental de fibromialgia em camundongos fêmeas
Authors	HEVELY CATHARINE DOS ANJOS SANTOS, JOÃO DA CRUZ FILHO, DANIEL BADAUÊ PASSOS JUNIOR, ANDRÉ SOUZA MECAWI, JOSIMARI MELO DESANTANA, DANILO LUSTRINO
Affiliations	Departamento de Fisiologia, UFS, Departamento de Biofísica, UNIFESP, Departamento de Fisioterapia, UFS
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A fibromialgia (FB) é caracterizada por dor musculoesquelética generalizada e é um dos principais diagnósticos de dor crônica. Embora sua fisiopatogenia ainda não seja totalmente conhecida, estudos prévios demonstraram uma possível associação da doença com maior índice de massa corporal e desregulação da homeostase glicêmica, sugerindo que estes pacientes podem desenvolver resistência à insulina. Todavia, os achados ainda não são totalmente conclusivos. Objective: Portanto, objetivou-se neste trabalho investigar parâmetros de sensibilidade insulínica e regulação glicêmica em um modelo experimental de FB em camundongos. Methods: Para tanto, foram utilizados camundongos fêmeas, com 8 a 12 semanas de idade, submetidos ao modelo de dor crônica induzida pela injeção dupla de 20 µL de NaCl 0,9% pH 7,2 (controle) ou pH 4,0 no músculo gastrocnêmio esquerdo, em intervalo de cinco dias, que mimetiza a hiperalgesia observada em pacientes FB. Results: A hiperalgesia mecânica foi confirmada por meio da avaliação do limiar de retirada da pata (PWT). Após a 2ª injeção, observou-se redução significativa do PWT ipsi e contralateral no grupo pH 4,0, desde o dia 6º [-36,5% vs. controle (CON); p<0,001] até o 12º (-42,5% vs. CON; p<0,001), comprovando a eficácia do modelo. No 11º dia, parte dos animais (n = 6/grupo) foi submetido ao jejum alimentar (JJ) noturno de 12 h (21:00 h – 9:00 h) e, em seguida, aos testes intraperitoneais de tolerância à glicose (ipTTG; 2 g/kg) e piruvato (ipTTP; 1,5 g/kg). Após 15 minutos da administração de glicose houve elevação na glicemia no grupo pH 4,0 vs. CON (+29,4%; p= 0,041) e na área sob a curva (AUC; mg/dL x 120min) do ipTTG (+29%; p= 0,026), demonstrando que o grupo pH 4,0 apresentou intolerância à glicose. Ademais, efeito significativo da administração de salina ácida foi detectado pela ANOVA two-way no ipTTP aos 60 min (+35,8%; p= 0,017) e 120 min (+33,73%; p= 0,03) vs. CON, além de maior AUC (30,04%; p<0,001), corroborando com os achados do teste anterior. Um grupo de animais (n= 5- 6/grupo) foi submetido ao JJ diurno de 4h (8:00 – 12:00 h) no 12º dia e, após, ao teste de tolerância à insulina (ipTTI; 0,75 U/kg). A ANOVA two-way demonstrou maior glicemia aos 60 min (+23,7%; p= 0,02) no grupo pH 4,0 vs. CON, assim como aumento na AUC (+15,21 vs. CON; p = 0,001). Finalmente, os animais passaram por avaliação de calorimetria indireta (n = 6-7/grupo). A ANOVA two-way demonstrou efeito significativo do modelo em ambos o consumo de oxigênio (VO2) (p = 0.012) e produção de dióxido de carbono (VCO2) (p=0.016), mas não no quociente respiratório (RER) e produção de calor. Conclusion: Assim, constatamos que o modelo experimental de FB em camundongos culmina em desbalanço da homeostase glicêmica, resultando em intolerância à glicose e resistência insulínica. E, não menos importante, que há outras alterações presentes no perfil metabólico desses animais que necessitam ser melhor investigadas para uma maior compreensão das características da fibromialgia. Support: CAPES e FAPITEC (nº processo: 019203.01456/2024-4). Protocol: 7045181223</p>



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Title	LIVER RESPONSIVNESS TO PHENYLEPHRINE IS NOT ALTERED IN NON-OBESE DIABETIC GOTO-KAKIZAKI RATS.
Authors	ANA LUIZA ALVES LOURENÇO, FRANCIELE PASQUINI DALL'AQUA, OTÁVIO VINÍCIUS CUSTÓDIO JORGE, THAIS TAKAKI BRAGA, MARIA FERNANDA SIQUEIRA, LUNNA BOSQUETTI UEMURA, MANOEL OSVALDO ESTEVAM FÁVARO, GIOVANNA PAIS GALVÃO ESTEVES, ROBERTO BARBOSA BAZOTTE, ROBERTO BARBOSA BAZOTTE, RUI CURI, RUI CURI, GISELE LOPES BERTOLINI, PRISCILA CASSOLLA
Affiliations	Physiological Sciences, UEL, Post Graduate Program in Physiological Sciences, UEM, Interdisciplinary Post Graduate Program in Health Sciences, UNICSUL, Butantan Institute, USP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The Goto-Kakizaki (GK) rat is a model of non-obese insulin resistance, which spontaneously develops type 2 diabetes mellitus with a chronology like that in humans. Although the phenylephrine stimulated glycogenolysis in the saturating concentration for Wistar rats is not altered in young GK rats, the capacity for glucose output can be different because the liver responsiveness to glycogenolytic agents is modulated by a wide variety of factors such as aging, animal species, fasting, and hypercortisolism. Objective: The main of this work was to evaluate liver responsiveness to phenylephrine, an alpha 1-adrenergic agonist in glucose production, glycogenolysis, and glycolysis. Methods: To this end, three days after confirmation of insulin resistance at the end of the 8th week of age by the insulin tolerance test (ITT), the animals (n = 7-10 each group) were submitted to in situ liver perfusion, through which an infusion was made at phenylephrine concentrations of 2 μM, 4 μM or 6 μM for the evaluation of the dose-response curve of alpha 1-adrenergic agonist on glucose production, glycogenolysis, and glycolysis in GK and control Wistar rats (C). Statistical analysis was performed using unpaired Student's t-test and one-way ANOVA followed by Tukey's test and $p < 0.05$ was adopted. Results: The ITT confirmed insulin resistance in the GK group ($p = 0.0147$). The hepatic response to phenylephrine was similar in GK animals at all concentrations for glucose output [2 μM, GK area under curve (AUC) 16.520 ± 2.065, C AUC 18.870 ± 2.567, $p = 0.9874$; 4 μM, GK AUC 10.950 ± 2.490, C AUC 10.130 ± 1.684, $p > 0.9999$, and 6 μM, GK AUC 10.890 ± 2.506, C AUC 13.920 ± 2.901, $p = 0.9444$], glycogenolysis [2 μM, GK AUC 18.31 ± 1.625, C AUC 20.64 ± 3.505, $p = 0.9831$; 4 μM, GK AUC 9.091 ± 1.015, C AUC 9.712 ± 1.113, $p > 0.9999$; and 6 μM, GK AUC 11.16 ± 2.094, C AUC 15.54 ± 2.776, $p = 0.6733$], and for glycolysis [2 μM, GK AUC 7.071 ± 0.986, C AUC 6.605 ± 1.346, $p = 0.9992$; 4 μM, GK AUC 4.546 ± 0.665, C AUC 4.473 ± 0.732, $p > 0.9999$; and 6 μM, GK AUC 3.262 ± 0.416, C AUC 5.698 ± 0.791, $p = 0.5295$]. Conclusion: Therefore, the liver capacity for glucose output, glycogenolysis, and glycolysis induced by phenylephrine were similar in GK and Wistar animals, thus this alpha 1-adrenergic agonist did not contribute to hyperglycemia in this model of non-obese insulin resistance. Support: FAPESP nº 2018/09868-7. Government of the State of Paraná, Paraná Science and Technology Council, and State Secretariat for Science, Technology, and Higher Education (SETI) (budget allocation # 4560.19.571.06.6153; eprotocol 21.234.745-0). Protocol: CEUA nº 019.2023</p>

Title	ANÁLISE DA RESISTÊNCIA À INSULINA, MORFOLOGIA E VIA DE SINALIZAÇÃO INFLAMATÓRIA NA PLACENTA DE RATAS COM PERIODONTITE APICAL
Authors	ANA CARLA THALEZ YWABUCHI NOBUMOTO, MARIA SARA DE LIMA COUTINHO MATTERA, BIANCA ELVIRA BELARDI, BRUNA DE OLIVEIRA ALVES, LORENA UMBELINO RODRIGUES, ANIELLY GONSALVES, ANNA CLARA CACHONI, MARIA CLARA VENCESLAU DOS SANTOS, ANGELA VERMELHO SARRACENI, ILANA YOSHIY DE ALMEIDA, DORIS HISSAKO MATSUSHITA
Affiliations	Ciências Básicas, Faculdade de Odontologia FOA/UNESP
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: In recent years, the relationship between oral inflammation and systemic disorders has become an area of great interest in the medical and dental scientific community. In this sense, studies have shown that maternal periodontal disease (PD) is associated with adverse gestational outcomes, such as low birth weight and preterm birth. Furthermore, it was found that periodontal pathogens induce changes in the placental structure. However, the literature is scarce regarding studies that investigated the relationship between maternal apical periodontitis (AP) and adverse pregnancy outcomes. AP is an oral inflammatory process in the region of the apex of the dental root associated with an increase in inflammatory cytokines that can contribute to systemic changes. Objective: The objective of the present study was to investigate insulin resistance and the inflammatory signaling pathway in the placenta of rats with AP and to investigate the effects of maternal AP on the health of the neonate. Methods: To this end, the 24 two-month-old Wistar rats (200g) were distributed into 3 groups: 1) control rats; 2) rats with 1 PA induced in the upper right 1st molar; 3) rats with 4 APs induced in the 1st and 2nd upper and lower molars on the right side. AP was induced using a carbon steel drill equipped with a 0.1 mm ball at the end. After 30 days of pulp exposure, rats from all groups were placed for mating. The rats were euthanized on the twentieth day of pregnancy to carry out the following experiments: 1) placental weight; 2) plasma glycemia using the glucose-oxidation method; 3) insulinemia using the ELISA method; 4) insulin resistance by HOMA-IR calculation; 5) degree of phosphorylation of JNK, IKK α/β and NF-κB p50 (Ser337) in the placenta using the Western blotting technique; 6) protein content of JNK, IKK α/β, NF-κB p50 and TNF-α in the placenta by Western blotting technique. In relation to newborns, the following analyzes were carried out: 1) capillary blood glucose. For statistical analysis, the normality of the data was statistically verified. They were performed by analysis of variance (ANOVA), followed by the Tukey test. The results were considered statistically significant when $p < 0.05$, using the statistical software Graph Pad Prism version 7.0 (GraphPad Software Inc., San Diego, CA, USA). Values were expressed as mean \pm standard error of the mean (SEM). Results: 1) there was a change in placental weight only in the PA4 group when compared to the CN and PA1 groups; 2) there was no increase in blood glucose, 3) there was hyperinsulinemia and insulin resistance according to the HOMA-IR index in groups PA1 and PA4 in relation to the CN group, as well as PA4 showing a higher value of this index in relation to PA1; 4) increased TNF-α content in the placenta of rats with 4PA when compared to the PA1 and CN groups; 5) no difference was observed in the degree of phosphorylation and content of JNK, IKK and NF-κBp50. Regarding the offspring, there was a reduction in capillary glycemia in the PA1 and PA4 groups when compared to the CN group. Conclusion: These partial data demonstrate that maternal BP can lead to changes in the placenta. The data presented reinforce that maintaining good maternal oral health is extremely important to prevent systemic changes that can affect the intrauterine environment and fetal development. Support: São Paulo Research Foundation (FAPESP) grant #2023/00536-0. Protocol: 0878-2022</p>

Title	Impacto do Glaucoma na Ritmicidade Circadiana e Atividade Termogênica do Tecido Adiposo Marrom em Camundongos
Authors	PALOMA ROBERTO ALVES, ELIZ MARIA FURTADO, PIETRA S. BARSANELE, LEONARDO V. DE ASSIS, MARIA NATHÁLIA MORAES
Affiliations	Ciências Biológicas, UNIFESP, Departamento de Fisiologia Geral, USP, Institute of Neurobiology, University of Lübeck
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A senescência do tecido adiposo marrom (TAM) resulta em diminuição da termogênese, atribuída ao `embranquecimento` das células, no qual as múltiplas gotículas multiloculares características se transformam em gotículas citoplasmáticas lipídicas uniloculares, típicas dos adipócitos brancos, cuja função primordial é estocar lipídios. No entanto, em camundongos machos <i>Mus musculus</i> DBA/2J de 12 meses, um modelo que carrega uma mutação espontânea na proteína GPNMB e desenvolve gradualmente glaucoma, observou-se a preservação da arquitetura celular do TAM, indicando maior atividade termogênica. No ensaio de calorimetria indireta, os camundongos glaucomatosos mostraram maior taxa de CO₂ exalado e RER elevado em resposta ao frio ambiental. O glaucoma afeta a ritmicidade biológica, prejudicando a sincronização do núcleo supraquiasmático (NSQ) devido à neurodegeneração das células ganglionares da retina. Em camundongos glaucomatosos, isso resulta em alterações no ritmo circadiano de <i>Per1</i> e <i>Vip</i> no relógio central. As alterações na maquinaria molecular do NSQ podem induzir modificações metabólicas, incluindo maior atividade termogênica no TAM. Além disso, as projeções das células ganglionares da retina (RGC) para outros núcleos hipotalâmicos como para o núcleo supraóptico, podem influenciar a termorregulação. Objective: Considerando que o trato retina-hipotálamo e o NSQ são alterados em consequência da morte das RGC, hipotetizamos que os animais glaucomatosos possam apresentar alterações na regulação termogênica no TAM Methods: Camundongos controle e portadores de glaucoma tiveram a temperatura do TAM monitorada por câmeras termográficas em temperatura termoneutra (30 °C) e em desafio de frio (17 °C). O TAM foi coletado a cada 4h por 24 h para análise de transcriptoma e de expressão gênica temporal (n=3-13). A análise estatística foi performada por ANOVA two way seguido de pós-teste de Bonferroni. Results: Observamos que em condição de termoneutralidade há aumento da temperatura do TAM em animais portadores de glaucoma. A análise do transcriptoma identificou que dentre os genes diferencialmente expressos há regulação negativa de processo biológico associado à regulação rítmica e para genes relacionados à biossíntese de lipídios Estes resultados suportam nossa hipótese, uma vez que a ativação da termogênese induz a lipólise e possui um claro perfil circadiano, o qual é originado por meio da interação dos genes do relógio. Buscando caracterizar o perfil temporal dos genes do relógio e da via termogênica de animais saudáveis e glaucomatosos, obtivemos como resultado a perda na oscilação temporal do grupo glaucomatoso quando comparado ao controle para os genes <i>Adrb3</i>, <i>Ppar-γ</i>, <i>Prdm16</i> relacionados à via termogênica e para os genes do relógio <i>Per2</i> e <i>Rev-erbα</i>. Aliado a isso, encontramos maior expressão gênica no grupo glaucomatoso em relação ao controle para o gene <i>Bmal1</i>, cuja deleção global ou específica no TAM potencializa obesidade induzida por dieta em camundongos. A proteína UCP1, a qual é responsável pela termogênese adaptativa apresentou maior expressão gênica nos animais glaucomatosos, além de menor expressão gênica para <i>Rev-erbα</i>, o qual reprime a transcrição de <i>BMAL1</i> e é um regulador negativo direto dos programas transcricionais termogênicos no TAM. Conclusion: Esses resultados indicam que a perturbação do ritmo circadiano causada pelo glaucoma pode afetar o controle metabólico do TAM, podendo fornecer perspectivas para abordagens terapêuticas de distúrbios metabólicos com impacto global. Support: FAPESP (2017/26651-9 e 2023/14439-6) Protocol: 8143290819</p>

Title	EFEITO DE VITAMINA D NO CONTEÚDO DE LIPÍDIOS NO TECIDO ADIPOSEO VISCERAL EM MODELO EXPERIMENTAL DE DIABETES MELLITUS EM RATOS
Authors	JÚLIA PIMENTEL SANTOS, MARIA CAROLINA SILVA AGUIAR, PEDRO ARTHUR AGUIAR SALES, EDIANNE SILVIA LUSTOSA CESAR, DIOGO CLETO CAVALCANTI, THAYNAR CAVALCANTE BATISTA, JOYCE LOPES MACEDO, AMANDA SUELLENN DA SILVA SANTOS OLIVEIRA, FRANCISCA VALDIRENE DE SOUSA NUNES, JOÃO PAULO JACOB SABINO, DANIEL DIAS RUFINO ARCANJO, MARIA DO CARMO DE CARVALHO E MARTINS
Affiliations	Departamento de Biofísica e Fisiologia, Universidade Federal do Piauí, UFPI
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A vitamina D tem sido apontada como um micronutriente com potencial ação no metabolismo da glicose e, desse modo, pode ser um recurso auxiliar para o controle dos agravos e complicações do diabetes mellitus Objective: Avaliar o efeito do tratamento com vitamina D no conteúdo de triglicérides e colesterol no tecido adiposo visceral em modelo experimental de diabetes induzido por dieta e estreptozotocina em ratos Methods: Foram utilizados 80 Rattus norvegicus Wistar, machos, com idade entre 08 e 12 semanas e peso corporal variando de 180 a 200 g. A indução do diabetes experimental foi realizada por meio de um protocolo com a oferta de ração hiperlipídica e normoproteica (DHLNP) ad libitum combinada com administração de estreptozotocina (STZ) 30 mg/Kg dissolvida em tampão citrato 10 mM e pH 4,5, por via intraperitoneal. A administração de STZ foi realizada após período de 5 semanas de manutenção com DHLNP. Os animais foram distribuídos aleatoriamente para compor grupos tratados por 4 semanas (n=7/grupo) e 8 semanas (n=9/grupo): (1) grupo controle não diabético (CN), (2) grupo controle diabético (CD), (3) grupo diabético tratado com metformina na dose de 150 mg/kg (MET); (4) grupo diabético tratado com vitamina D na dose de 0,25 µg/kg/dia (VD 0,25) via oral. Os animais dos grupos CN e CD receberam apenas veículo (óleo de girassol). Para comparações múltiplas entre os grupos, utilizou-se a Análise de Variância (ANOVA) seguida do pós-teste de Tukey. Foi utilizado o programa estatístico GraphPad Prism 8.0.1 (Graph Pad Software, Inc., San Diego, CA, EUA), sendo o nível de significância estabelecido em p<0,05. Results: Em relação à glicemia de jejum, os grupos tratados com vitamina D por 4 semanas apresentaram valores médios significativamente menores (p<0,05) do que os do grupo CD (CN: 99.29 ± 2.35; CD: 513,90 ± 17,98; MET: 459.00 ± 9.55; VD0,25: 410,60 ± 28,55). Também o tratamento com vitamina D por 8 semanas resultou em diminuição da glicemia em relação a CD (CN: 82,00 ± 2,56; CD: 454,20 ± 19,91; MET: 419,10 ± 15,24; VD0,25: 383,30 ± 13,14). Em relação ao peso relativo da gordura visceral (g/100g) não foram observadas diferenças significativas entre os grupos experimentais tratados por 4 ou 8 semanas. Quanto ao conteúdo de lipídios no tecido adiposo visceral, o grupo tratado com vitamina D na dose de 0,25 µg/kg durante 4 semanas apresentou valores significativamente menores de colesterol total (CT) (p<0,05) quando comparado a CD (CN: 4.40 ± 0.16; CD: 5,93 ± 0,15; MET: 5.60 ± 0.27; VD0,25: 5,15 ± 0,11), sem diferenças em relação ao conteúdo de triglicérides (TG). Resultados semelhantes também foram observados em animais submetidos ao tratamento por 8 semanas, com valores de CT significativamente menores (p<0,05) quando comparados a CD (CN: 3,71 ± 0,09; CD: 5,99 ± 0,40; MET: 5,45 ± 0,44; VD0,25: 4,81 ± 0,09), sem diferenças nos valores de TG Conclusion: A suplementação com vitamina D durante quatro e oito semanas resultou em melhora no controle glicêmico, evidenciado pela redução da glicemia de jejum, e no conteúdo de colesterol na gordura visceral em animais com diabetes com características de diabetes mellitus tipo 2 em humanos. Support: Fundação de Amparo à Pesquisa do Estado do Piauí, FAPEPI; Programa Pesquisa para o SUS – PPSUS – CHAMADA FAPEPI/SESAPI/MS-Decit/CNPq Nº 004/2020. Protocol: Comissão de Ética no Uso de An</p>

Title	Microplastics exposure during gestation and lactation alters biometric, biochemical, hormonal and behavioral parameters in Wistar rat dams and offspring
Authors	NATHÁLIA MEDEIROS NEHME, NELYANA DE OLIVEIRA SERPA, ROSIANE APARECIDA MIRANDA, LUANA LOPES DE SOUZA, EGBERTO GASPAR DE MOURA, VITOR HUGO SANTOS DUARTE PINHEIRO, ALEX CHRISTIAN MANHÃES, ANDREA CLÁUDIA FREITAS FERREIRA, IALA MILENE BERTASSO, PATRICIA CRISTINA LISBOA
Affiliations	Ciências Fisiológicas, UERJ, Fisiologia, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Worldwide, more than 350 million tons of plastic/year are produced, a scenario that was intensified with the Covid pandemic. Plastic components can act as endocrine disruptor chemicals and their residues of various sizes dispersed in the air, soil, water and food have already been found in the placenta and breast milk, being associated with impacts on the endocrine and cognitive system of offspring. Objective: Here, we studied if exposure to microplastics (MP) during gestation and lactation can cause dysfunction in the dam and offspring of both sexes at weaning, puberty and adulthood. Methods: The experimental design was approved by the Animal Care and Use Committee of the Biology Institute of the State University of Rio de Janeiro (031/2022; 032/2022). Nulliparous Wistar rats were mated for 24 h (2 females:1 male). From the 7th gestational day until weaning, dams received vehicle (Filtered water–control group; n=9) or 10 µm polystyrene microparticles (25 µg/kg body weight–MP group; n=8). The biochemical composition of milk was studied during lactation period (days 10 and 18). Biometric and biochemical parameters of dams, male (M) and female (F) offspring were evaluated at weaning (21 days-old), puberty (45 days-old) and adulthood (120 days-old). Behavioral tests (food preference, elevated plus maze and open field) were performed at puberty and adulthood. Data were analyzed using Student’s t test, considering $p < 0.05$ as significant. Results: MP dams had lower body mass during pregnancy (-16%, $p = 0.0134$) and lower plasma cholesterol at weaning (-34%, $p = 0.0381$). Milk lipids content, food intake, visceral fat mass, blood glucose, plasma triglycerides, plasma leptin and insulin were not changed in MP dams. At birth, MP males and females showed body weight and nasoanal length similar to controls. From birth to weaning, MP males and females showed lower weight gain (M=-10%, $p = 0.0426$; F=-13%, $p = 0.0193$). At weaning, pups of both sexes had higher plasma triglycerides (M=+93%, $p = 0.0457$; F=103%, $p = 0.0490$), while only MP females had higher plasma cholesterol (+40%, $p = 0.0107$). At this age, MP pups showed unchanged food intake, visceral fat mass, blood glucose, leptinemia and insulinemia. At 45 days-old, male offspring of MP group showed lower plasma cholesterol (-27%, $p = 0.0167$) and triglycerides (-39%, $p = 0.0004$). At 120 days-old, MP males had lower food intake (-3%, $p = 0.0071$) and plasma leptin (-43%, $p = 0.0419$). In the food preference test, MP males preferred to eat less the high-fat diet (-10%, $p = 0.0134$). In the open field test, regardless of age, MP males showed an increase in anxiety-like behavior ($p < 0.05$). At puberty and adulthood, MP females did not show significant changes in the biometric, biochemical and behavioral parameters studied. Conclusion: Our preliminary findings suggest that perinatal exposure to microplastics affects body mass and lipid metabolism of dams and pups at weaning. Furthermore, we evidence that early microplastics exposure leads to sex-dependent changes both in puberty and adulthood, with male offspring being most affected. Support: FAPERJ, CNPq, CAPES Protocol: CEUA 031/2022; CEUA 032/2022</p>

Title	Effects of nanoplastics exposure in a metabolic programming model.
Authors	NELYANA OLIVEIRA SERPA, NATHALIA MEDEIROS NEHME, LUANA LOPES DE SOUZA, ROSIANE APARECIDA MIRANDA, EGBERTO GASPAR DE MOURA, ALEX CHRISTIAN MANHÃES, VITOR HUGO SANTOS DUARTE PINHEIRO, ANDREA CLAUDIA DE FREITAS FERREIRA, IALA MILENE BERTASSO, PATRÍCIA CRISTINA LISBIA
Affiliations	Departamento de ciências fisiológicas, UERJ, Fisiologia, UFRJ
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Nanoplastics potentially act as endocrine-disrupting chemicals, but the impact of exposure to these contaminants on metabolic programming remain poorly understood. Objective: Here we investigated the short- and long-term impacts of exposure to nanoplastics during gestation and lactation on the endocrine-metabolic profile of offspring of both sexes. Methods: The experiments were approved by the Animal Care and Use Committee of the Biology Institute of the State University of Rio de Janeiro (CEUA 031/2022; 032/2022). Wistar rats were paired for 24h (2 females: 1 male). From the 7th day of gestation until the end of lactation, dams received by intragastric gavage filtered water (control group, n=9) or 100 nm polystyrene nanoparticles (25 µg/kg body mass; NP group, n=8). Biometric and biochemical parameters of dams, male (M) and female (F) offspring at birth, weaning (postnatal day 21, PN21), puberty (PN45) and adulthood (PN120) were studied. Behavioural parameters were analyzed at PN45 and PN120. Student's t-test was used for statistical analysis. Results: NP dams showed lower body mass during gestation (-19%, P=0.0098) and lower plasma cholesterol at weaning (-31%, P<0.05). Food intake, visceral fat mass, plasma glucose, triglycerides, leptin and insulin of dams were unchanged at weaning. At birth, the NP pups of both sexes were heavier (M: +5%, P<0.05; F: +8%, P=0.0005) and larger (M: +3%, P<0.05; F: +5%, P<0.0001). Until weaning, the NP pups of both sexes had unchanged body mass gain, naso-anal length, percentual of fat and lean mass. At PN21, only NP males showed higher TG (M: +76%, P<0.05). Other plasma parameters such as glucose, cholesterol, leptin and insulin were unaltered. At PN45, NP females had lower fat mass (-17%, p<0.05) and higher lean mass (+2%, p=0.045). In this age, NP offspring of both sexes showed lower TG levels (-39% and -38%, p<0.05). At PN120, NP females showed higher food intake (+3%, p<0.010). In the food preference test, NP males preferred to eat less of the standard diet (-50%, p<0.05) and more of the high-fat diet (+12%, p<0.05). In this same test, NP females showed lower preference for standard chow (-80%, p<0.01). Plasma leptin and insulin levels remained unchanged in NP offspring during puberty and adulthood. In the elevated plus maze (EPM) and open field (OF) tests, only NP males, regardless of age, showed higher anxiety-like behaviour (p<0.05). No changes were observed in locomotor activity in the OF or EPM. NP females showed no change in both behaviour tests. Conclusion: These data evidence that perinatal nanoplastics exposure can influence the offspring at different ages in a sex-dependent manner. Furthermore, adult male offspring show preference for a diet rich in fat, which can be associated with its the anxious profile. Support: FAPERJ, CAPES e CNPQ Protocol: CEUA 031/2022; 032/2022</p>

Title	Reduction in mitochondrial ROS production in white adipose tissue of animals treated with Doxorubicin and pre-treated with Calotropis Procera protein extracts.
Authors	DANIELLE CARVALHO FONSECA FALANGA DE OLIVEIRA, SAULO CHAVES MAHALHAES, ARIEL FALANGA DE OLIVEIRA, MARCIO VIANA RAMOS, ARICLECIO CUNHA DE OLIVEIRA, NILBERTO ROBSON FALCÃO DO NASCIMENTO
Affiliations	Ciências da Saúde, UECE
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Doxorubicin (Doxo) is a potent chemotherapy drug from the anthracycline class, however, it has non-specific selectivity, presenting adverse effects on other tissues, such as white adipose tissue (WAT). The damage occurs due to redox imbalance, mitochondrial damage and cellular apoptosis due to the activation of caspases by Doxo. There is a search for drugs that minimize these effects, including plant extracts. Calotropis Procera is abundant in the Brazilian Northeast and has several biological effects taking into account the different parts of the plant. Pharmacological properties such as pro- and anti-inflammatory, antipyretic, neuromuscular blocking and antioxidant activities stand out. The LP extract is composed of chitinases, proteases, lecithins, enzymes related to antioxidant metabolism and osmotin. PII is made up of proteases and osmotin. Studies from our laboratory showed that both Lp and PII led to improved oxidative metabolism, with less ROS production and increased mitochondrial density. Objective: To evaluate the effect of treatment with Calotropis Procera protein fractions associated with the acute use of Doxo. Methods: 24 male Wistar rats were used, kept in a vivarium with a 12/12h light/dark cycle, water and food ad libitum. The animals were between 12 weeks old, weighing between 250 and 300g. Divided into 4 groups (n=6): C (saline), Doxo (DX, 15 mg/kg + saline), Lp (DX, 15 mg/kg + Lp 5 mg/kg), PII (DX-15 mg/ kg + PII, 5 mg/kg). A single dose of Doxo or saline was administered on the second day of treatment in combination with saline, Lp or PII for 3 days. On the fourth day, the animals were euthanized and TAB (subcutaneous and periepididymal) removed, mitochondrial isolation to evaluate activity using the Oxigraph Oroborus and ROS production. Results: In the production of mitochondrial ROS, in the subcutaneous tissue there is a difference between Control (3.292±0.5); LP (1.068 ± 0.17) and PII (0.5486 ± 0.09), PII was also different from the Doxo group (2.72 ± 0.87). Periepidymal BAT, LP (0.9042± 0.1583) and PII (0.3958 ± 0.04) groups were different from the control (2.848 ± 0.47). Conclusion: We observed that treatment associated with LP and PII protein extracts reduces mitochondrial ROS production in WAT. Support: CAPES Protocol: 05198059/2019 (Aditivo)</p>



Title	Unveiling the role of IAPP dysfunction in diabetes pathophysiology
Authors	ÍLIA ALVES ^{1,A *} , ANDREIA GOMES ^{1*} , RITA ANDRADE ^{2*} , JOÃO F. RAPOSO ² , ROGÉRIO RIBEIRO ² , REGINA MENEZES ¹ & LUÍS MONTERIO RODRIGUES ¹
Affiliations	1 Universidade Lusófona CBIOS –Research Center for Biosciences & Health Technologies 2APDP – Associação Protectora dos Diabéticos de Portugal
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Diabetes mellitus (DM) is characterized by hyperglycemia resulting from defects in insulin secretion (IS), action, or both. Central to DM is insulin-producing β-cells dysfunction, exacerbated by the deposition of islet amyloid polypeptide (IAPP) fibrils within the pancreatic islets. IAPP (or amylin) is co-secreted with insulin by β-cells. Under physiological conditions, IAPP plays a role in regulating glucose levels and gastric emptying. Objective: In pathological states, IAPP processing can become dysregulated, leading to the formation of toxic fibrils that contribute to β-cell apoptosis and impair IS, creating a vicious cycle that accelerates diabetes progression. Methods: A cross-sectional study was conducted in March-June 2022 (APDP Ethics Committee approval code 103/2021). A total of 153 participants, including 53 with T1DM (35%), 49 with T2DM (32%), and 51 without diabetes (33%; Control group), were recruited. Sociodemographic data were collected through interviews. Blood samples were analyzed for HbA1c, glucose, insulin, C-peptide, IAPP, pro-IAPP, pro-insulin, lipid profile, and glucagon using standard laboratory procedures and enzyme-linked immunosorbent assay (ELISA). Statistical analyses were performed using ANOVA followed by post hoc multiple comparison tests. Correlations between variables were assessed using the Spearman correlation test. Results: T2DM and Control groups were predominantly women (57.1% and 58.8%, respectively, $p < 0.001$). The T2DM group was older on average than the T1DM and Control groups (58.5 ± 10.1 years, 45.0 ± 12.9 years, and 40.0 ± 11.9 years, respectively, $p < 0.001$). T2DM participants had a BMI indicative of obesity, whereas T1DM and Control participants were overweight (30.5 ± 5.95 kg/m², 25.5 ± 4.03 kg/m², and 25.1 ± 4.09 kg/m², respectively, $p < 0.001$). In T2DM, both men and women exhibited high cardiovascular risk (CVR), evidenced by waist circumference (WC) (107.0 ± 16.5 cm for men and 99.0 ± 11.2 cm for women, $p = 0.007$ and $p < 0.001$) and an Atherogenic Index of Plasma (AIP) of 0.450 ± 0.314, $p < 0.001$. T1DM participants showed a moderate AIP risk (0.121 ± 0.239, $p < 0.001$), with a notable WC trend in women (84.1 ± 10.8 cm, $p < 0.001$). T2DM participants were diagnosed over a decade ago in 51.0% ($n = 25$) of cases, while in 86.8% ($n = 46$) of T1DM participants disease duration surpasses 20 years ($p < 0.001$). HbA1c and FG levels were similar between T1DM and T2DM, exceeding recommendations and higher than Control ($p < 0.001$). T2DM participants had elevated levels of pro-insulin, insulin, C-peptide, pro-IAPP, and pro-insulin/insulin compared to T1DM and Control ($p < 0.05$ for all). HbA1c positively correlated with years since diagnosis (YSD) ($\rho = 0.738$, $p < 0.001$) and negatively with C-peptide ($\rho = -0.315$, $p < 0.001$). FG positively correlated with HbA1c ($\rho = 0.647$, $p < 0.001$) and pro-insulin/insulin ($\rho = 0.563$, $p < 0.001$), but negatively with C-peptide ($\rho = -0.631$, $p < 0.001$). AIP positively correlated with BMI ($\rho = 0.372$, $p < 0.001$), C-peptide ($\rho = 0.514$, $p < 0.001$), and pro-insulin ($\rho = 0.566$, $p < 0.001$). Pro-IAPP/IAPP positively correlated with YSD ($\rho = 0.264$, $p < 0.001$), FG ($\rho = 0.232$, $p < 0.001$), and pro-insulin/C-peptide ($\rho = 0.222$, $p < 0.01$), and negatively with C-peptide ($\rho = -0.207$, $p < 0.05$) and IAPP/insulin ($\rho = -0.511$, $p < 0.001$). Conclusion: Increased levels of pro-IAPP, IAPP/insulin, and pro-insulin/insulin ratios observed in this study indicate that IAPP dysregulation is associated with β-cell dysfunction, contributing to impaired glucose regulation, insulin resistance, and an increased CVR in individuals with DM. Support: FCT under DOI: 10.54499/UIDP/04567/2020 and DOI: 10.54499/UIDB/04567/2020. R.M. (DOI:10.54499/CEECINST/00002/2021/CP2788/CT0004) and A.G. are funded by FCT Scientific Employment Stimulus contracts. COFAC/ILIND Research Excellence Grant (FAZER+/ILIND/CBIOS/1/2023). Protocol: APDP Ethics Committee approval code 103/2021</p>



Title	Dietary Supplementation of Grape Pomace Flour Reduces Plasma Cholesterol Concentration and Modulates Oxidative Stress
Authors	LUÍS MONTEIRO RODRIGUES ^{1,A} , RAPHAELA CASSOL PICCOLIB, MARISA NICOLAIA, PAULA PEREIRAA,C,D, ROSELIA MARIA SPANEVELLOB, FRANCIELI MORO STEFANELLOB, MARIA LÍDIA PALMAA, REJANE GIACOMELLI TAVARESA,E,F*
Affiliations	1 Sociedade Portuguesa de Fisiologia a Center for Research in Biosciences & Health Technologies (CBIOS), Universidade Lusófona; bPPGBBio Federal University of Pelotas; cCenter for Natural Resources and Environment (CERENA), Instituto Superior Técnico da Universidade de Lisboa; dEPCV, Universidade Lusófona; ePPGNA Federal University of Pelotas; fPPGMCF Federal University of Pelotas
Session	4-Fisiologia Endócrina e Metabolismo
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Wine making industry generates a large amount of byproducts that can be utilized in functional foods, thereby mitigating environmental repercussions and collaborating in the control of metabolic diseases, such as dyslipidemia. This is characterized as a disorder in lipid metabolism, representing a significant risk for atherosclerotic cardiovascular disease (ASCVD). Within this context, grape pomace flour (GPF), obtained after grape processing, has been evaluated Objective: This study aimed to investigate the effects of administering GPF from 'Arinto' and 'Touriga Nacional' varieties on weight gain, feed and water consumption, as well as serum lipidic profile, and oxidative stress parameters in the liver of adult male Wistar rats. Methods: The serum and liver tissue used in the present study were obtained from adult male Wistar rats. Experimental dyslipidemia was induced by a single intraperitoneal administration of Tyloxapol (300mg/kg) on the 89th day of the experimental period. Rats were divided into five groups: Control (CT), Dyslipidemia (DYS, $DYS+Orlistat$ (50mg/kg) intragastrically ($DYS+ORL$), $DYS+10\%$'Arinto' GPF ($DYS+WGPF$) and $DYS+10\%$'Touriga Nacional' GPF ($DYS+RGPF$). On the 90th day, the animals were euthanized, and the samples were collected. Subsequently, serum analyses of triacylglycerol (TG), total cholesterol (TC), and high-density lipoprotein (HDL) was measured, and an aliquot of the hepatic homogenate was used to analyze the concentrations of reactive oxygen species (ROS), thiobarbituric acid reactive substances (TBARS), and catalase (CAT) enzyme activity. Results: Experimental dyslipidemia induces no significant differences in feed consumption, water intake, or total weight gain among the groups ($P>0.05$). Regarding the biochemical profile, Tyloxapol acute administration significantly increased TG levels ($P<0.01$), with para tendency of reduction in the $DYS+WGPF$ ($P>0.05$) and $DYS+RGPF$ ($P>0.05$) groups. Additionally, the $DYS+RGPF$ showed a significant increase in TC compared to the CT group ($P<0.01$), that reflected in a enhancement of HDL-cholesterol levels compared to the DYS and $DYS+ORL$ groups, suggesting a cardiovascular protection enhancement by the HDL profile ($P<0.05$, both). The redox status evaluation demonstrated that Tyloxapol exposure led to a significant enhancement of ROS levels ($P<0.001$). However, pre-treatments with Orlistat, WGPF, and RGPF were able to protect against the increase in ROS levels caused by the experimental induction protocol ($P<0.001$, all). Furthermore, the experimental induction of dyslipidemia significantly increased the levels of TBARS ($P<0.001$). However, pre-treatments with Orlistat, WGPF, and RGPF were able to protect against lipid peroxidation ($P<0.01$, $P<0.001$, and $P<0.001$, respectively). Finally, treatment with RGPF was able to increase the antioxidant enzymatic activity of CAT ($P<0.05$). Conclusion: These findings suggest that GPF consumption could act as a dyslipidemia-adjuvant therapy by positively modulating cholesterol levels and antioxidant profile. Support: This work was funded in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) – Finance Code 001, CNPq and FAPERGS. Protocol: All of the procedures were approved by the Institutional Ethics Committee on the Use of Animals of the Federal University of Pelotas (CEUA 033578/2022-14).</p>



Title	Long-Term Effects of COVID-19: A One-Year Follow-Up Study on Cytokines Levels and Hematological Parameters in Moderate and Severe Cases
Authors	REBECCA SALOMÃO, VICTORIA ASSIS, KRAIN MELO, LEANDRA SILVA, ISABELLA SILVA ALMEIDA, LEANDRO GOMES DE JESUS FERREIRA, ROCHELLE ROCHA COSTA, JOÃO LUIZ QUAGLIOTTI DURIGAN, RITA DE CASSIA MARQUETI DURIGAN
Affiliations	Faculdade de Ceilândia, Universidade de Brasília
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The severity of COVID-19 can vary among individuals, resulting in unpredictable outcomes and the development of a post-COVID-19 syndrome associated with poorer prognoses and increased mortality rates. Objective: This study examined cytokines levels and hematological parameters in recovered COVID-19 patients over one year to evaluate the long-term effects. Methods: This longitudinal observational study involved three groups: (a) moderate COVID-19 (n=22), (b) severe COVID-19 (n=18) and (c) control (n=30). The COVID-19 groups were assessed 4 times over the year, while the control group was evaluated once. Blood samples were collected for cytokines and blood cell count, C-reactive protein (CRP), red cell distribution width % (RDW), and neutrophil to lymphocyte ratio (NLR). Statistical analysis used SPSS 22.0 with significance at $p < 0.05$. GEE method was adopted, using “group” and “assessments” as factors. Results: The severe COVID-19 group exhibited higher levels of IL-6 and IL-8 compared to the other groups ($p < 0.001$). CRP demonstrated a group-assessment interaction ($p < 0.001$), with the severe group showing higher levels compared to the control group. An interaction between group and assessment was noted for absolute monocyte count ($p < 0.001$), with the severe group having higher values than the other groups. For white blood cell count and NLR, the severe group had higher levels ($p < 0.001$) than the other groups. A group-assessment interaction was found for red blood cell count ($p < 0.001$), where levels increased in the second and third assessments in both moderate and severe groups. The severe group showed higher levels of RDW in all assessments ($p < 0.001$). Conclusion: The findings suggest systemic inflammation and hemogram disturbances in post-COVID patients. Elevated levels of IL-6 and IL-8, as well as in NLR and RDW highlight disease severity and mortality risks. Monitoring inflammatory and hematological parameters emphasizing the need for targeted interventions to manage long-term complications in severe COVID-19 survivors. Support: FAPDF (Process: 00193-00000773/2021-72) Protocol: CEP/FCE-CAEE: 45043821.0.0000.</p>



Title	RELATIONSHIP BETWEEN PLASMA METALLOPROTEINASE PROFILES AND POST-INFECTION COMPLICATIONS IN MODERATE AND SEVERE COVID-19 CASES
Authors	REBECCA SALOMÃO DE CARVALHO, MAYARA ANANIAS SOUZA, VICTORIA LYSSA ASSIS DE MENDONÇA ¹ , LEANDRO GOMES DE JESUS FERREIRA, ISABELLA DA SILVA ALMEIDA, LEANDRA DA SILVA, ROCHELLE ROCHA COSTA, JOÃO LUIZ QUAGLIOTI DURIGAN, RITA DE CÁSSIA MARQUETI
Affiliations	1. Laboratory of Molecular Analysis, Faculty of Ceilândia, UnB, 2. Laboratory of Muscle and Tendon Plasticity, Faculty of Ceilândia, UnB, 3. Nursing Course, Faculty of Ceilândia, UnB, 4. Faculty of Physical Education, University of Brasília, UnB
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Post-COVID-19 syndrome involves persistent symptoms lasting over 12 weeks after acute SARS-CoV-2 infection, with no alternative diagnosis. The role of matrix metalloproteinases (MMPs) in inflammation following COVID-19, especially in those with moderate and severe disease one-year post-infection, remains unclear. Objective: To investigate the longitudinal profile of MMPs in individuals recovering from moderate and severe COVID-19, during the one-year post-infection. Methods: This is a longitudinal observational study including n=270, both sexes, aged 18 to 80 years. Groups: (1) control (n=30), (2) moderate COVID-19 (n=120), and (3) severe COVID-19 (n=120). Four assessments were conducted over one-year: (1) between the 21st and 30th days, (2) between 31 and 90 days, (3) between 91 and 180 days, (4) between 181 and 360 days. Blood samples were collected to perform MMPs analysis using the zymography technique. To verify the differences the Generalized Estimating Equations (GEE) method was adopted, using “group” and “assessments” as factors. Results: A group-assessment interaction was found for isoforms pro and active MMP9 (p<0.001). The severe group presented higher levels of MMP9 compared to all other groups. For pro MMP2, a main effect was observed between groups (p<0.001), with the severe group showing elevated levels compared to the control and moderate groups. An interaction between group and assessment was observed for active MMP2 (p<0.001), with the moderate group exhibiting decreased levels compared to the control and severe groups during assessments 1, 2, and 3. Conclusion: Based on these findings, MMPs appear to serve as potential predictors of chronic inflammatory complications following COVID-19 infection within the first year. Support: FAPDF (Process: 00193-00000773/2021-72). Protocol: 45043821.00000.8093.</p>

Title	Efeitos do Treinamento Isométrico de Handgrip associado ao Exercício Aeróbico na Função Endotelial de Idosas Hipertensas
Authors	LEONARDO AUGUSTO FARIA, TATIANE CRISTINA RODRIGUES, GIOVANA EDUARDA DIAS SANTOS, LENICE KAPPES BECKER
Affiliations	Educação Física, UFOP, Universidade Federal de Ouro Preto
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introdução: O endotélio desempenha um papel central na fisiopatologia da aterosclerose e a dilatação mediada por fluxo (DMF) é um método não invasivo bem estabelecido que avalia a função endotelial. A disfunção do endotélio pode ser um dos primeiros sinais detectáveis de aterosclerose e uma resposta prejudicada da DMF está relacionada a fatores de risco cardiovascular, sendo um preditor independente de eventos cardiovasculares. Objective: Objetivos: Investigar os efeitos cardiovasculares do treinamento de prensão manual isométrica (Handgrip) combinado com o exercício aeróbico em idosas hipertensas por meio da avaliação da Dilatação Mediada por Fluxo (DMF) na artéria braquial. Methods: Métodos: Indivíduos de 55 a 74 anos com hipertensão estágio 1 ou 2 foram divididos em dois grupos. Ambos os grupos realizaram o protocolo de exercícios aeróbicos e Handgrip nas diferentes fases do estudo, com crossover entre elas. O protocolo de prensão palmar consistiu em 4 contrações isométricas de 2 minutos, com prensão a 30% da contração isométrica voluntária máxima, 3 vezes/semana por 8 semanas. Foi realizado avaliação física, anamnese, aferição da pressão arterial (PA), avaliação da dilatação mediada por fluxo na artéria braquial durante e após treinamento. O Protocolo de DMF foi uma adaptação do protocolo Expert consensus and evidence based recommendations for the assessment of flow-mediated dilation in humans. Results: Resultados: Amostra homogênea, com adesão de 75% ao treinamento. Não houve diferenças significativas na força de prensão palmar e na composição corporal, nem nos parâmetros cardiovasculares entre os momentos de avaliação ($p > 0,05$). Observou-se um aumento significativo na dilatação mediada por fluxo no treinamento combinado quando comparado com o isolado ($p = 0,03$). Conclusion: Conclusão: Os resultados deste estudo indicaram uma amostra homogênea, com uma adesão satisfatória de 75% ao treinamento. Embora não tenham sido observadas diferenças estatisticamente significativas na força de prensão palmar, composição corporal e parâmetros cardiovasculares entre os momentos de avaliação ($p > 0,05$). A combinação de exercícios Handgrip e exercício aeróbico demonstrou melhorias na função endotelial, sugerindo benefícios para a saúde cardiovascular. Metanálises corroboram esses achados, destacando a redução significativa no risco de eventos cardiovasculares para cada incremento na dilatação média da artéria braquial. Contudo, é importante reconhecer a limitação do estudo devido ao tamanho amostral reduzido. Isso destaca a necessidade de dar continuidade à pesquisa para garantir que os resultados possam ser aplicados de forma mais ampla. Essa importância é ressaltada pela frequente utilização desse método na literatura científica, tornando essencial ampliar a amostra para uma compreensão mais abrangente da eficácia dessa intervenção ao longo do tempo e em diferentes contextos. Support: Proppi-UFOP, Fapemig. Protocol: 53200421.3.0000.5150</p>

Title	Redox profile of the cardiac ventricle of Wistar rats in adaptation to linear or polarized training
Authors	DOUGLAS SANTOS BATISTA, AMANDA ALVES DE ALMEIDA, JÚLIA DE OLIVEIRA BORGES, THIAGO MACÊDO LOPES CORREIA, MAIARA RAULINA DE JESUS DIAS, REGIANE RIBEIRO DIAS, RAFAEL PEREIRA DE PAULA, SAMUEL SANTOS BITTENCOURT PEREIRA, PEDRO LUCIANO MACEDO DE ANDRADE LOPES, AMÉLIA CRISTINA MENDES DE MAGALHÃES GUSMÃO
Affiliations	Programa de Pós graduação Multicêntrico em Ciências Fisiológicas, Universidade Federal da Bahia
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The beneficial effects of regular physical exercise are well established and studied in the literature, recognized for their non-pharmacological therapeutic effects in treating or preventing chronic diseases. Considering that different training intensities exert metabolic and cardiovascular adaptations, it is believed that other types of training can exert different effects after the same period and volume of physical training. However, despite the importance of the topic, no studies were found that evaluated differences between the effects of linear or polarized training in an animal model. Objective: To investigate the adaptive effects of linear or polarized training on the redox state and antioxidant capacity in the ventricle of male Wistar rats. Methods: Initially, 18 4-month-old Wistar rats, sedentary or who performed physical exercise on a treadmill, were used and distributed into 3 experimental groups: Sedentary Group (SED, n=6), Linear Training (LIN, n=6) and Polarized Training (POL, n=6). After four months of training/control, the groups were euthanized. The antioxidant capacity in the ventricle was measured through the activity of the enzymes catalase and glutathione peroxidase (Gpx), in addition to immunostaining for GPx and superoxide dismutase (Sod). Oxidative damage to proteins was measured through carbonyl proteins, and lipid peroxidation was estimated by testing thiobarbituric acid reactive substances (TBARS). This study was approved by the CEUA of IMS/CAT-UFBA (Protocol nº 088/2020). All variables of interest in this study were subjected to the Shapiro-Wilk normality test. Comparisons between the 3 groups were performed by one-way ANOVA. Depending on the normality tests, the Bonferroni adjustment and the appropriate post hoc test were applied to the procedures. Differences were considered significant when $p\text{-value} < 0.05$. Results: Both trainings determined a reduction in the levels of TBARS (SED: 7.22 ± 1.37; LIN: 2.45 ± 0.99; POL: 2.03 ± 0.81, $P < 0.05$) and carbonyl proteins (SED: 4.95 ± 0.42; LIN: 3.00 ± 0.78; POL: 1.76 ± 0.86, $P < 0.05$) and increased Gpx activity (SED: 0.37 ± 0.04; LIN: 0.49 ± 0.05; POL: 0.60 ± 0.04, $P < 0.05$) when compared to the SED group. No differences were observed in relation to the activity of the catalase enzyme. The POL group showed a lower concentration of carbonyl proteins and higher GPx activity than LIN group. LIN and POL training also resulted in increased immunostaining for GPx (SED: 0.29 ± 0.046; LIN: 0.51 ± 0.10; POL: 0.52 ± 0.018, $p < 0.0001$) and SOD (SED: 0.29 ± 0.046; LIN: 0.51 ± 0.10; POL: 0.52 ± 0.018, $p < 0.0001$) in relation to the SED group. Conclusion: The results of the present study point to an improvement in the redox balance in the cardiac ventricle of animals subjected to linear or polarized training. The differences observed between training modalities, with a relative superiority of polarized training when it comes to Gpx, were insufficient to determine the advantage of either protocol conclusively. Support: CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior) Protocol: CEUA of IMS/CAT-UFBA (Protocol</p>

Title	Cardiac mitofusins expression is not modulated by dynamic resistance training of rats fed high-calorie diet
Authors	ANDRÉ HIDEAKI QUARESMA UEDA, MARIANA MENDES SILVA REIS, MURILLO SILVA CARDOSO, ANA CAROLINE RIPPI MORENO, KAREN CRISTINA REGO GREGORIO, CAROLINE PANCERA LAURINDO, MARIA TEREZA NUNES, MARCOS FERNANDO SOUZA TEIXEIRA, PATRICIA MONTEIRO SERAPHIM
Affiliations	Fisiologia e Biofísica, Universidade de São Paulo, USP, Química e Bioquímica, Universidade Estadual Paulista, UNESP, Fisioterapia, Universidade Estadual Paulista, UNESP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Obesity is the consequence of the excessive accumulation of fat mass that can impact cardiac fitness, as it is associated with alterations on mitochondrial function in various organs, such as heart. Mitofusins are responsible for mitochondrial fusion and, in this way, play a vital role in heart function, since the heart muscle requires a large amount of energy to contract and pump blood. Objective: We aimed to investigate whether the high-calorie diet associated to a dynamic resistive training (DRT) can modulate mitofusins MFN1 and MFN2 expression in the heart of male rats. Methods: All the interventions were previously approved by the local CEUAs, proc. No. 01/2017. Wistar rats were divided into 4 groups: Sedentary Control (SC), Sedentary Obese (SO), Exercised Control (EC) and Exercised Obese (EO), (n=6 animals/group). CS and CE ingested standard chow and water, SO and EO ingested standard chow and water plus cookies, chocolate, mortadella, and soda during 12 weeks. EC and EO performed DRT by climbing a ladder with an incremental attached 30g-load to the tail of the animal, 4 rep/day, 3x/week, during 12 weeks. Statistical analysis were performed using two-way ANOVA, with Tukey's post-test, considering p<0.05. Results: Final body weight was increased in the SO (537.7±15.7, p<0.0001) compared to the other groups (SC: 426.0±14.1; EC: 396.3±13.9; EO: 447.6±15.1). Fat mass was heavier in the SO group (15.0±1.3, p<0.0001 vs. SC and EC; p<0.05 vs. EO) than in the other groups (SC: 5.50±0.4; EC: 5.61±0.8; EO: 9.67±0.7), while DRT reduced (p<0.001) the fat mass in the EO compared to SC and EC. The O group showed a higher feed efficiency coefficient (~68%, p<0.0001) compared to other groups. According to the serum analysis, there was no significant change in cholesterolemia among the groups. However, the glycemia of the SO group (219± 9.922, p<0.0001) was 85% and ~40%-higher than the glycemia of EC (119.6± 17.19), and the glycemia of SC (162.3± 13.17) and EO (153.1± 13.09) groups. Triglyceridemia of the SO group (239.1±75.93, p<0.0001) was extremely elevated compared to the other groups (SC: 57.38±17.20; EC: 60.05±7.95; EO: 77.93± 2.96). Cardiac MFN1 and MFN2 protein expression was unchanged among the groups (MFN1 – SC: 0.73±0.12; SO: 1.13±0.35; EC:1.16±0.32; EO:1.03±0.21; MFN2: SC:1.0±0.33; SO:1.25±0.35; EC: 1.35±0.4; EO: 1.40±0.45). Conclusion: The high-calorie diet caused obesity, accompanied by a heavier fat mass, and alterations in the glycemia and tryglyceridemia. DRT was efficient to reduce fat mass and body weight, and serum parameters. However, neither the high-calorie diet nor DRT seem to participate in the modulation of the expression of MFN1 and MFN2 mitofusins in the heart. Support: NENHUM Protocol: Proc. No. 01/2017, CEUAs, FCT/</p>



Title	Evaluation of the Performance of a Hypotensive Peptide Extracted from Scorpion Venom in Endurance Physical Activity in Animals
Authors	PEDRO HENRIQUE MAYRINK SOARES, GUSTAVO DE OLIVEIRA ZANETTI, NICIA SOARES, GABRIELA C MAGALHÃES, DAWIT ALBERIO P GONÇALVES, THIAGO VERANO-BRAGA
Affiliations	Fisiologia, UFMG
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The proven benefits of physical activity include lowering blood pressure, glycemic control, weight management, and treatment of anxiety and depression. Recent studies in hypertensive rats have shown that regular aerobic training can alleviate chronic hypertension. However, while light to moderate aerobic exercise offers well-established benefits, endurance physical activity leads to the generation of free radicals and reactive oxygen species, causing an imbalance in the REDOX system. This event is known as `overtraining syndrome,` which is detrimental to athletes' health and performance. The hypothesis of this study is that KPP, a vasoactive peptide derived from a scorpion peptide, can eventually be used to improve performance in endurance physical activity due to its antioxidant and vasodilatory effects. Objective: The aim of this study is to evaluate the outcomes of the oral treatment with KPP in an experimental model of endurance physical activity. Methods: C57BL/6 male mice (n=12) were used in the study and were divided into 3 groups: (A) KPP, (B) Ang-(1-7) and (C) Saline, representing each treatment. On day 1, the animals underwent surgery for the installation of temperature sensors and a SHAM procedure done with random animal selection. On day 8, mice were acclimatized to the 2 and 4 paw grip strength test and began treadmill acclimatization, which occurred from day 8 to day 12 as follows: Day 1: 3 minutes of rest, 5m/min (5 minutes), 6m/min (3 minutes); Day 2: 3 minutes of rest, 6m/min (5 minutes), 8m/min (3 minutes); Days 3-4: 3 minutes of rest, 5m/min (5 minutes), 8m/min (5 minutes); Day 5: 3 minutes of rest, incremental load test (test ending 10 seconds before fatigue zone). On day 12, the strength test was performed. On day 15, the animals began the incremental load tests (starting at 10m/min and increasing 3m/min every 3 minutes, ending 5 seconds on the shock grid) before starting treatment in room temperature (24°C) and warm (34°C) environment. On day 22, the animals began oral treatment with KPP (1mg/kg, 3h before the test), Ang-(1-7) (30µg/kg, 2h before the test), or saline (3h before the test). After 8 days of treatment, the animals were subjected again to the tests. Results: There was no statistical difference in the maximum 2-paw grip strength test represented by the force in grams (A= 128.6 ± 8.2; B= 117.0 ± 9.4; C = 136.1 ± 13.2) nor in the maximum 4-paw grip strength test (A= 356.6 ± 5.3; B= 355.5 ± 20.8; C= 335.5 ± 5.2). In the incremental treadmill tests, we also did not obtain statistical significance in the parameter of maximum speed and duration of the tests, at both temperatures: speed in room temperature: (A= 30.3 ± 1.35 ; B= 28.9 ± 1.78 ; C= 27.7 ± 0.8), speed in warm environment: (A= 31.1 ± 1.3 ; B= 30.4 ± 1.0 ; C=26.5 ± 0.5), duration in room temperature (A= 21.6 ± 1.4 ; B= 20.1 ± 2.0 ; C= 19.0 ± 0.8), duration in warm environment (A= 22.2 ± 1.6 ; B= 21.6 ± 1.1 ; C= 17.7 ± 0.8). Conclusion: More experiments are needed to test the beneficial aspects of chronic treatment with KPP and Ang-(1-7) in endurance physical activity. Support: INCT-Nanobiofar, CNPq, Fapemig and Capes Protocol: CEUA-UFMG; protocolo 241/2023</p>



Title	Efeitos da suplementação oral de HPβCD-angiotensina-(1-7) em atletas recreativos de mountain bike: um estudo cruzado
Authors	DANIEL MALTA OLIVEIRA, SAMARA SILVA DE MOURA, FRANCISCO DE ASSIS DIAS MARTINS-JÚNIOR, EMERSON CRUZ DE OLIVEIRA, DANIEL BARBOSA COELHO, DAISY MOTTA-SANTOS, ROBSON AUGUSTO SOUZA DOS SANTOS, LENICE KAPPES BECKER
Affiliations	DEEFD, UFOP, DEFF, UFMG
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A suplementação com Angiotensina-(1-7) [Ang-(1-7)] tem recebido considerável atenção devido aos seus possíveis efeitos ergogênicos no desempenho físico. Os efeitos de uma única dose de Ang-(1-7) no desempenho de atletas de mountain bike (MTB) durante testes de carga progressiva realizados até o início da fadiga voluntária já foram demonstrados anteriormente. Objective: Foi verificar os efeitos de Ang-(1-7) em protocolo de exercício aeróbico (prova de tempo) a fim de avaliar a temperatura muscular (termografia) e níveis de óxido nítrico. Methods: Foram selecionados vinte e um atletas de ciclismo do sexo masculino, 18 anos, que praticavam MTB há pelo menos 3 anos, com um volume de treino semanal de pelo menos 5 dias por semana e participação em provas regionais/nacionais nos últimos 6 meses. Os participantes receberam cápsulas contendo uma formulação oral de HPβCD-Ang-(1-7) (0,8 mg) e HPβCD-placebo (apenas HPβCD) e realizaram uma prova de ciclismo de 20 km contra o relógio (TT20km). Um período de washout de 7 dias foi aplicado entre placebo e HPβCD-Ang-(1-7) (crossover). Os dados foram coletados antes e depois da prova de ciclismo para avaliar a radiação de calor muscular por meio da termografia, e níveis de óxido nítrico no plasma e na urina. Results: A suplementação com HPβCD-Ang-(1-7) aumentou os níveis de óxido nítrico urinário no grupo submetido ao TT20km em repouso (HPβCD-placebo $9,25 \pm 0,97$ nmol; HPβCD-Ang-(1-7) $12,24 \pm 3,60$ nmol; $p = 0,0402$) e não aumentou após o exercício (HPβCD-placebo $14,5 \pm 5,54$ nmol [$p = 0,039$]; HPβCD-Ang-(1-7) $18,1 \pm 5,96$ nmol [$p = 0,4961$]). Além disso, não foram observadas diferenças entre níveis de nitrito plasmático em repouso ou após o exercício. Em relação à termografia, não foram observadas diferenças entre os grupos em repouso (HPβCD-placebo $26,5 \pm 1,2$ °C; HPβCD-Ang-(1-7) $27,1 \pm 2,80$ °C) ou após o exercício (HPβCD-placebo $27,0 \pm 1,40$ °C; HPβCD-Ang-(1-7) $26,7 \pm 1,70$ °C). Conclusion: De acordo com este estudo, observou-se que a suplementação com HPβCD-Ang-(1-7) aumentou os níveis de óxido nítrico na urina em repouso, mas não alterou os níveis de óxido nítrico no plasma e nem a radiação de calor muscular em atletas de ciclismo do sexo masculino. Support: Pró-Reitoria de Pesquisa, Pós-Graduação e Inovação Protocol: 14912519.4.0000.5150</p>

Title	Effects of Ovariectomy and Resistance Training on the mitochondrial function and energy metabolism of left ventricular cardiomyocytes
Authors	REGIANE ALVES PINTO, CHRISTOPHER BARSAQUE GARCIA, DIEGO FELIPE ARMININI CAVALINI, JOÃO PEDRO MAIA DE OLIVEIRA DA SILVA, ANDERSON FERREIRA DA CUNHA, ROGER FRIGERIO CASTILHO, GILBERTO EIJI SHIGUEMOTO
Affiliations	Departamento de Ciências Fisiológicas, UFSCAR Universidade Federal de São Carlos, Departamento de Genética e Evolução, UFSCAR Universidade Federal de São Carlos, Departamento de Bioenergética e Metabolismo Celular, FCM/UNICAMP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The menopause causes hormonal changes that affect various physiological functions and fertility. Estradiol, an important female hormone, is crucial for cardiovascular protection, cholesterol regulation and brain function. However, the decrease in estrogens during menopause increases the risk of cardiovascular diseases, such as heart failure, due to inflammation and fibrosis in the heart, leading to left ventricular (LV) dysfunction. Studies indicate that mitochondrial dysfunction can contribute to changes in the metabolism of cardiomyocytes, which normally oxidize fatty acids, but in pathological conditions become predominantly glycolytic. Resistance training (RT) has emerged as a promising therapeutic strategy to prevent these mitochondrial metabolic changes and the consequent dysfunction. Objective: Investigate the effects of ovariectomy (OVX) and reduced estrogen levels on the function and mitochondrial energy metabolism of LV cardiomyocytes. In addition, to explore the impact of RT as a preventive measure of these adverse effects Methods: 20 young adult Wistar rats were divided into four groups (INT-SED, INT-RT, OVX-SED, and OVX-RT). OVX was performed when the rats reached 13 weeks of age, and RT began one week after surgery, with 3 sessions per week over 12 consecutive weeks. Euthanasia and tissue collection took place 48 hours after the 20th RT session. Analyses conducted on LV biopsies: 1- Gene expression (RT-qPCR) of the Electron Transport Chain complexes (ETC: CI, CII, CIII, CIV and ATPS) and CS; 2- Mitochondrial respiration using High Resolution Respirometry (Oroboros®, Innsbruck, Austria). Results: Body mass (BM) of the animals: the OVX-SED group had a significantly higher BM (357.4±18.1 g) than the other groups. Maximum workload: both trained groups had a significant increase in MW (771.88±2.1 g) at the end of the RT compared to the initial week. Respirometry: a significant decrease in oxygen consumption in the OVX-SED group in S3 and S3Suc (53.0 and 63.3 pmol/sec*mg) compared to the other groups; RT increased oxygen consumption in S3 and S3Suc (OVX-RT = 104.1 and 113.09; INT-RT = 97.72 and 110.36 pmol/sec*mg). ETC gene expression: OVX produced a significant reduction in the gene expression of all ETC complexes in the sedentary group (OVX-SED, CI = 0.74, CII = 0.77, CIII = 0.94, CIV = 0.76, ATPS = 0.82 AU) when compared to the sedentary control group (INT-SED, CI = 1.08, CII = 1.12, CIII = 1.29, CIV = 1.34, ATPS = 1.16 AU); RT significantly increased gene expression in all ETC complexes of both trained groups (INT-RT, CI = 1.82, CII = 1.41, CIII = 1.74, CIV = 1.75, ATPS = 2.74 AU; OVX-RT, CI = 1.21, CII = 1.51, CIII = 1.37, CIV = 2.35, ATPS = 1.48 AU) compared to both sedentary groups. Conclusion: OVX produced a significant decrease in the oxygen consumption of LV cardiomyocytes in the coupled respiratory states (S3 and S3Suc), as well as in the gene expression of the ETC complexes, demonstrating metabolic deficiency from the stimulation of complexes I and II together. Resistance training was effective in increasing oxygen consumption in the coupled states (S3 and S3Suc), as well as increasing the gene expression of ETC complexes in both trained groups, determining an improvement in mitochondrial metabolic efficiency. Support: CAPES Protocol: 4381011222</p>

Title	ACUTE EFFECT OF RESISTANCE TRAINING ON IRISIN, PGC-1A EXPRESSION AND CARDIOPROTECTION ON WISTAR RATS.
Authors	ANTONIA FREZ, LUCAS MONTEIRO DE CARVALHO, AINÁ EIRAS DOMINGOS, ROBERTO VICTOR FIGUEIREDO DE OLIVEIRA GONÇALVES, EMERSON LOPES OLIVARES, ANA KÉSSIA DO NASCIMENTO GOMES, ANDERSON LUIZ BEZERRA DA SILVEIRA
Affiliations	Departamento de Educação Física e Desportos (DEFD), Universidade Federal Rural do Rio de Janeiro, ., Universidade Federal do Rio de Janeiro, Departamento de Ciências Fisiológicas (DCFis), Universidade Federal Rural do Rio de Janeiro
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Irisin is a 112 amino acids protein with effects ranging from improved energy metabolism to neuroprotection. Despite its numerous benefits, few studies have investigated the effect of a single session of resistance training on irisin secretion and its influence on cardioprotection. Objective: To investigate the acute effect of resistance training on cardioprotection and on irisin and PGC-1α levels in the skeletal and cardiac muscle of wistar rats. Methods: The resistance training followed the protocol of Hornberger Jr. and Farrar (2004). Eighteen male Wistar rats were used and then divided into a resistance training group (TR n=9) and a control group (n=9). The heart was collected and subjected to an ischemia and reperfusion protocol to analyze cardiac function. Muscle and heart tissues were used to analyze the expression of irisin and PGC-1α by RT-PCR. The Shapiro-Wilk test and Two way ANOVA with Tukey's post hoc verification were used. In addition, effect size was calculated using the Cohen's d method, where values were defined as: small (<0.2), medium (<0.5) and large (>0.8). Results: With regard to cardiac function data, when comparing the groups, there was no significant difference in left ventricular developed pressure (LVDP) during reperfusion (p>0.05) or in the final minute (20.5 \pm 6.5 vs. 25.7 \pm 6.7), and the effect size was small: 0.27. The results were repeated for left ventricular end-diastolic pressure (LVEDP) throughout reperfusion, as well as in the final minute (100.8 \pm 6.05 vs. 86.5 \pm 6.3). However, the effect size was 0.81, symbolizing a relevant clinical effect. For the speed of contraction (+dP/dt) and relaxation (-dP/dt), there was no significant difference in any of the comparisons (669.45 \pm 185.33 vs. 735.04 \pm 183.55)(100.80 \pm 6.05 vs. 86.58 \pm 6.35), with a small effect size of 0.12 for maximum +dP/dt and 0.11 for minimum -dP/dt. There was also no significant difference in the infarct area (24.10 \pm 3.74 vs. 22.05 \pm 3.16) and the effect size was also small, 0.20. In addition, there were no significant changes in FNDC5 mRNA concentrations in skeletal muscle tissue (0.21 \pm 0.17 vs. 0.15 \pm 0.19), with an effect size of 0.29, as well as in cardiac tissue (1.13 \pm 0.52 vs. 1.86 \pm 1.00), the effect size was 0.69. There was a significant decrease in PGC-1α concentrations in skeletal muscle in the trained group (0.08 \pm 0.03 vs. 0.034 \pm 0.02), with a large effect size of 2.86. In contrast, there was no significant difference in cardiac tissue (1.00 \pm 0.77 vs. 1.26 \pm 0.73), with an effect size of 0.35. Conclusion: One session of resistance training does not induce cardioprotection, but it does seem to initiate the mechanism for this protection. In addition, a training session did not increase irisin expression in skeletal and cardiac muscle, but there was a trend towards an increase in skeletal muscle tissue. High-intensity training reduced the expression of PGC-1α in skeletal muscle and variations in its expression could lead to physiological and metabolic consequences. Support: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brasil (CAPES), Finance Code 001. Protocol: 15/2022</p>

Title	High-intensity interval training alleviates cisplatin hepatotoxicity by regulating the hepatic polarization of M1 and M2 macrophages in female rats.
Authors	LARA FABIANA LUZ MALHEIRO, CAROLINE ASSUNÇÃO OLIVEIRA, ERIKA AZENATHE BARROS MÉRCEDES, FERNANDA SANTOS PORTELA, LAÍS MAFRA DE BENEDICTIS, JÚLIA MAFRA DE BENEDICTIS, AMÉLIA CRISTINA MENDES DE MAGALHÃES, TELMA DE JESUS SOARES, PATRÍCIA DA SILVA OLIVEIRA, FABRÍCIO FREIRE DE MELO, LILIANY SOUZA DE BRITO AMARAL
Affiliations	Universidade Federal da Bahia Instituto Multidisciplinar em Saúde, UFBA/CAT
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cisplatin (CP) is a highly effective antineoplastic drug, but its lack of selectivity causes several cytotoxic effects, including hepatotoxicity. The imbalance of inflammatory cytokines and excessive macrophage infiltration contribute to CP-induced liver injury. Exercise training can regulate the inflammatory response by modulating cytokines and the polarization of macrophages from their pro-inflammatory (M1) to anti-inflammatory (M2) phenotype, thus attenuating hepatotoxicity. Objective: The objective was to compare the effects of preconditioning with high-intensity interval training (HIIT) and low-intensity continuous training (LIT) on the balance of inflammatory cytokines and macrophage polarization of the M1 and M2 phenotypes in the liver from rats with CP-induced hepatotoxicity. Methods: To this purpose, 28 Wistar female rats, weighing 190–220g at 10 weeks of age, were divided into four groups (n=7): control and sedentary (C+S), treated with CP and sedentary (CP+S), treated with CP and LIT (CP+LIT), and treated with CP and HIIT (CP+HIIT). Training protocols consisted of running on a motorized treadmill, 5 days a week, for 8 weeks before CP treatment. At the end of the 8 weeks of training, the rats received a single injection of CP (5 mg/kg i.p.), and 7 days after the injection, they were sacrificed. Liver samples were collected for analysis of M1 (iNOS) and M2 (arginase 2) gene expression (RT-qPCR), ED-1 immunostaining (a nonspecific marker of macrophages), and TNF-α and IL-10 concentrations (ELISA). Data were expressed as mean \pm mean, standard deviation, and statistical significance was determined at $p < 0.05$. The study was approved by CEUA under protocol no. 056.2018. Results: The results showed an increase in the immunostaining of positive ED-1 cells in the CP+S group when compared to C+S (34.0\pm8.1 vs. 23.3\pm7.6, respectively) ($p < 0.05$), with HIIT being the training protocol with a more pronounced reduction (27.9\pm5.7) compared to CP+LIT (30.4\pm8.1) ($p < 0.05$). CP treatment also increased gene expression in both M1 macrophages (11.4\pm2.5) and M2 macrophages (8.6\pm2.1) compared to C+S (1.0\pm0.4; 1.0\pm0.7, respectively) ($p < 0.05$), but HIIT was only capable of reducing M1 macrophages in relation to LIT (6.1\pm1.1 vs. 11.1\pm1.8, respectively) and increasing M2 macrophages (12.7\pm1.5 vs. 9.4\pm1.0, respectively). Furthermore, the M1/M2 ratio increased in the CP+S group when compared to C+S (1.6\pm0.5 vs. 1.0\pm0.4, respectively), while HIIT promoted a more prominent reduction in relation to CP+LIT (0.5\pm0.1 vs. 1.2\pm0.2, respectively). Our results demonstrate that the groups treated with CP showed increased of TNF-α and IL-10 protein expressions (56.6\pm11.3; 42.8\pm6.0, respectively) compared to C+S (9.8\pm3.7; 14.7\pm4.8, respectively). However, HIIT reduced the TNF-α expression when compared to CP+LIT (29.3\pm5.3 vs. 53.4\pm5.6), while it promoted a greater increase in IL-10 expression than LIT (71.1\pm9.5 versus 42.6\pm6.6). The TNF-α/IL-10 ratio increased in the group treated with CP in relation to the control (1.4\pm0.4 vs. 0.7\pm0.2), and HIIT again proved to be more effective in reducing this effect in relation to the other training protocol (0.4\pm0.1 vs. 1.3\pm0.3). Conclusion: The present study suggests that physical preconditioning with HIIT was more effective than LIT in modulating hepatic inflammation via greater IL-10 production and predominance of M2 macrophage polarization in rats with CP-induced hepatotoxicity. Support: CNPq e Fapesb Protocol: 056.2018.</p>

Title	O treinamento resistido melhora o perfil mitocondrial em ratos com ou sem obesidade
Authors	PRISCILA ARISA SASAKI, MURILLO SILVA CARDOSO, ANA CAROLINE RIPPI MORENO, LARISSA AYUMI MASUYAMA, KAREN CRISTINA REGO GREGORIO, CAROLINE PANCERA LAURINDO, MARIA TEREZA NUNES, PATRÍCIA MONTEIRO SERAPHIM
Affiliations	Fisioterapia, FCT/UNESP, Fisiologia e Biofísica, USP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O consumo de dieta hipercalórica é um dos principais fatores para o desenvolvimento da obesidade. A obesidade é uma doença metabólica que está ligada ao comprometimento da dinâmica e função mitocondrial. O treinamento físico é uma das abordagens mais antigas, econômicas e promissoras para tratar essa condição. Objective: Investigar o impacto do treinamento de resistência (TR) na expressão de proteínas da atividade mitocondrial em fibra muscular glicolítica-oxidativa rápida (OR) de ratos com alimentação de dieta hipercalórica (DH). Methods: Ratos machos Wistar, com 45 dias, pesando 200g, foram divididos em 6 animais por grupo: Controle Sedentário (C), Treinado (T), Obeso sedentário (O) e Obeso treinado (OT). Ratos OT e O foram alimentados com dieta hipercalórica (chocolate, biscoitos, salsicha, refrigerante e água), enquanto ratos C e T alimentados com ração padrão e água durante 12 semanas. O TR consistiu em treino de escalada com carga fixada ao corpo, com aumento de 50% para 100% durante 12 semanas. O músculo gastrocnêmio foi removido sob anestesia para análise de expressão gênica e proteica por RT-qPCR (genes NRF1, MFN2, TFAM, Fis1) e Western blotting (NRF2, MFN1, MFN2, OXPHOS complexo CI, C5 e proteínas TFAM). Foi realizada punção intracardíaca para coleta de sangue para análise bioquímica. Foi utilizado o teste ANOVA TWO-WAY, considerando $p < 0,05$ como nível de significância. Todos os procedimentos envolvendo animais foram previamente aprovados pelos CEUAs locais nº 01/2017. Results: O grupo O apresentou maior massa corpórea do que os grupos C e T ($P < 0,01$). A massa gorda aumentou 3x ($P < 0,01$) no grupo O ($14,99 \pm 1,771g$) em comparação com os grupos C ($5 \pm 0,56g$) e T ($5,9 \pm 0,91g$). O peso muscular foi semelhante entre os grupos. A glicemia foi maior no grupo O ($219 \pm 9,9$ mg/dL, $P < 0,05$) em comparação com o grupo C ($162,3 \pm 13,17$ mg/dL); os triglicerídeos estavam elevados no grupo O ($239,1 \pm 7,53$ mg/dL, $P < 0,05$) em comparação com os grupos C ($57,38 \pm 17,2$ mg/dL) e T ($60,05 \pm 7,95$ mg/dL). O TR promoveu aumento de 3x mais nos níveis de expressão dos genes NRF1, MFN2 e TFAM nos grupos T e OT em comparação com o grupo O ($P < 0,05$), e promoveu diminuição (3x, $P < 0,05$) na expressão do gene Fis1 em T e OT em comparação com o grupo O. Os níveis de proteína NRF2 foram reduzidos em OT em comparação com os grupos T e O ($P < 0,01$). Nenhuma alteração foi observada nos níveis de proteína TFAM, MFN1 e MFN2 entre os grupos. Para a expressão da proteína dos complexos OXPHOS (CI-CV), apenas no grupo T houve aumento da expressão CII em comparação com C e O ($P < 0,05$). Conclusion: A DH provocou o desenvolvimento da obesidade, visto pelo aumento da massa gorda e do peso corpóreo. O TR foi capaz de diminuir o progresso de instalação da obesidade, evitando o ganho exagerado da massa gorda mesmo nos animais DH. O TR possibilitou a prevenção de alterações séricas, como aumento da glicemia e da trigliceridemia. A DH não influenciou na expressão de proteína mitocondrial em fibra OR. O TR aumentou a transcrição de genes relacionadas à biogênese mitocondrial, sem alterar o conteúdo de proteínas, propondo um regulação pós-transcricional na fibra muscular OR. O complexo respiratório CII aumentou com o TR, sugerindo maior capacidade respiratória em treinados, com ou sem obesidade. Portanto, concluímos que a DH promoveu a obesidade, mas não impactou nas proteínas mitocondriais na fibra muscular OR, e o TR evitou o prejuízo causado pela DH, com melhora do perfil mitocondrial. Support: Proc PIBIC 114092/2022-2; CAPES 001 Protocol: CEUA nº 01/2017</p>

Title	EFFECTS OF THERAPEUTIC OR LIFELONG PHYSICAL TRAINING ON INFLAMMATORY MARKERS AND REDOX BALANCE IN MUSCLE IN AN ANIMAL MODEL OF AGING AND OBESITY
Authors	SAMUEL SANTOS BITTENCOURT PEREIRA, THIAGO MACÊDO LOPES CORREIA, AMANDA ALVES DE ALMEIDA, MAIARA RAULINA DE JESUS DIAS, JÚLIA DE OLIVEIRA BORGES, REGIANE RIBEIRO DIAS, DOUGLAS SANTOS BATISTA, RAILDO DA SILVA COQUEIRO, RAFAEL PEREIRA, TELMA DE JESUS SOARES, AMÉLIA CRISTINA MENDES DE MAGALHÃES GUSMÃO
Affiliations	Programa de Pós Graduação Multicêntrico em Ciências Fisiológicas, UFBA, UNIVERSIDADE FEDERAL DA BAHIA
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The association between aging and obesity is closely linked to the establishment of sarcopenia, mainly by promoting changes in body composition, inflammatory profile, and antioxidant capacity. On the other hand, physical exercise is an important strategy against the muscle outcomes resulting from this association, being an alternative for the prevention and treatment of obesity, as well as for mitigating the effects of aging on health. Objective: To evaluate the effects of therapeutic or lifelong training on changes in body composition, inflammatory cytokines, and redox balance in the gastrocnemius muscle of Wistar rats at the early stages of aging in a model of diet-induced obesity. Methods: 32 male Wistar rats (300-350g, initial age = 4 months, final age = 14 months) were allocated into four aged groups (n=8/group): sedentary (ASed), sedentary + high-fat diet (HFD) (ASed+HFD), therapeutically trained + HFD (ATT+HFD), which started training at 12 months of age, and lifelong trained + HFD (ALT+HFD), which began training at four months of age. The gastrocnemius muscle was weighed and stored for further analysis. The sum of visceral fat deposits (EAT, RPAT, and MAT) was used to determine visceral adipose tissue (VAT) weight. Total abdominal adipose tissue (TAAT) was determined by summing VAT and abdominal subcutaneous adipose tissue. The gene expression of TNF-α, IL-6, and IL-10 cytokines was evaluated using qPCR. The expression of antioxidant capacity markers, including Nrf2, SOD-1, Catalase, and GPx-1, was also quantified using this method. The CEUA of IMS-UFBA approved the study (Protocol: 079/2020). The Student's t-test was used to compare the ASed and ASed+HFD groups. Comparisons between the ASed+HFD and trained groups were performed using One-Way ANOVA. Differences were considered significant when $p < 0.05$. Results: In aged animals fed with HFD, both ALT and ATT training showed reduced gene expression of TNF-α (ALT: 1.7 ± 0.2; ATT: 0.9 ± 0.1; ASed: 4.8 ± 0.3; $p < 0.0001$) and IL-6 (ALT: 0.9 ± 0.02; ATT: 0.7 ± 0.2; ASed: 4.8 ± 0.2; $p < 0.0001$), and increased gene expression of IL-10 (ALT: 4.5 ± 0.3; ATT: 3.4 ± 0.2; ASed: 0.3 ± 0.02; $p < 0.0001$). Regarding antioxidant capacity markers, in aged animals fed with HFD, both trainings increased the gene expression of SOD-1 (ALT: 3.2 ± 0.2; ATT: 3.0 ± 0.1; ASed: 0.6 ± 0.06; $p < 0.0001$), Catalase (ALT: 3.3 ± 0.2; ATT: 3.4 ± 0.1; ASed: 0.5 ± 0.06; $p < 0.0001$), GPx-1 (ALT: 4.1 ± 0.2; ATT: 2.9 ± 0.1; ASed: 0.6 ± 0.06; $p < 0.0001$) and Nrf2 (ALT: 3.1 ± 0.2; ATT: 2.9 ± 0.2; ASed: 0.9 ± 0.1; $p < 0.0001$). Additionally, the lifelong training group was more significant than therapeutic training in increasing the gene expression of GPx-1 (ALT: 4.1 ± 0.2 vs. ATT: 2.9 ± 0.1, $p < 0.05$) and IL-10 (ALT: 4.5 ± 0.3 vs. ATT: 3.4 ± 0.2, $p < 0.05$). Conclusion: Both training regimes protected the gastrocnemius muscle from deleterious changes caused by the high-fat diet in aged animals. The training promoted reduced gene expression of tissue inflammatory markers and increased expression of anti-inflammatory cytokine and antioxidant capacity markers. Moreover, lifelong training was more effective in improving the gene expression of IL-10 and the enzyme GPx-1. Support: CNPq Protocol: Protocol: 079/2020</p>

Title	Effects of consuming invertebrate flour on the nutritional and body composition of rats undergoing strength training
Authors	ADILSON DE BARROS MARTINS, EMERSON CRUZ DE OLIVEIRA, WANDERSON GERALDO DE LIMA, DANIEL BARBOSA COELHO, LEONARDO AUGUSTO GONÇALVES FARIA, HELEN SEIDEL, PEDRO HENRIQUE CARLOS GONÇALVES, DOUGLAS FELIX COELHO, LARISSA PEDROSA TAVARES FRANÇA, RAFAEL DA SILVA ANDRADE, LENICE KAPPES BECKER
Affiliations	DEEFD, UFOP, DECBI, UFOP, DEMSC, UFOP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: When searching for dietary supplements that can help improve the body composition of physically active individuals, it is important to consider environmentally sustainable options. One such option is using invertebrates as a food source. Surprisingly, there are no studies evaluating the consumption of cricket flour as a dietary supplement in combination with resistance training. Objective: The aim of this study is to examine the effects of cricket flour (<i>Gryllus assimilis</i>) intake on the nutritional and body composition parameters of rats undergoing resistance training. Methods: : Thirty male Wistar rats, two months old and averaging 200 grams at the beginning of the study, were divided into 4 groups: Control (C; n = 9), Trained (T; n = 6), Supplemented (S; n = 9), and Trained Supplemented (TS; n = 6). The supplemented rats received an average of 1.98g of cricket flour added to commercial feed as a supplement. The training consisted of 5 weekly sessions, each comprising 4 sets of 10 jumps per day, with a 1-minute recovery between sets, performed in water with a load attached to the tail. The load was increased weekly based on the rats' body mass: 1st week = 25% of body mass; 2nd week = 30%; 3rd and 4th weeks = 35%; 5th week = 45%; and 6th week = 50%. Results: the results showed that training led to a reduction in final weight ($p = 0.0217$) and weight gain ($p = 0.0203$). Additionally, supplementation resulted in improved food efficiency ($p = 0.0136$) and food conversion ($p = 0.0331$). Furthermore, training led to a reduction in epididymal fat ($p < 0.0001$) and an increase in fat-free mass ($p = 0.0047$). This was determined using the Anova Two Way, and the difference was considered statistically significant when the p-value was less than 0.05. Conclusion: : in conclusion, it was found that supplementing with <i>Gryllus assimilis</i> flour along with strength exercise training improves nutritional and body composition parameters. Support: CNPq, CAPES, FAPEMIG, Pró-Reitoria de Pesquisa, Pós-Graduação e Inovação da Universidade Federal de Ouro Preto–PROPI-UFOP Protocol: 2018/14</p>

Title	Vagal and splenic participations modulate adiposity and serum iron levels in hypothalamic-obese exercised rats.
Authors	CAROLINE DE MAMAN OLDRA, GIOVANA FANHANI TESSARO, ELLEN CAROLINA ZAWOSKI GOMES, EVELINE CRISTIANE BATISTA SCHMIDT HELENE, AMANDA ROCHA FUJITA, KÉSIA ZANUZO, SABRINA GRASSIOLLI
Affiliations	Endocrine Physiology and Metabolism Laboratory, UNIOESTE
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The vagus nerve (VN) and spleen participate in the inflammatory processes related to obesity and metabolic dysfunctions. Hypothalamic obese rats exhibit vagal hyperactivity and splenic abnormalities, events that could be related to iron imbalance. Exercise promotes anti-adiposity and positive health effects on metabolism. However, its impact on iron control is unknown. Objective: Here, we evaluated the impact of VN and spleen ablation on adiposity and serum iron levels in hypothalamic obese rats subjected to swimming training. Methods: Ethical approval (n° 16-22). Hypothalamic obesity (Ho) was induced by high doses (4 g/kg) of monosodium glutamate administered in the first post-natal days (PND). At 60 PND, Ho rats were subjected to surgeries: total vagotomy (vag), splenectomy (spl), vag+spl, or sham. At 80 PND, Ho groups were randomly subdivided into exercised (Ex) or sedentary (Sd). The Ex groups swam daily for 4 weeks in a heated pool with an overload attached to the tail. At PND 120, Ho rats were weighed (g) and naso-anal length (NAL, cm) recorded to obtain the Lee Index (LI). After euthanasia, white adipose tissue (WAT) from inguinal (I) and retroperitoneal (R) depots was excised and weighed. Blood was collected, and the serum was used for biochemical assays of glucose, triglycerides, total cholesterol, and iron. The TyG (triglyceride/glucose) index was used as an indicator of insulin resistance. Results: Ho-Ex rats showed smaller LI (5.4%), triglycerides (44.9%), total cholesterol (36.4%), and TyG values (6.4%) compared to Ho-Sd rats, which was not observed in glucose. However, serum iron levels were 47% higher in Ho-Ex compared to Ho-Sd. Ho-vag and Ho-vag+spl groups showed reductions in WAT-R (47.0%) compared to Ho-Sd, an effect lost by spl. Similarly, WAT-R was reduced by approximately 45% and 43% in Ho-vag-Ex and Ho-vag+spl-Ex groups compared to Ho-Sd and Ho-Ex, respectively. In Ho-vag-Ex rats, there was a reduction of triglycerides (53.9%), TyG (8.6%), and total cholesterol (48.2%) compared to Ho-Sd, which was not observed in glucose. Ho-spl-Ex, Ho-vag+spl-Ex, and Ho-vag-Ex rats showed a rise of approximately 50% in serum iron levels compared to Ho-Sd rats. Conclusion: VN and spleen ablation enhances the anti-adiposity effects of exercise and reduces serum iron levels in hypothalamic obese rats. Support: Graduate Support Program for financial assistance to an Educational or Research Project, with process number 88881.594204/2020-01 and assistance number 1359/2020. Protocol: Ethics Committee approval 16-2</p>



Title	Evaluation of physical performance of obesity-prone and obesity-resistant rats induced by different dietary compositions.
Authors	DANIEL SESANA DA SILVA, MATHEUS CORTELLETTI, LUCAS FURTADO, JOCTAN CORDEIRO, KIANY MIRANDA, ANA PAULA LIMA LEOPOLDO, ANDRÉ SOARES LEOPOLDO
Affiliations	Programa de pós graduação em Ciências Fisiológicas, Universidade Federal do Espírito Santo
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The global obesity epidemic arises from complex genetic and environmental factors like diet and physical activity. Investigating factors influencing obesity susceptibility is crucial. Obesity-prone (OP) and obesity-resistant (OR) rats show that OR rats have enhanced lipid oxidation. Despite gaps in understanding OR metabolism, evidence suggests physically active OR rats outperform in training due to heightened ATP generation. Objective: This study aims to investigate physical performance, cardiorespiratory, and metabolic adaptations of OP and OR rats. Methods: Wistar rats underwent 23 weeks of obesity exposure, initially randomized into SD (standard diet, n=39) and HFD (high-fat diet, n=39) groups. Rats were classified as OP and OR in each diet, forming SD-OR (n=13), SD-OP (n=13), HFD-OP (n=13), and HFD-OR (n=13) groups. Adiposity, nutrition, and metabolism were analyzed. An incremental speed test in the 23rd week assessed aerobic capacity and performance. Results: Initial body masses were similar among groups: SD-OR (n=11,104±13g), SD-OP (n=13,111±12g), HFD-OR (n=10,96±15g), and HFD-OP (n=11,109±9g). The SD-OP group (n=13,602±21g) exhibited a higher final body mass compared to the SD-OR group (n=11,520±41g). Similarly, the HFD-OP group (n=11,601±79g) showed a lower final body mass than the HFD-OR group (n=10,496±27g). The SD-OR group (n=11, 24.6±1.3g/day) exhibited higher food consumption compared to the HFD-OR group (n=15, 8.1±1.3g/day). Similarly, the SD-OP group (n=13, 26.8±1.4g/day) also showed higher food consumption than the HFD-OP group (n=11, 17.3±2.1g/day). Additionally, the SD-OP group (n=13, 26.8±1.4g/day) had a higher food consumption than the SD-OR group (n=11, 24.6±1.3g/day). Furthermore, the HFD-OR (n=10, 3.28±0.20%) and HFD-OP (n=11, 3.63±0.21%) groups exhibited elevated feed efficiency values compared to the SD-OR (n=11, 2.76±0.17%) and SD-OP (n=13, 2.99±0.17%) groups, respectively. The SD-OR group (n=11, 54.5±6.0ml/min/kg^{0.75}) achieved a higher VO₂max compared to the SD-OP group (n=12, 32.0±4.00ml/min/kg^{0.75}). Additionally, the SD-OR group (n=11, 328±70m) also covered a greater distance than the SD-OP group (n=12, 248±84.8m), and the SD-OR group (n=11, 31.4±2.2min) spent more relative time than the SD-OP group (n=12, 22.3±3.2min). Similarly, the HFD-OR group (n=9, 33.9±4.4m/min) exhibited higher speed than the HFD-OP group (n=11, 26.7±5.4m/min), and the HFD-OR group (n=9, 370±88m) covered a greater distance than the HFD-OP group (n=11, 234.5±95.2m). Conclusion: The high-fat diet (DH) contributed to increased body mass and adiposity in obesity-prone animals (POb), highlighting its role in obesity development. The study also reveals potential metabolic advantages in obesity-resistant animals (ROb), emphasizing enhanced lipid oxidation and endurance during physical tests. This research provides valuable insights into the intricate connections among diet, metabolism, and obesity-related outcomes. Support: : Espírito Santo Research and Innovation Support Foundation – FAPES Protocol: Aug-21</p>



Title	EFFECTS OF OVARIECTOMY AND RESISTANCE TRAINING ON THE FUNCTION AND MITOCHONDRIAL STRESS BIOMARKERS OF LIVER AND SKELETAL MUSCLE IN RATS: CROSSTALK BETWEEN LIVER AND MUSCLE
Authors	CHRISTOPHER BARSAQUE GARCIA, REGIANE ALVES PINTO, DIEGO FELIPE ARMININI CAVALINI, JOÃO PEDRO MAIA DE OLIVEIRA DA SILVA, ANDERSON FERREIRA DA CUNHA, ROGER FRIGERIO CASTILHO, GILBERTO EIJI SHIGUEMOTO
Affiliations	Ciências Fisiológicas, UFSCar, Genética e Evolução, UFSCar, Bioenergetica e metabolismo celular, UNICAMP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The hormonal decline in menopause can lead to mitochondrial dysfunction, predisposing women to diseases such as sarcopenia and non-alcoholic fatty liver disease (NAFLD). Evidence indicates that there is a metabolic crosstalk between the liver and skeletal muscle, currently targeted at mitochondrial biomarkers. MOTS-c plays a role in regulating glucose uptake and lipid metabolism, acting on the crosstalk between the two tissues. In this context, resistance training (RT) has been shown to be effective, as it improves mitochondrial function and helps prevent and treat sarcopenia and NAFLD in menopausal women.</p> <p>Objective: Investigate the effects of ovariectomy and RT on mitochondrial function and the mitochondrial stress biomarker MOTS-c in the crosstalk between liver and skeletal muscle. Methods: 20 young adult Wistar rats were divided into 4 groups (INT-SED, INT-RT, OVX-SED and OVX-RT). Ovariectomy was performed at 13 weeks of age. RT was performed weekly (3x/week) for 20 weeks. The tissues were euthanized and collected 48 hours after the 20th RT session. The following analyses were carried out on liver and gastrocnemius muscle tissue biopsies: 1) Gene expression (RT-qPCR) of the electron transport chain complexes (ETC: CI, CII, CIII, CIV and ATPS) and MOTS-c, 2) Oxygen consumption by High Resolution Respirometry (pmol/sec*mg, Oroboros®). Statistical analysis was carried out by One-Way ANOVA followed by Fisher's Post-hoc test (P<0.05). Results: Body mass: the OVX-SED group (357.4±18.1 g) was significantly larger than the other groups. Maximum workload: both trained groups had a significant increase in MW (771.88±2.1 g) at the end of the RT compared to the initial week. Liver respirometry: significant decrease in oxygen consumption of the OVX-SED group in the S3Succ (46.2±7.4 pmol/sec*mg) compared to the other groups; RT increased oxygen consumption in the S3Succ of both trained groups (OVX-RT=78.2±23.7; INT-RT=86.7±36.9 pmol/sec*mg). Respirometry of the gastrocnemius: a significant decrease in oxygen consumption in the OVX-SED group in the S3Succ (34.8±9.4 pmol/sec*mg) compared to the other groups; RT increased oxygen consumption in the S3Succ of both trained groups (OVX-RT=36.4±6.5; INT-RT=40.3±7.3 pmol/sec*mg). RT-qPCR of ETC and MOTS-c in the liver: reduction in gene expression of CIV and ATPS in the OVX-SED group (0.71 and 0.71 AU) compared to INT-SED; RT increased gene expression of CII in both trained groups (OVX-RT=1.20; INT-RT=1.30±0.3 AU); RT increased gene expression of MOTS-c in both trained groups (OVX-RT=2.29±2.2; INT-RT=2.19±1.0 AU). RT-qPCR of ETC and MOTS-c in the gastrocnemius: reduction in CIII gene expression in the OVX-SED group (0.87±0.3 AU) compared to INT-SED; reduction in CIV gene expression in the OVX-SED group (0.59±0.2 AU) compared to the other groups; RT increased CIV gene expression in both trained groups (OVX-RT=1.49±0.6; INT-RT=1.62±0.5 AU); RT increased MOTS-c gene expression in the OVX-RT group (1.25±0.3 AU) compared to OVX-SED. Conclusion: Ovariectomy produced mitochondrial dysfunction in the liver and gastrocnemius, reducing gene expression of ETC proteins and MOTS-c. However, RT as a non-pharmacological intervention was effective in preventing this damage. The increase in MOTS-c gene expression in the trained groups (INT-RT and OVX-RT) indicates the presence of mitochondrial biomarkers that confirm crosstalk between liver and muscle tissues promoted by exercise. Support: National Council for Scientific and Technological Development (CNPq). Protocol: 4381011222</p>



Title	EFFECTS OF AEROBIC TRAINING ON THE OXIDATIVE BALANCE OF THE SOLEUS MUSCLE OF OVERNOURISHED RATS DURING THE LACTATION
Authors	JONATA HENRIQUE DE SANTANA, DEISIANE DE ARAUJO CORREIA, DEYVISON GUILHERME MARTINS SILVA, ELENILSON MAXIMINO BERNARDO, ALLIFER ROSENDO PEREIRA, MARIANA PINHEIRO FERNANDES, CLAUDIA JACQUES LAGRANHA
Affiliations	Graduate Program in Nutrition, Physical Activity and Phenotypic Plasticity, UFPE, CAV, Graduate Multicentric Program in Physiological Sciences, UFPE, CAV, Graduate Program in Neuropsychiatry and Behavioral Science, UFPE, Graduate Program in Nutrition, UFPE
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Physical inactivity and inappropriate diets have contributed to the increase in obesity rates. Studies indicate that obesity is associated with excessive production of reactive oxygen species, which can trigger metabolic disorders in skeletal muscle, such as insulin resistance Objective: To evaluate the effects of aerobic training on the oxidative balance of the soleus muscle of overnourished rats during the lactation Methods: Rats of the Wistar lineage were used and, after the birth, they were divided into normonourished (N, n=9 pups/mothers) and overnourished (O, n=3 pups/mothers) groups, which had a litter reduction on the 3rd day; on the 21st the weaning occurred. On the 23rd day of life, the rats were subdivided into two more groups, now according to the physical training protocol, forming the untrained and trained groups (NNT, NT, ONT and OT). The trained groups were subjected to a moderate intensity training program, carried out on an ergometric treadmill for rats for 4 weeks, with a frequency of 5 days/week, 60 min/day and at 50% of the maximum treadmill running capacity. At 54 days of life, the rats were euthanized for tissue collection, where biomarkers of oxidative stress, antioxidant enzyme activity, REDOX balance (GSH/GSSG ratio) and quantification of total thiol levels were subsequently evaluated. The study was approved by the Ethics Committee on the Use of Animals (CEUA) of the UFPE Biosciences Center (nº 117/2022), following the regulations of the National Council for the Control of Animal Experimentation (CONCEA). For statistical analysis, the Two-way ANOVA test was used, and the results were shown as mean \pm SEM considering significant $p < 0.05$ Results: Our data showed that there was a reduction (29%) of carbonyls levels in the NT group (NNT: 17.13 ± 0.740, n= 6; NT: 12.08 ± 0.359 nmol/mg of protein, n= 6, $p = 0.0001$) and in OT (16%) (ONT: 18.92 ± 0.872, n= 6; OT: 15.85 ± 0.520 nmol/mg of protein, n= 6, $p = 0.0199$); with regard to the enzyme antioxidant system there was a reduction in superoxide dismutase (SOD) activity (18%) in ONT (NNT: 110.04 ± 5.243, n= 8; SNT: 90.39 ± 2.735 U/mg of protein, n= 6, $p = 0.0200$) and an increase in OT (21%)(ONT: 90.39 ± 2.735, n= 6; OT: 109.16 ± 4.272 U/mg of protein, n= 6, $p = 0.0418$); catalase (CAT) activity decreased (20%) in ONT (NNT: 85.38 ± 2.938, n= 8; ONT: 68.98 ± 2.208 U/mg of protein, n= 6, $p = 0.0068$) and increased in OT (32%) (ONT: 68.98 ± 2.208, n= 6; OT: 90.52 ± 5.568 U/mg of protein, n= 6, $p = 0.0015$). The reduced glutathione (GSH) levels reduced (27%) in ONT (NNT: 24.92 ± 0.284, n= 6; ONT: 18.12 ± 0.350 mM/mg of protein, n= 6, $p < 0.0001$) and increased in OT (34%) (ONT: 18.12 ± 0.350, n= 6; OT: 24.29 ± 0.606 mM/mg of protein, n= 6, $p < 0.0001$). The oxidized glutathione (GSSG) levels reduced (27%) in OT (ONT: 1.119 ± 0.045, n= 6; OT: 0.811 ± 0.040 mM/mg g of protein, n= 6 $p = 0.0002$) Conclusion: Overnutrition causes a reduction in the enzymatic antioxidant activity and on the levels of non-enzymatic antioxidants, while the aerobic training attenuates these effects and reduces the levels of protein oxidation markers in the soleus muscle of overnourished rats during the lactation Support: CAPES, FACEPE. Protocol: nº 117/2022</p>

Title	Modulação das vias de Estresse Oxidativo e Inflamatórias na Carcinogênese da Bexiga Urinária e Efeitos do Docetaxel Emulsificado em Nanopartícula de LDE Associado ao Treinamento Físico Aeróbico em Ratos Sprague-Dawley.
Authors	VICTOR ROGÉRIO GARCIA BATISTA, ALLICE SANTOS CRUZ VERAS, MARIA EDUARDA ALMEIDA TAVARES, RAFAEL RIBEIRO CORREIA, REBECA VIEIRA E MAGALHÃES RODRIGUES, MATEUS MACHADO FRIGO, GIOVANA RAMPAZZO TEIXEIRA
Affiliations	Educação Física, UNESP, Ciências Básicas, UNESP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O câncer de bexiga (BCa) é uma das malignidades mais comuns do trato urinário, sendo o quarto tipo de câncer frequente em homens. A biotecnologia quimioterápica utilizando a nanoemulsão de LDE apresenta resultados importantes na redução de tumores sólidos com grande versatilidade e mínima toxicidade. O potencial preventivo do exercício físico (Ex) contra o câncer tem seu mecanismo de ação amplamente demonstrado. Pouco se sabe sobre os efeitos relativos da combinação de quimioterápicos em entrega de drogas associado ao exercício físico no tratamento do BCa. Objective: Investigar os efeitos do exercício físico aeróbico associado ao LDE-docetaxel nas vias inflamatórias e de estresse oxidativo do câncer de bexiga. Methods: 40 ratos Sprague-Dawley, aos 50 dias de vida os animais receberam via intraperitoneal 1 dose única de 65mg/kg de 7,12-dimetilbenzantraceno (DMBA). O período de indução ocorreu por 91 dias, e os animais receberam ração e água ad libitum. Dividimos os animais em 4 grupos (n=10): BCa (BCa induzido), BCa+Ex (BCa induzido e Ex), BCa+LDE-DTX (BCa induzido e tratados LDE-docetaxel), BCa+LDE-DTX+Ex (BCa induzido, tratado com LDE-docetaxel, e Ex). O protocolo de Ex ocorreu durante 8 semanas, com duração de 30 minutos por sessão, 5x por semana, com 60% da capacidade máxima dos animais. A molécula de LDE foi preparada e associada ao quimioterápico docetaxel, totalizando 6 doses (uma por semana na concentração de 2mg/kg). Aos 189 dias de idade os animais foram submetidos a eutanásia e a bexiga urinária coletada e pesada. CEUA 02/2020. As análises estatísticas foram obtidas por meio do teste One Way-ANOVA, seguido do pós-teste de Tukey com $p \leq 0,05$. Results: Os animais do grupo BCa+LDE-DTX ($p=0,0088$) apresentaram redução significativa no peso corporal inicial em comparação ao grupo BCa. No final do experimento, os animais do grupo BCa ($p=0,0279$) redução significativa no peso corporal em relação ao grupo LDE-DTX+Ex, sem diferenças em comparação aos demais grupos. Contudo, ao olharmos para o ganho de peso durante a experimentação não se houve diferença entre os grupos. O grupo BCa apresentou aumento significativo no peso absoluto da bexiga urinária em comparação aos grupos BCa+Ex ($p=0,0068$), LDE-DTX ($p=0,001$) e LDE-DTX+Ex ($p=0,0002$). O peso relativo da bexiga urinária foi significativamente maior no grupo BCa em comparação com BCa+Ex ($p=0,0091$), LDE-DTX ($p=0,0002$) e LDE-DTX+Ex ($p<0,0001$). A quantidade dos mastócitos foi maior no grupo BCa ($2,38 \pm 0,57$) quando comparado aos grupos BCa+Ex ($p=0,023$) e LDE+DTX ($0,027$). A citocina anti-inflamatória de IL-10 nos animais tratados com exercício BCa+Ex ($0,83 \pm 0,02$), LDE-DTX ($0,800 \pm 0,09$) e os LDE-DTX+Ex ($0,86 \pm 0,22$) apresentaram maior expressão em comparação ao grupo BCa ($0,69 \pm 0,10$). A expressão da citocina inflamatória IL-6 foi maior no grupo LDE-DTX comparado aos demais grupos. Marcadores NF-κB, ao compararmos a expressão entre os grupos não apresentaram diferença significativa. A Capacidade Antioxidante Total do grupo LDE-DTX+Ex, apresentou níveis reduzidos quando comparado aos grupos BCa ($p=0,030$) e BCa+Ex ($p=0,041$). A peroxidação Lipídica e a enzima SOD não apresentaram diferença significativa entre os grupos. Conclusion: 8 semanas de exercício físico aeróbico associado ou não ao LDE-DTX, promove a redução do peso da bexiga urinária, redução de mastócitos e redução da capacidade antioxidante no microambiente tumoral, mas não modifica a inflamação tecidual significativamente. Support: Financiamento: Este estudo foi financiado pelos projetos FAPESP (Processo:2020/16310-2; 2020/16166-9, 2021/14514-2 e 2023/13014-1). Protocol: Feb-20</p>



Title	ELUCIDATION OF THE CRITICAL ROLE OF MUSCLIN IN THE MODULATION OF PHYSIOLOGICAL RESPONSES DURING CARDIOPULMONARY EXERCISE TESTING
Authors	ANTONIO ALVES DE FONTES-JUNIOR, ANA PAULA RENNÓ SIERRA, MARIA FERNANDA CURY BOAVENTURA
Affiliations	Instituto de Ciências da Atividade Física e do Esporte, UNICSUL, Escola de Educação Física e Esportes, USP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Skeletal muscle is increasingly recognized as an endocrine organ. The identification and understanding of myokines, such as musclin, have the potential to expand our knowledge of muscle function both at rest and during exercise, as well as to reveal how muscle communicates with other organs and influences the overall metabolism of the body. Objective: This study aims to investigate the correlation between pretest plasma musclin levels and several physiological variables during cardiopulmonary exercise testing. Methods: Seventy-five healthy endurance athletes between the ages of 30 and 55 (mean \pm 41.4) with no history of cardiovascular disease participated in this study. Blood samples were collected to determine plasma musclin levels by enzyme-linked immunosorbent assay before and immediately after the athletes underwent CPET. The test was performed using a treadmill protocol (TEB Apex 200, TEB, São Paulo, Brazil) with a fixed incline of 1% and a speed starting at 8km/h and increasing by 1km/h per minute until the runner reached maximal exhaustion. Exhaled gas analysis was performed with a breath-by-breath system (Quark CPET, Cosmed, Rome, Italy) at the first, second and third thresholds (AT, RC and Pico, respectively). Correlations between Musclin and CPET parameters were performed using Spearman's test. Statistical significance was accepted at the $p < 0.05$ level in all analyses. Results: The data showed significant and moderate correlations between MUSCLINA_PRE and PETO2_AT_DELTA ($r = 0.406$, $p = 0.0005$), VE_VCO2_AT_DELTA ($r = 0.4432$, $p = 0.0002$), FAT_Kcal/MIN AT_POST ($r = 0.3894$, $p = 0.0006$), CURVE_DELTA ($r = 0.4029$, $p = 0.0004$) and VO2@AT_DELTA ($r = 0.3124$, $p = 0.009$). We also observed moderate and significant negative correlations between MUSCLINE_PRE and RQ_RC_POST ($r = -0.4844$, $p < 0.0001$), RQ_RC_DELTA ($r = -0.3633$, $p = 0.004$), TEMPO_PICO_DELTA ($r = -0.3736$, $p = 0.0033$), and RQ_PICO_DELTA ($r = -0.3311$, $p = 0.0092$). The positive correlation between Musclin levels and variables such as PETO2_AT_DELTA and VE_VCO2_AT_DELTA suggests that higher pre-exercise Musclin levels are associated with better ventilatory capacity and gas exchange, which are essential for cardiorespiratory performance. In addition, the correlation with FAT_Kcal/MIN AT_POST indicates a possible influence of Musclin on the efficiency of energy metabolism after exercise. On the other hand, the negative correlations observed with RQ_RC_POST, RQ_RC_DELTA, TEMPO_PICO_DELTA and RQ_PICO_DELTA suggest a possible modulatory role of Musclin in the regulation of the respiratory quotient and the duration of maximal effort. These negative associations may reflect a physiological adaptation in which Musclin helps to optimize the use of energy substrates and exercise efficiency, possibly delaying fatigue. Conclusion: These findings suggest that musclin may act as an important modulator of cardiorespiratory and metabolic processes during exercise, influencing both performance and recovery. Further studies are needed to elucidate the exact mechanisms by which musclin exerts these effects, but our results highlight its potential as a relevant biomarker in the context of exercise physiology. Support: This research was funded by the São Paulo State Research Foundation (FAPESP), grant number [2018/26269]. Protocol: Approval number: 3.895.058</p>



Title	Effect of a high-fat diet and physical exercise on the compound action potential of the sciatic nerve of Wistar rats.
Authors	PALOMA KATLHEEN MOURA MELO, FRANCISCA TAYNÁ DA SILVA GOMES, ALEXIA MIRANDA MORAIS, LAVÍNNYA YÁSKARA DE AQUINO MATOSO, IVANA ALICE TEIXEIRA FONSECA, PAULO LEONARDO ARAUJO DE GOIS MORAIS, JOSÉ RODOLFO LOPES DE PAIVA CAVALCANTI
Affiliations	Neurologia Experimental, UERN
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The study of electrophysiology in the sciatic nerve is essential to understand neuromuscular functions and dysfunctions. In relation to a high-fat diet and physical exercise, it is essential to understand how these factors influence neuromuscular health. Physical exercise, on the other hand, can improve nerve function by increasing neuroplasticity and reducing inflammation and oxidative stress. Objective: To analyze the effect of a high-fat diet and physical exercise on the compound action potential of the sciatic nerve of Wistar rats. Methods: This is an experimental study . Wistar rats, aged 22 days, with a diet and physical exercise protocol were used, being fed with control (7%) and high-fat (48%) diets and subdivided into sedentary and exercised, for a period of 8 weeks. The experimental intervention period began after weaning, with males, divided into 4 groups (n=12, each) with a high-fat diet and forced physical training, carried out on a treadmill. To record the compound action potential (PAC) in the conduction velocity of the myelinated fibers of the sciatic nerve, pulses of 40 V and 0.1 ms were used; for non-myelinated fibers the pulse was 60 V and 1.5 ms, delivered at a frequency of 0.2 Hz. The results were expressed as mean and their corresponding standard error. After data collection, the Shapiro-Wilk distribution normality test was used. One-way Analysis of Variance (ANOVA) was used to compare groups, and post-hoc, respecting the assumptions of normality, Tukey when normally distributed or Kruskal-Wallis (Dunn's test) when not. Statistical significance was considered when the results showed a probability of occurrence of the null hypothesis was less than 5% (P<0.05). The software used was GraphPad Prism 8 (GraphPad Software) Results: After analyzing the PAC of the NCs, we verified changes in the amplitude and speed of the 1st and 2nd components of the PAC. The speed of the 1st and 2nd components was 94.5 mV ± 23.15m/s and 32.722 mV ± 12.88m/s, without showing a significant difference between the groups. A high-fat diet can negatively affect nerve function, contributing to inflammation and oxidative stress, which are harmful to nerve health. Studies have shown that a high-fat diet can lead to changes in nerve conduction and the integrity of the sciatic nerve, resulting in peripheral neuropathies. These changes can be detected using electrophysiological techniques, which measure the speed of nerve conduction and the response of the muscles innervated by the sciatic nerve. Conclusion: The high-fat diet groups did not cause PAC block in peripheral nerves; while physical exercise helped maintain driving speed. Therefore, physical exercise may be a possible strategy for treating neuropathic pathologies. Sciatic nerve electrophysiology therefore serves as a valuable tool to investigate the complex interactions between diet and physical exercise, helping to identify effective interventions to prevent and treat neuropathies associated with poor eating habits and a sedentary lifestyle. Support: Coordination for the Improvement of Higher Education Personnel Foundation (CAPES). Protocol: 10510522.2</p>

Title	Jaboticaba berry (<i>Myrciaria jaboticaba</i>) consumption improves redox balance and accelerates muscle recovery following exercise-induced muscle damage: a randomized, placebo-controlled trial.
Authors	OLAVO JOÃO FREDERICO RAMOS JUNIOR, THIAGO SILVEIRA ALVARES
Affiliations	Centro Multidisciplinar UFRJ Macaé, Universidade Federal do Rio de Janeiro
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Jaboticaba berries have demonstrated high antioxidant activity with a potential health benefit. However, their functional properties have not been demonstrated in humans. Objective: This study aimed to examine the effect of Jaboticaba berry Juice (JBT) intake on recovery from exercise-induced muscle damage (EIMD), which is known to increase oxidative stress, muscle soreness, decrease muscle function and muscle quality. Methods: Twenty-four trained participants were randomly allocated to consume 250 mL of JBT (containing approximately 1,060 mg of total polyphenols) or a fruitflavored placebo drink (PLA) for seven days. On day 4, participants performed 6 x 10 maximal isokinetic eccentric contractions of the elbow flexors. Results: Plasma-reduced glutathione (GSH), myoglobin (Mb), muscle soreness (DOMS), maximal isokinetic voluntary contraction (MVCisok), and functional (MQf) and morphological (MQm) muscle quality were assessed before and 2h, 24h, 48h and 72h after EIMD. Results: The EIMD protocol increased Mb levels ($p < 0.001$) and DOMS ($p < 0.001$) and reduced GSH levels ($p < 0.001$), MVCisok ($p < 0.001$), MQf ($p < 0.001$), and MQm ($p = 0.028$). JBT intake increased GSH levels ($p = 0.001$), decreased DOMS ($p < 0.001$), and accelerated the recovery of muscle strength ($p = 0.004$) and muscle quality functional ($p = 0.002$) and morphological ($p = 0.006$) in the following days after the eccentric exercise when compared to control. Conclusion: The consumption of jaboticaba berry polyphenols may alleviate the symptoms of muscle damage in resistance-trained participants. Support: This work was supported by the Fundação de Amparo a Pesquisa do Estado do Rio de Janeiro – FAPERJ (SEI-260003/001179/2020 and SEI-260003/016456/2021) Protocol: protocol CAAE: 25801019.9.0000</p>



Title	Effects of NKB agonist on exercise performance and thermoregulation during acute physical exercise in Wistar rats
Authors	MARCIO OSVAN REZENDE ROCHA XAVIER, ALESSIA AGUIAR DE FREITAS, KAOMA STEPHANI DA COSTA SILVA, RAPHAEL ESCORSIM SZAWKA, GLAUBER DOS SANTOS FERREIRA DA SILVA
Affiliations	Fisiologia Farmacologia, UFMG
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Thermoregulation during aerobic exercise is crucial due to its direct impact on performance. The conversion of chemical energy into mechanical energy is not entirely efficient, resulting in heat generation. During acute continuous exercise, this process increases the body's internal temperature (T_{abd}) and, consequently, the peripheral temperature (T_{skin}), promoting increased heat dissipation. The neuropeptide NKB activates heat-sensitive neurons in the median preoptic area (MPOA), resulting in heat dissipation. Therefore, we hypothesized the NKB agonist improves acute physical exercise performance and changes the thermoregulation in acute exercise. Objective: To evaluate the thermoregulatory changes induced by Senktide (senk), an agonist of the neuropeptide NKB, during acute aerobic exercise. The aim is to investigate how the neuropeptide NKB agonist influences the performance of these animals during physical activity, as well as to analyze their thermoregulatory responses. Methods: Male Wistar rats (CEUA 421/2018), 10 to 11 weeks old weighing 300g, were used in this study, previously habituated to a metabolic treadmill for five consecutive days, for 10 minutes each day. Subsequently, the rats underwent surgery for the implantation of a guide cannula in the central nervous system, specifically in the lateral ventricle (LV). For the implantation of an abdominal temperature sensor, a small incision was made in the abdominal muscle. To assess tail temperature, a subdermal temperature sensor (biotag) was inserted 2 cm from the base of the tail. The animals were divided into 2 groups: Senktide (N=10) and PBS vehicle (n=11). The thermal variables were then measured: internal/abdominal temperature (T_{abd}) and skin tail temperature (T_{skin}). These animals were re-habituated to the treadmill and then subjected to progressive exercise to perform a maximum test and achieve 60% performance. Senktide or vehicle was administered into the LV, and the run until exhaustion was initiated. Results: In the present study, we observed that the microinjection of senk significantly increased the running time of the animals during the exercise protocol compared to the vehicle group ($P<0.001$). Additionally, the treatment with Senk also elicited a greater running distance compared to animals in the PBS group ($P=0.006$). The work performed during exercise was also significantly higher in animals receiving the senk compared to the PBS group ($P<0.001$). For the thermal variables, we observed significant differences in the minimum T_{skin} ($P=0.0131$) when comparing senk with PBS, although there was no significant difference in the maximum T_{skin} values. Regarding T_{abd}, we did not observe differences in either the minimum or maximum T_{abd} temperature values. Conclusion: The thermoregulatory changes induced by the NKB agonist, senktide, demonstrated a positive effect on improving performance during acute aerobic exercise, leading to increased running time, distance, and work performed during the exercise protocol. In addition to the observed T_{skin} changes, further analyses are being conducted to better understand how thermal variables impact the enhanced performance associated with senktide. Future experiments will be conducted to elucidate the underlying mechanisms. Support: FAPEMIG, CAPES and CNPq Protocol: CEUA 421/2018</p>



Title	Study of Gamma-Aminobutyric Acid supplementation in combination with exercise on the food intake of overweight/obese women
Authors	LARISSA VITALINA DE MEDEIROS PIRES, ADILSON DE BARROS MARTINS, CRISTINA OLIVEIRA TRINDADE, RAIANNE DOS SANTOS BALEIRO, THAINÁ GOMES PEIXOTO, FERNANDA GUIMARÃES DRUMMOND E SILVA, DANIEL BARBOSA COELHO, EMERSON CRUZ DE OLIVEIRA, LENICE KAPPES BECKER
Affiliations	Escola de Educação Física, UFOP, DCBI, UFOP, Escola de Nutrição, UFOP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Gamma-Aminobutyric Acid (GABA) has demonstrated potential for improving quality of life and reducing stress in previous studies. GABA supplementation has also been shown to increase growth hormone levels, which may aid in the mobilization of fatty acids and lead to weight loss. Objective: This study aims to investigate the effects of GABA dietary supplementation combined with functional exercises on the food intake of overweight/obese women. Methods: Thirty overweight/obese and sedentary women participated in the study. In a double-blind randomized design, they were divided into two groups, both performing physical exercises three times a week for 12 weeks. One group received 200 milligrams of GABA (treatment) daily, and the other group received a placebo, until the end of the experiment. The Food Frequency Questionnaire (FFQ) was used to collect information on food and dietary intake. Results: The study observed that the placebo group had a higher protein intake of 1.66 (1.16 – 5.06) [median (minimum – maximum) g/kg/day] compared to the GABA group's intake of 0.92 (0.47 – 2.71) at the beginning of the study. This was determined through the Mann Whitney test, and the difference was statistically significant with a p-value of 0.0057. At the end of the study, the only significant difference between the two groups was in vitamin B6 intake. The placebo group had a median intake of 2.01 (0.36 – 36.65) [median (minimum – maximum) mg/day], while the GABA group had a median intake of 1.08 (0.18 – 2.76), p-value of 0.0052. Conclusion: In conclusion, the supplementation of GABA alongside physical training did not have any adverse effects on food intake in overweight and obese women who were undertaking a physical training program. Support: CNPq, CAPES, FAPEMIG, Pró-Reitoria de Pesquisa, Pós-Graduação e Inovação da Universidade Federal de Ouro Preto–PROPPi-UFOP Protocol: 40000620.3.0000.5150</p>



Title	Efeito da Síndrome Metabólica e da Atividade Física no Lazer na Memória em Mulheres Pré-menopausa e Pós-Menopausa
Authors	ARTHUR POLVEIRO DA SILVA, GABRIEL PEINADO COSTA, ADRIANO CORREA, MATHEUS MARTINS MOREIRA, ANA LIVIA PINHEIRO CANTARIM, LETÍCIA DETORE DEVELEY, JÚLIA CUNHA SANTOS OLIVEIRA, ÁTILA ALEXANDRE TRAPÉ, CAMILA DE MORAES
Affiliations	Grupo de Estudos e Pesquisa em Educação Física e Saúde Coletiva, USP, Grupo de Estudos e Pesquisa em Exercício Físico e Condições Especiais de Saúde, USP
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A síndrome metabólica (SM) é considerada um fator de risco para o declínio cognitivo patológico, que demanda monitoramento já na meia idade, devido aumento da produção de biomarcadores associados à neurodegeneração e ao comprometimento de fatores neuroprotetores. As mulheres podem estar especialmente vulneráveis a fatores de risco neurodegenerativos durante o envelhecimento reprodutivo, em razão das repercussões neuroendócrinas e vasculares relacionadas à transição menopausal. No entanto, estratégias não farmacológicas como a prática de atividade física no lazer (AFL), apresentam-se como abordagens promissoras diante de seus impactos positivos sobre parâmetros cardiometabólicos e cognitivos. Objective: Verificar se há efeito da SM, do estágio reprodutivo e da prática de AFL sobre o desempenho cognitivo no domínio da memória em mulheres de meia idade e início da faixa etária idosa. Methods: Utilizou-se a classificação da SM segundo a International Diabetes Federation; classificou-se o estágio reprodutivo segundo a recomendação do STRAW+10; a AFL nos últimos 12 meses foi avaliada pelo questionário de atividade física habitual de Baecke e o desempenho cognitivo no domínio da memória pelo Exame Cognitivo de Addenbrooke. Dados analisados por regressão linear generalizada, distribuição gama, nível de significância de 5% e descritos pelo coeficiente beta [IC95%] da diferença média entre os grupos. A diferença entre os grupos foi verificada pelo método de bootstrap BCa [IC95%] 10.000 reamostragens. Results: Participaram 40 mulheres com 50±6 (40-60) anos de idade e 14±3 anos de escolaridade. Destas, 62,5% foram classificadas como pós-menopausa com a ocorrência do período menstrual final há 7,5±6 anos. 31% das participantes apresentaram critérios e foram classificadas com SM. As que pertenciam ao grupo pré-menopausa sem SM (24,2 [23,4; 25,0]) apresentaram desempenho cognitivo no domínio da memória superior às participantes pré-menopausa com SM (20,8 [20,0; 22,5]) e pós menopausa sem SM (22,0 [20,7; 23,3]) e com SM (22,1 [20,9; 23,2]). Não houve diferença entre o desempenho das participantes pós-menopausa com e sem SM. Com a inclusão da covariável AFL ($\beta = 1,314 [0,123; 2,321]$ $p=0,010$) a diferença previamente verificada entre as participantes pré-menopausa sem SM (23,9 [22,9; 24,8]) e pós-menopausa sem SM (22,0 [21,0; 23,0]) e com SM (22,3 [20,8; 23,9]) deixou de ser significativa. Conclusion: Foi demonstrado o efeito negativo da SM sobre o desempenho de memória durante a pré-menopausa. A prática de AFL apresenta um efeito positivo no desempenho de memória. Quando consideramos a prática de AFL, o efeito negativo da SM se mantém para as mulheres pré-menopausa, porém, o desempenho inferior das participantes pós-menopausa com e sem SM quando comparadas à participantes pré-menopausa sem SM deixa de ser significativo. Os resultados demonstram que a transição menopausal é um período crítico no que se refere ao desempenho de memória, reforçando a importância da promoção de políticas públicas voltadas à saúde da mulher que incluam uma abordagem multidisciplinar, considerando estratégias farmacológicas e não farmacológicas como a prática de AFL para a manutenção da função cognitiva nesta população. Support: CAPES (Código de Financiamento 001) Protocol: 58595122.0.0000.5659</p>

Title	EFFECT OF PHARMACOLOGICAL AND NON-PHARMACOLOGICAL THERAPY ON MEMORY AND LEARNING IN THE ADHD EXPERIMENTAL MODEL
Authors	ANTONIA FREZ, ROBERTO VICTOR FIGUEIREDO DE OLIVEIRA GONÇALVES, ANA KÉSSIA DO NASCIMENTO GOMES, ANDERSON LUIZ BEZERRA DA SILVEIRA, -
Affiliations	Departamento de educação física e desporto, UFRRJ
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is defined as a neurodevelopmental dysfunction that is evident in childhood and can also have effects in adolescence and adulthood. Psychopharmacological interventions are commonly used for treatment; although they present positive effects, various adverse effects caused by prolonged use prompt the search for non-pharmacological approaches. Therefore, evidence suggests that resistance training can be used to achieve responses similar to those of psychostimulants, reducing the characteristic symptoms of ADHD. Objective: To investigate the effect of high-intensity resistance training, with or without pharmacological therapy, on memory and learning in an experimental model of ADHD. Methods: The study was approved by the Animal Use Ethics Committee of UFRRJ under the number 23083.014058/2020-15. Forty rats, aged 6-week-old, were separated into four groups: control (ADHDct), trained (ADHDtr), pharmacotherapy (ADHDmp), and trained + pharmacotherapy (ADHDtr+mp). Behavioral assessments were conducted using the Barnes Maze test and the passive avoidance test. Pharmacological treatment consisted of the orogastric administration of methylphenidate hydrochloride at a therapeutic dose of 2 mg/kg, in a concentration of 0.2 mg/mL. Non-pharmacological therapy consisted of 6 weeks of high-intensity resistance training, using a validated ladder-climbing protocol. For statistical analysis, variables were subjected to the Shapiro-Wilk normality test, and parametric analyses were conducted using one-way and two-way ANOVA. Welch's correction was applied for one-way ANOVA, and Tukey's post-hoc test was used for two-way ANOVA. Data were presented as mean \pm standard error of the mean. The significance level adopted was $p < 0.05$. Results: Memory was evaluated using the Barnes Maze test, where the parameter analyzed was the time taken by the animal to enter the escape box. A significant reduction was observed between sedentary ADHDct vs. trained ADHDct (ADHDct: 52.6 ± 19.5 vs. ADHDtr: 32.1 ± 13; $p = 0.0038$), sedentary ADHDct vs. sedentary ADHDmp (ADHDct: 77 ± 7 vs. ADHDmp: 45.4 ± 5.6; $p = 0.0007$), and sedentary ADHDct vs. trained ADHDmp (ADHDct: 37.1 ± 7.6 vs. ADHDmp: 62.8 ± 14.1; $p < 0.0001$). Additionally, when evaluating learning through the passive avoidance test, a significant difference was demonstrated between sedentary ADHDct vs. trained ADHDct (ADHDct: 77.8 ± 6.3 vs. ADHDtr: 270.4 ± 17; $p < 0.0001$), sedentary ADHDct vs. sedentary ADHDmp (ADHDct: 64.4 ± 10.1 vs. ADHDmp: 180.2 ± 11.6; $p = 0.0001$), and sedentary ADHDct vs. trained ADHDmp (ADHDct: 122.3 ± 57.8 vs. ADHDmp: 254.4 ± 13; $p < 0.0001$). Moreover, there was a significant difference between sedentary ADHDmp vs. trained ADHDmp (ADHDmp: 180.2 ± 11.6 vs. ADHDmptr: 254.4 ± 13; $p = 0.0036$). Conclusion: Resistance training has proven to be an effective and low-cost non-pharmacological therapy for improving memory and learning in an experimental model of ADHD, with benefits similar to those of pharmacological treatment. Support: This study was partly funded by the Coordination for the Improvement of Higher Education Personnel, Brazil (CAPES), Funding Code 001. Protocol: nº 23083.014058/2020-15.</p>

Title	Modulatory effects of aerobic physical exercise on body mass and redox state in regions of the central autonomic nervous system in juvenile rats overnourished in lactation
Authors	ELENILSON MAXIMINO BERNARDO, JONATA HENRIQUE DE SANTANA, ALLIFER ROSENDO PEREIRA, DEISIANE DE ARAUJO CORREIA, DEYVISON GUILHERME MARTINS SILVA, CLAUDIA JACQUES LAGRANHA, MARIANA PINHEIRO FERNANDES, DAYANE APARECIDA GOMES-
Affiliations	Fisiologia e Farmacologia, UFPE, Centro Acadêmico de Vitória, UFPE, Nutrição, UFPE
Session	8-Fisiologia do Exercício
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Being overweight or obese in the early stages of life, linked to sedentary behavior, is associated with the development of cardiometabolic diseases in adulthood and premature death. Regular exercise is related to modulations in the autonomic central nervous system and reduced morbidity and mortality.</p> <p>Objective: To evaluate the effects of exercise on body mass and REDOX balance in the brainstem and hypothalamus of 54-day-old rats subjected to overnutrition during lactation. Methods: This study was approved by the ethics committee (protocol nº 0117/2022). Wistar rats were used, and the groups were divided from the 3rd day of life into normonourished (N) (n=9) and overnourished (S) (n=3). At 23 days, they were subdivided into untrained normonourished (NNT), untrained overnourished (SNT), trained normonourished (NT) and trained overnourished (ST), and at 24 days of life, the physical training protocol was started at 50% of the maximum running capacity on a treadmill, 60 minutes a day, 5 days a week, for 4 weeks and at 60 days, the animals were sacrificed and the brainstem and hypothalamus were collected for biochemical analysis. Data were expressed as a percentage. The significance level was maintained at 5% ($p < 0.05$) for all analyses. Statistical analyses were performed using GraphPad Prism 9.5.0 software. Results: During lactation, we observed an increase in body mass of 15% at 7 ($p = 0.001$), 14% at 14 ($p = 0.0207$), and 21% at 21 ($p < 0.0001$) days of life. Group S increased by 11% at 54 days of life ($p < 0.0001$) compared to group N. Group S showed a 30% reduction in citrate synthase (CS) activity compared to group N in the soleus muscle ($p = 0.0134$). However, exercise increased CS activity in the extensor digitorum longus muscle by 55% in the NT and 66% in the ST compared to their control groups ($p < 0.0001$, respectively), and in the soleus only the ST group showed a 40% increase compared to SNT ($p = 0.0317$). Regarding biomarkers of oxidative stress, the SNT group increased malonaldehyde levels compared to NNT by 57% in the brainstem and 23% in the hypothalamus ($p < 0.0001$ and $p = 0.0253$, respectively). However, only the ST group showed a 28% reduction compared to the SNT in the brainstem ($p = 0.0006$) and the hypothalamus by 22% (0.0041). Furthermore, physical exercise reduced carbonyl levels compared to untrained in brainstem ($p < 0.0001$, $p = 0.0001$), while in the hypothalamus, only ST was reduced compared to SNT ($p = 0.0079$). As for enzymatic antioxidant defense, CAT increased by 67% only in the NT group compared to NNT in brainstem ($p < 0.0298$). GST had a 46% reduction in activity in the SNT group compared to NNT in the brainstem ($p < 0.0327$), and interestingly, it showed a 53% increase in the SNT group compared to NNT in the hypothalamus ($p < 0.0080$). In non-enzymatic antioxidant defenses, only the ST group showed a 64% increase in GSH compared to SNT in the brainstem ($p < 0.0001$). In the hypothalamus, the SNT group showed a 34% reduction compared to NNT ($p < 0.0001$); on the other hand, exercise increased by 49% ($p < 0.0001$). In the GSSG results, only the NT group showed a 29% reduction compared to the NNT in the hypothalamus ($p < 0.0137$) Conclusion: Overnutrition during lactation leads to early overweight, damaging oxidative metabolism and enzymatic and non-enzymatic antioxidant defenses in the brainstem and hypothalamus; however, exercise reduces these effects. Support: Fundação de Amparo à Ciência e Tecnologia de PE (FACEPE) e Fundação, Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Protocol: nº 0117/2022</p>

Title	DEHYDRATION-INDEPENDENT DORMANCY DURING DRY WINTER IN A SUBTROPICAL LIZARD
Authors	ANÉ GUADALUPE-SILVA, DEREK F. CAMPOS, LIVIA S. HERVAS, LUCIANE H. GARGAGLIONI, KÊNIA CARDOSO BÍCEGO-
Affiliations	Morfologia e Fisiologia Animal, UNESP
Session	1-Fisiologia Comparada
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The availability of water is critical for animal survival, especially during seasonally dry phases. The tegu lizard (<i>Salvator merianae</i>) exhibits seasonal physiological fluctuations, with high metabolic activity in spring (reproduction) and summer, followed by gradual metabolic reductions in autumn, and eventually enters in dormancy during the dry winter in southeastern Brazil. Previous studies indicate that metabolic reduction during winter is independent of ambient temperature, suggesting no effects of ambient temperature on dormancy of this ectothermic vertebrate. However, there is no evidence of how water supply influences this metabolic suppression during dry season (winter). Objective: Therefore, the present study aimed to evaluate the influence of dehydration on the pattern of metabolic and behavioral reduction during winter in southeastern Brazil, in female and male tegu lizards. Methods: We experimentally exposed tegus of both sexes to control and dehydration conditions during the pre-dormancy (April and May), dormancy (June and July) and post-dormancy (August and September) phases. We monthly assessed plasma osmolality, hematocrit, body mass, rostro-cloacal length, body temperature (Tb) and activity rate (ODBA). Results: Dehydrated animals showed higher osmolality and Tb compared to hydrated lizards ($p < 0.01$), despite the fact that osmolality did not correlate with Tb ($R^2 = 0.169-0.27$; $p > 0.05$ for females and $R^2 = 0.148-0.472$; $p > 0.05$ for males). Increased osmolality during dehydration did not affect ODBA ($R^2 = 0.103-0.125$; $p > 0.05$ for females and $R^2 = 0.054-0.248$; $p > 0.05$ for males), hematocrit ($p > 0.05$), and body mass ($p > 0.05$). Conclusion: Our results suggest that tegus exhibit a synchronized reduction in activity and metabolism during dry winter in southeastern Brazil, regardless their hydration status. This reinforces the idea that these animals do not undergo estivation (metabolic reduction during dry season) but rather enter a state of hibernation (metabolic reduction during winter). Additionally, males seem to be more sensitive to dehydration, as a reduction in their locomotion-associated behaviors was observed, in contrast to females. Support: FAPESP (2021/10910-0; fellowships 2022/13834-6, 2023/00852-9, 2022/13835-2), CNPq (309899/2022-2), CAPES (master fellowship 88887667389/2022) Protocol: CEUA 580/22</p>

Title	Thermal tolerance of Golden Mussel (<i>Limnoperna fortunei</i>, Dunker 1857)
Authors	FERNANDA ARAUJO FERNANDES, KETLYN GARCIA GREZZANA, LEONARDO PUSSIELDI BASTOS, SUELEN RODRIGUES SANTIAGO, PEDRO GAYER DE ARAUJO, GIULLIANO BATELOCHI GALLO, VIVIANE PRODOCIMO, LUCIANA RODRIGUES DE SOUZA BASTOS
Affiliations	Laboratório de toxicologia e avaliação ambiental, LACTEC, Departamento de Fisiologia, UFPR, China Three Gorges Corporation, CTG
Session	1-Fisiologia Comparada
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: <i>Limnoperna fortunei</i> (Mytilidae) commonly known as the Golden Mussel, is an invasive freshwater bivalve species native to Asia. As an invasive species, it has a number of characteristics that give it physiological plasticity which allows with survival, reproduction and dispersal in several habitats. Studies have shown the effect of temperature in reproduction and survival, however, thermal tolerance of <i>L. fortunei</i> at different developmental stages have not been evaluated. Objective: The aim of this study is evaluate the thermal tolerance of golden mussel in five stages and determine lethal temperature (LT50) for each developmental classes. Methods: The larval samples were obtained on Três Lagoas (MS) and the other specimens was obtained on Foz do Iguaçu (PR). The experimental temperatures was 30, 35, 40 and 50°C. The mean value for control group was 23.32°C. The tolerance experiments occurred during 60 min for larvae and 96 h to other stages. We use Probit analysis to calculate lethal temperatures for 10, 50, 90 and 99% of specimens. Statistical difference between stages was performed by Kaplan-meyer and Log-rank test. Results: Lethal temperature (LT50) for mussels belonging to Class I (Larvae) was 37.79°C (n=307/ml), Class II (Post-larvae) 30.44°C (n=80), Class III (Juveniles I) 32.55°C (n=80), Class IV (Juveniles II) 34.65°C (n=80) and Class V (Adults) 34.68°C (n=80). No statistically significant difference between classes II, III, IV and V was found, witch corroborates with other studies. Although, <i>L. fortunei</i> shows thermal tolerance the sensibility to increased temperature did not differing between classes, except for larval that resist to 60 min of exposure. Larval stage was more sensitive than others. Conclusion: The lethal temperature (LT50) for <i>L. fortunei</i> is ~34°C. Values from 40°C causes mortality in first 24h. Larvae LT 50 (37.79°C) is higher than other stages (30.44°C-34.68). Determine thermal limits of this species may be a powerful tool to development technique to control. Support: China Three Gorges Corporation and Lactec Institutes Protocol: N.A.</p>

Title	EFFECTS OF GLYPHOSATE EXPOSURE ON EARTHWORMS AND PREDICTION OF TOXICITY BY MATHEMATICAL MODELING
Authors	DIOVANA GELATI DE BATISTA, JULIANA FURLANETTO PINHEIRO, ISADORA SULZBACHER OURIQUE, MARIA EDUARDA TODENDI DE BRAGAS, LETÍCIA MARIÁ CASSOL GÖRCK, LUCAS MACHADO SULZBACHER, ANTÔNIO AZAMBUJA MIRAGEM, PAULINE BRENDLER GOETTEMES FIORIN, RAFAEL Z. FRANTZ, THIAGO GOMES HECK
Affiliations	Programa de Pós Graduação em Modelagem Matemática e Computacional, UNIJUÍ, Curso de Medicina, UNIJUÍ, Curso de Biomedicina, UNIJUÍ, Escola Estadual Técnica 25 de Julho, EET25, Curso de Licenciatura em Ciências Biológicas, IFFar, Programa de Pós Graduação em Atenção Integral à Saúde, UNIJUÍ
Session	1-Fisiologia Comparada
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Glyphosate-based herbicides (GBH) are the most used pesticides; however, they may threaten the health of non-target organisms. In this way, earthworms are bioindicators of soil health and have been used as models to study the immune system and for the elaboration of toxicological predictive models.</p> <p>Objective: In this study, we investigated if exposure to GBH at agricultural doses induces mortality and alters the body mass, behavior, and immunological profile of earthworms. We used these data to develop a mathematical model to predict toxicity. Methods: 348 adult <i>Eisenia andrei</i> earthworms (0.27 ± 0.06 g) were divided into 5 groups: Control (C, native soil), G1.5, G3, G6, and G9 (soils exposed to GBH at doses $\sim 1.5, 3.0, 6.0$ and 9.0 L/ha). Each experimental unit (EU) contained 100g of soil/animal, with 5% organic matter with water (control) or GBH (Roundup®, Original DI, Monsanto, 44.5% w/v). We conducted a 168-h Toxicity Test (n=60) to analyze body mass and mortality rate, and the soil temperature was verified. Also, we applied a 48-h Avoidance Test, in which the EU was divided in half (water/GBH) at different doses of GBH (n=144), and the avoidance behavior was calculated $[(AB = ((C-G)/n) * 100)]$, where C and G were the n° of animals found on the control or GBH sides, respectively. Finally, we performed a 48-h Toxicity Test to evaluate the effects of GBH (n=144) on the earthworm's immune profile. The coelomocytes were collected, and cell viability (trypan blue), density, and total cell count were measured. Data were expressed as mean \pm s.d. and analyzed by one- or two-way ANOVA (or Kruskal-Wallis test), followed by Tukey's (or Dunn's) multiple comparisons test and Pearson Correlation, considering $P < 0.05$. Results: Exposure to GBH induced mortality in earthworms at the highest dose (MT, Mortality%: C=0; G3=10; G9=30*; *P=0.028 vs. C; Relative Risk=1.30; CI95% 1.06-1.30). Furthermore, the earthworms that survived the highest dose had a reduction in body mass (BM, Body mass g: C=0.23\pm0.02; G3=0.22\pm0.02; G9=0.20\pm0.03*; *P<0.01 vs. C, F(2,48)=5.7). The GBH decreased the soil temperature (AUC °C.h-1: C=313\pm8; G3= 262\pm6*; G9=228\pm6*; *P<0.001 vs. C, F(2, 9)=133.4). We found a correlation between the soil temperature at the end of the experiment and the body mass of animals (r=0.681; P=0.01). The G6 presented avoidance behavior (AB, %: C=-28\pm61; G1.5=55\pm50; G3=44\pm81; G6=83\pm18*; *P=0.01). Finally, when the animals had no option to avoid GBH, G3 and G6 groups reduced cell viability (CV, Cell viability%: C=76\pm19; G1.5=64\pm22; G3=57\pm29*; G6=56\pm21*; *P\leq0.01 vs. C), without altering total cell count or cell density (P>0.2). Thus, we built a model to predict the effects of exposure to GBH: $F(x) = \{MT = \log(1 - pp) = \beta_0 + \beta_1 \times [GBH]; BM = \alpha_0 + \alpha_1 \times [GBH]; AB = \gamma_0 + \gamma_1 \times [GBH]; CV = \delta_0 + \delta_1 \times [GBH]\}$, with intercept ($\beta_0, \alpha_0, \gamma_0, \delta_0$) and GBH dose coefficient ($\beta_1, \alpha_1, \gamma_1, \delta_1$). Simulating for an animal (0.22g), the predicted results would be (mean-IC95%): MT(%): C=0(0-0); G1.5=0.15(0.05-0.25); G3=0.45(0.35-0.55); G6=0.75(0.65-0.85); BM(g): C=22(22-22); G1.5=21(20-21); G3=20(19-21); G6=18(16-19); AB(%): C=0(0-0); G1.5=30(20-40); G3=60(50-70); G6=90 (80-100); CV(%): C=100(100-100); G1.5=95(85-100); G3=80(70-90); G6=60(50-70). Conclusion: Exposure to GBH at an agronomic dose or higher threatens earthworm survival and immune defense and provides evidence for a mathematical model to predict GBH toxicity. Support: This study was partially supported by the Coordination for the Improvement of Higher Education Personnel (CAPES) in Brazil, under grant 001, and by the Brazilian National Council for Scientific and Technological Development (CNPq) under grants 307926/2022-2 and 405546/2023-8 to TGH, and 309425/2023-9 to RZF. Protocol: N.A.</p>





Title	HOW SEX AFFECTS ANOXIA RESISTANCE IN TRACHEMYS SCRIPTA
Authors	SOFIA LOPES BASÍLIO DA SILVA MATOS, KAOMA STEPHANI DA COSTA SILVA, ANGELITA MARIE STABILE, RAPHAEL E SZAWKA, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI
Affiliations	Department of Animal Morphology and Physiology, UNESP, Department of Physiology and Biophysics, UFMG
Session	1-Fisiologia Comparada
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Freshwater turtles can tolerate oxygen depletion conditions, such as anoxia, by drastically lowering their metabolic rate. In the environment, these anoxic periods, dependent on temperature, can endure up to forty days. Despite the number of studies regarding several aspects of anoxia resistance in turtles, no research has ever evaluated if this response is sex-dependent. Objective: Therefore, this research assessed metabolic, respiratory, and molecular differences between male and female adults of <i>Trachemys scripta</i> exposed to anoxia, hypoxia, and normoxia. Methods: In total, 107 adults of <i>Trachemys scripta</i>, split into 68 females and 39 males, were previously acclimatized to 12°C water. Four days before the experiments, the right subclavian artery was cannulated. On the day of the exposure, before and after the experiments, blood gases and lactate were measured, and by the end, tissue was collected for further analyses. Ventricle HIF-1 expression was quantified by western blot, plasma steroids were estimated by ELISA kits, and catecholamine concentration in the forebrain and hindbrain was obtained by HPLC. To analyze the data, each variable was compared by two-way ANOVA, considering sex and treatment as factors. As to the blood gases analysis, a one-way ANOVA was added to compare before and after conditions. Results: The results described here are only the sex-related differences significant results ($P < 0.05$), presented as mean \pm error. Males presented lower PaO₂ in all conditions, lower pH after hypoxia and anoxia exposure, and higher plasma lactate. The ventricular HIF1-α expression exhibited a male-biased increase compared to females during anoxia (males: 2.18 ± 0.592 vs females: 1.62 ± 0.698 relative expression). Males did not present any significant changes during exposures for any of the catecholamine concentrations tested (all presented in pg/ug). Females, on the other hand, exhibited variable concentrations of catecholamines when faced with atmospheric oxygen changes. Regarding female's brainstem, hypoxia decreased noradrenaline (NORA, males: 16.72 ± 3.369 vs females: 9.51 ± 1.921), dopamine (DA, males: 3.22 ± 0.385 vs females: 1.92 ± 0.356), 5-HT metabolite (5-HIAA; males: 8.33 ± 0.924 vs females: 3.36 ± 0.867), and 5-HT (males: 21.312 ± 3.936 vs females: 11.37 ± 2.613). In addition, females presented a lower DA metabolite (DOPAC)/ DA ratio (males: 0.49 ± 0.09 vs females: 0.18 ± 0.022). In the diencephalon, females had higher NORA and DA concentrations than males (males: 12.83 ± 2.75 vs females: 16.07 ± 1.01, and males: 18.46 ± 4.34 vs females: 25.03 ± 2.13, respectively) under normoxia. After hypoxia exposure, DOPAC/DA ratio was also higher in females (males: 0.12 ± 0.016 vs females: 0.66 ± 0.004). Conclusion: Our results indicate that females adjust their metabolism to atmospheric composition through rapid changes in catecholamine concentrations, particularly in the brainstem, maintaining higher PaO₂, pH, and lactate levels. In contrast, males recruit long-term mechanisms by increasing the transcription of HIF-1. This sex difference could be attributed to sex hormones, the sex influence on size, and since females retain eggs – its calcium could buffer lactate. Support: FAPESP and CNPq Protocol: local CEUA committee (233/2022)</p>



Title	TRIAxIAL ACCELERATION AS A PROXY FOR THE METABOLIC RATE OF TEGU LIZARDS SALVATOR MERIANAE
Authors	JOÃO VITOR PARIS XAVIER, LUCAS APARECIDO ZENA, TIAGO FABRÍCIO CARABOLANTE, ANE GUADALUPE SILVA, MELISSA BARS CLOSEL, LUCIANE HELENA GARGAGLIONI, KÊNIA CARDOSO BÍCEGO
Affiliations	Departamento de Morfologia e Fisiologia Animal, UNESP, Department of Biological and Environmental Sciences, GU
Session	1-Fisiologia Comparada
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Animals expend energy on various physiological processes and interactions with the environment, regulating their metabolic rate according to the energetic demands required at any given time. Measurements of oxygen consumption ($\dot{V}O_2$) are well-defined for inferences of metabolic rate under aerobic conditions. However, this approach becomes limiting in the case of measurements in freely behaving animals, both in captivity and in the field. In these cases, minimally invasive methodologies capable of storing energy expenditure data over long periods have gained increasing attention. Triaxial accelerometers are capable of detecting acceleration in the three orthogonal axes X, Y, and Z, and have been increasingly used as proxies for metabolic activity in different species. The tegu lizard, <i>Salvator merianae</i>, exhibits significant metabolic variation throughout the year, characterized by hibernation in winter and facultative endothermy during reproduction in spring. Objective: The hypothesis tested was that there is a high correlation between $\dot{V}O_2$ of <i>S. merianae</i> and the overall dynamic body acceleration (ODBA) measured by accelerometers. Methods: For this, 10 female tegu lizards (1.5-3.2 kg body mass) were used, each one equipped with a leather vest containing an accelerometer fixed in the scapular region. These animals were individually placed in a 48-liter chamber for O_2 consumption measurements by open-flow respirometry, allowing simultaneous determination of $\dot{V}O_2$ and ODBA. The experimental protocols were approved by the local Animal Ethics Committee (CEUA; protocol no. 008948/18). The experiments were conducted with the same individuals in September (reproduction), December (post-reproduction), May (pre-hibernation), and July (hibernation). Results: A linear regression model between ODBA and $\dot{V}O_2$ ($R^2 = 0.64$) for the entire set of seasons, considering the repetition in each season, showed a significant relationship between ODBA and $\dot{V}O_2$ ($P < 0.001$). When each season was analyzed separately in a repeated measures model, a significant correlation was observed in all seasons. In this case, winter, the season with the lowest metabolic activity, showed the highest correlation level ($R^2 = 0.74$; $P < 0.001$), while spring, the season with the highest metabolic activity, showed the lowest correlation level between the two variables ($R^2 = 0.62$; $P < 0.001$). Summer ($R^2 = 0.66$; $P < 0.001$) and autumn ($R^2 = 0.71$; $P < 0.001$) presented intermediate correlations. Conclusion: The lowest correlation between ODBA and $\dot{V}O_2$ in spring may indicate that the metabolic increase in females is not only due to their behavioral activity, which can be detected by accelerometers, but also to folliculogenesis and vitellogenesis processes. In conclusion, the positive correlation between ODBA and $\dot{V}O_2$ in tegu lizards indicate a possible application of this methodology during all seasons of the year. Support: FAPESP (2021/10910-0), CNPq (309899/2022-2). Protocol: CEUA; protocol no. 008948/18</p>

Title	Vida na escuridão: respostas metabólicas e cardiorrespiratórias à variação de temperatura e hipóxia ambiental da espécie troglóbica de bagre cavernícola, <i>Ancistrus cryptophthalmus</i> Reis, 1987 (Siluriformes: Loricariidae)
Authors	LEONARDO DE ASSIS, DEREK FELIPE DE CAMPOS, SOFIA LOPES BASÍLIO DA SILVA MATOS, MARIA ELINA BICHUETTE, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI BATALHÃO
Affiliations	Departamento de Morfologia e Fisiologia Animal, UNESP
Session	1-Fisiologia Comparada
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: As ações antrópicas atuam de forma negativa ao meio ambiente, como desmatamento, poluição e eutrofização de meios aquáticos. A fauna cavernícola, em geral, pode ser considerada muito frágil e altamente ameaçada. Este fato só se agrava quando citamos as espécies consideradas troglóbicas (só constituem populações fonte dentro de habitats subterrâneos). O presente estudo pretende compreender a tolerância à hipóxia ambiental (baixa concentração de oxigênio no ambiente) e a sensibilidade térmica do bagre cavernícola <i>Ancistrus cryptophthalmus</i>, que habita cavernas da região de São Domingos, Goiás, e é uma espécie troglóbica classificada como Em Perigo (EN) na Lista Oficial da Fauna Brasileira Ameaçada de Extinção de 2022. Objective: Avaliar a tolerância à hipóxia ambiental e a sensibilidade térmica do bagre cavernícola <i>Ancistrus cryptophthalmus</i>, que habita cavernas da região de São Domingos, Goiás, e é uma espécie troglóbica classificada como Em Perigo (EN) na Lista Oficial da Fauna Brasileira Ameaçada de Extinção de 2022. Methods: Os animais utilizados nos experimentos foram coletados com a Licença SISBIO (nº 90904-1) e mantidos em laboratório com autorização da CEUA (Protocolo nº 9520/23) da UNESP/FCAV. As análises preliminares foram feitas em câmara respirométrica (respirometria intermitente). Foram realizados testes de tolerância à hipóxia (100%, 50%, 25%, 12,5% e 5% O₂) e variação de temperatura (19, 20, 21 e 22°C) com medição de frequência de ventilação branquial (fB) e análise comportamental. Os indivíduos foram adaptados por 24 horas na câmara antes do início do protocolo experimental. Os testes foram visualizados por uma câmara infravermelho (noturna) para evitar interferência de luz no comportamento do animal de caverna. Results: As análises preliminares indicaram uma baixa taxa metabólica (MO₂ = 37,8 mgO₂.kg⁻¹.h⁻¹) e baixo ponto crítico de oxigênio (PO₂crit – 0,02% O₂). A redução de O₂ e alteração da temperatura promoveu aumento da fB e alterou a movimentação do animal: -100%O₂ à 19°C a fB foi de 42ml/min e o peixe não se movimentou; em 50%O₂ à 20°C, a fB foi de 125 ml/min e o animal apresentou muita movimentação corporal; em 25%O₂ à 21°C, a fB foi de 171 ml/min e ocorreu extrema movimentação corporal; em 12,5%O₂ à 22°C, a fB foi e 132 ml/min e houve muita movimentação corporal; e em 5%O₂ à 22°C, a fB foi de 113 ml/min e o animal ficou letárgico. Conclusion: Nossos dados preliminares mostram que a espécie <i>Ancistrus cryptophthalmus</i> tem aumento da ventilação branquial durante a hipóxia e apresenta PO₂ crítica 0,02% O₂. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Protocol: 9520/23</p>

Title	Sleep Deprivation is a risk factor predisposing to severe chemotherapy-associated intestinal mucositis
Authors	JOÃO LUCAS SILVA PINHEIRO, LUCAS HENRIQUE MARQUES RODRIGUES, VICTÓRIA MARTINS RODRIGUES DOS SANTOS, LORENA DUARTE DA SILVA, ANA LUIZA COSTA FERREIRA, CECÍLIA LOURENA OLÍMPIA ARAGÃO DA CUNHA, ARTHUR VINÍCIOS TENÓRIO DA SILVA, MARCELLUS HENRIQUE LOIOLA PONTE SOUZA, LUIZ ALBERTO REIS MATTOS JUNIOR, RENAN OLIVEIRA SILVA DAMASCENO
Affiliations	Department of Physiology and Pharmacology, UFPE, Department of Physiology and Pharmacology, UFC, Center for Medical Sciences, UFPE
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Intestinal mucositis is an adverse effect related to chemotherapy with 5-fluorouracil (5-FU), due its lack of specificity for tumor cells, with a significant impact on quality of life and therapeutic successes of cancer patients. Associated with this, sleep disorders are common in these patients, which reduces immune response, worsen inflammation and impair its cognitive abilities. Objective: To investigate the impact of sleep deprivation (SD) on 5-FU-induced intestinal mucositis. Methods: Balb/c mice (7-8 weeks old, 20-25g, n=6, Protocol nº 82/2021) received 5-FU (450 mg/kg, i.p.) associated or not with SD. The ponderal curve, leukocytes, morphometry, oxidative stress and inflammation markers, and gastrointestinal (GI) motility were evaluated after 3 days. Results: 5-FU reduced leukocytes count (2596.0±257.9 cells/mm³; P<0.05) and ponderal curve (-14.1±1.0%), compared to control (6433.0±218.5 cells/mm³ and +1.7±1.0%, respectively). Compared to 5-FU, SD+5-FU animals (-15.0±0.8%) had no alteration in ponderal curve, but exacerbated leukopenia (1568.0±206.1 cells/mm³; P<0.05). 5-FU also reduced (P<0.05), compared to control, villus height and crypt depth in the jejunum (480.0±20.5 vs 650.3±19.8 µm and 137.3±9.5 vs 248.2±16.8 µm, respectively) and ileum (362.5±17.8 µm vs 427.1±21.2 and 129.7±6.2 vs 239.5±13.0 µm, respectively). These effects of 5-FU were intensified (P<0.05) in SD+5-FU mice in the jejunum (352.4±45.1 µm and 116.5±6.5 µm, respectively) and ileum (295.2±10.5 µm and 141.3±8.0 µm, respectively). Moreover, 5-FU (679.5±146.1 and 229.1±35.5 mg/g tissue, respectively) increased (P<0.05) NP-SH consumption in both segments, compared to control (1156.0±110.0 and 587.4±51.7 mg/g tissue, respectively). This effect of 5-FU was potentiated in SD+5-FU animals (162.5±19.3 and 58.2±11.2 mg/g of tissue, respectively; P<0.05). About oxidative stress, compared to control, the MDA and 4-HNE levels were increased (P<0.05) in 5-FU group in the jejunum (26.3±1.2 µM/mg tissue vs 19.6±0.6 µM/mg tissue and 0.153 ± 0.008 OD vs 0.109±0.004 OD) and ileum (23.1±1.2 µM/mg tissue vs 18.5±0.8 µM/mg tissue and 0.15±0.01 OD vs 0.108±0.005 OD). However, SD+5-FU potentiated these effects of 5-FU on 4-HNE production (0.20±0.01 OD) in the jejunum, but not in the ileum, while MDA production was not changed in any of the segments (25.3±1.1 µM/mg tissue and 21.3±1.5 µM/mg tissue, respectively). 5-FU administration (0.9±0.2 and 1.0±0.3 UMPO/mg of tissue, respectively) also increased MPO activity in both segments, compared to control (0.21±0.04 and 0.37±0.07 UMPO/mg of tissue, respectively). Furthermore, SD+5-FU (2.9±0.6 and 2.0±0.3 UMPO/mg of tissue; P<0.05) intensified the effects of 5-FU. About GI motility, 5-FU delayed emptying gastric, compared to control (29.1±2.4% vs 16.9±1.7%; P<0.05), while SD+5-FU (29.2±2.0%) did not alter this parameter, compared to 5-FU group. Compared to control, 5-FU provoked a delay in intestinal transit (2.43±0.06 vs 2.72±0.09), which was intensified in SD+5-FU animals (2.08±0.07). Conclusion: SD worsens 5-FU-induced intestinal mucositis, which was associated with intense inflammation and oxidative stress. These data provide a basis for a management clinical of cancer patients undergoing chemotherapy with 5-FU. Support: CNPq and FACEPE. Protocol: Protocol nº 82/2021.</p>

Title	Carbon monoxide, an endogenous gaseous mediator, regulate cholera toxin-induced secretory diarrhea: Evidence for its direct interaction with toxin
Authors	LORENA DUARTE DA SILVA, JOÃO LUCAS SILVA PINHEIRO, LUCAS HENRIQUE MARQUES RODRIGUES, VICTÓRIA MARTINS RODRIGUES DOS SANTOS, LARISSA GONÇALVES MACIEL, THIAGO DE SOUZA LOPES ARAÚJO, CECÍLIA LOURENA OLÍMPIA ARAGÃO DA CUNHA, ANA LUIZA COSTA FERREIRA, CONCEIÇÃO DA SILVA MARTINS, DAYANE APARECIDA GOMES, EDUARDO CARVALHO LIRA, MARCELLUS HENRIQUE LOIOLA PONTE SOUZA, JAND-VENES ROLIM MEDEIROS, RENAN OLIVEIRA SILVA DAMASCENO
Affiliations	Department of Physiology and Pharmacology, UFPE, Department of Fundamental Chemistry, UFPE, Biotechnology and Biodiversity Center Research, UFDPar, Department of Physiology and Pharmacology, UFC
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Carbon monoxide (CO) is a gasotransmitter produced from heme oxygenase (HO) enzymes, with key role in controlling digestive functions, such as maintenance of mucosal integrity, blood flow regulation and ion transport. However, the effect of CO has not been studied in choleric diarrhea. Objective: To evaluate the effects of the HO-1/CO signaling on cholera toxin-induced diarrhea and its mechanisms of action. Methods: BALB/c mice (25-30g; 8 weeks old; n=6; Protocol nº 17/2019) received CORM-2 (a CO donor), iCORM (inactive CORM-2), Hemin (a HO-1 inducer) or ZnPP (a HO-1 inhibitor) and were inoculated with cholera toxin (CT; 100 µL; 0.5 or 1 µg) or PBS into the intestinal loops. After 4 h, the mice were euthanized and samples were collected to evaluate intestinal fluid, Cl⁻ ion, intestinal absorption, vascular permeability, histology, bilirubin, immunohistochemistry for HO-1, and CO-CT interaction. Results: CT increased (P<0.05) the loop weight/length ratio (0.093±0.006 g/cm), Cl⁻ secretion (24.6±4.1 mg/dL) and vascular permeability (11.8±0.6 µg/mg tissue), compared to PBS group (0.053±0.003 g/cm, 2.7±0.7 mg/dL, 5.0±0.6 µg/mg tissue, respectively). However, CORM-2 (0.064±0.004 g/cm, 10.5±1.0 mg/dL and 7.4±1.0 µg/mg tissue, respectively) or Hemin (0.071±0.007 g/cm, 12.2±0.8 mg/dL and 7.2±0.6 µg/mg tissue, respectively), but not iCORM (0.086±0.007 g/cm), reduced (P<0.05) these parameters altered by CT. The effects of Hemin were reversed (P<0.05) by ZnPP (0.11±0.01 g/cm and 23.5±3.6 mg/dL). Furthermore, ZnPP did not alter the loop weight/length ratio (0.110±0.009 g/cm) or Cl⁻ secretion (30.4±7.3 mg/dL) increased by CT, but potentiated (P<0.05) the effects when a submaximal dose of CT (0.10±0.01 vs 0.069±0.003 g/cm and 25.4±4.9 mg/dL vs 14.8±2.5 mg/dL, respectively) was used. The intestinal absorption was not altered by CORM-2, Hemin or ZnPP, compared to the PBS group. CT also altered the crypt-villus architecture (3.2±0.1 µm), compared to PBS group (4.8±0.7 µm). However, this harmful effect was prevented by CORM-2 (4.3±0.2 µm). Mice inoculated with CT had increased (P<0.05) HO-1 expression and bilirubin levels (9.2±0.6 mg/g tissue), compared to PBS group (5.9±0.8 mg/g tissue). Fluorometric analysis showed reduced (P <0.05) fluorescence emission when CT was incubated with CORM-2 (309.0±5.2 AUC), compared to CT alone (805.0±4.3 AUC). A Stern-Volmer plot was made at 25° and 45 °C, where its linear profile indicated that only one type of fluorescence quenching occurred, while the decreasing slope with increasing temperature suggests static CO-CT interaction. Elisa data showed that CORM-2 did not alter the GM1-bound CT. However, pre-incubation of CT with CORM-2 (2 µM: 41.2±0.8; 20 µM: 42.5±0.9 and 200 µM: 29.3±1.7%) revealed a decreased (P<0.05) GM1-bound CT, compared to CT alone. Finally, molecular docking showed that CO occupies a cavity close to the NAD⁺ binding site and interacts with residues Ile 64, Ser 68 and Gln 111, suggesting that it may inhibit CTA and affect its intracellular signaling. Conclusion: CO regulate CT-induced secretory diarrhea, with control of fluid secretion, Cl⁻ efflux, and preservation of the crypt-villus and reduction of the vascular permeability. Its antisecretory effect occurs by direct of CO with toxin, which reduce its binding to the GM1 receptor. Our results suggest an application of CO in the management of cholera diarrhea. Support: CNPq and FACEPE. Protocol: Protocol No. 0017/2019</p>

Title	Sleep deprivation modulates ethanol-induced gastric injury in rodents: Insights from oxidative stress
Authors	VICTÓRIA MARTINS RODRIGUES DOS SANTOS, LUCAS HENRIQUE MARQUES RODRIGUES, LORENA DUARTE DA SILVA, JOÃO LUCAS SILVA PINHEIRO, ARTHUR VINÍCIOS TENÓRIO DA SILVA, RENAN OLIVEIRA SILVA DAMASCENO
Affiliations	Department of Physiology and Pharmacology, UFPE
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Good quality sleep is crucial for maintaining health and regulating physiological functions. Thus, alterations in sleep patterns have been linked to onset of gastrointestinal disorders, such as colitis and exacerbation of intestinal mucositis (unpublished data). Conversely, sleep deprivation has been shown to potentially enhance immune responses to infections and increases antioxidant responses in rat brain regions. However, the impact of sleep deprivation on the gastric mucosa, particularly regarding oxidative injury, remains unclear. Objective: To evaluate the impact of sleep deprivation on ethanol-induced gastric injury in rodents. Methods: Male Swiss mice (8 weeks old, 25-30g; n=6; Protocol nº 22/2024) were subjected to 72h of sleep deprivation (SD), followed by ethanol (SD+E) or saline via gavage. Another group underwent SD followed by 7 days of recovery sleep (Rebound group). Control groups received only ethanol or saline. After 1h, mice were euthanized, stomach were opened, photographed, and samples were collected for oxidative stress analysis, including non-protein sulphhydryl groups (NP-SH), reduced glutathione (rGSH) and 4-hydroxynonenal (4-HNE). The macroscopic gastric injury was measured with Image J® software. In other experiment, Evans blue was administered via the retro-orbital plexus 30 min before euthanasia to assess gastric vascular permeability. Results: SD reduced ($P<0.05$) gastric injury ($32.0\pm4.6\%$) compared to the ethanol group ($54.2\pm5.2\%$). However, animals with recovered sleep ($49.7\pm9.4\%$) showed a reversal ($P<0.05$) of this protective effect, with no difference ($P>0.05$) compared to the ethanol group ($65.7\pm10.7\%$). Neither SD nor REB animals exhibited macroscopic injury. About oxidative stress, SD prevented reductions in gastric antioxidant defense by ethanol, evidenced by higher NP-SH (882.9 ± 97.3 mg/g tissue vs 518.6 ± 88.6 mg/g tissue; $P<0.05$) and rGSH (19.0 ± 1.2 mg/g tissue vs 11.7 ± 2.0 mg/g tissue; $P<0.05$), compared to the ethanol group. SD and saline control groups had baseline levels of NP-SH (1166 ± 194.6 and 1643 ± 153.5, respectively), and rGSH (23.57 ± 1.5 and 37.33 ± 2.4, respectively). These findings were supported by decreased lipid peroxidation, measured by 4-HNE levels (0.24 ± 0.03 O.D.; $P<0.05$) in SD+E animals compared to the ethanol group (0.35 ± 0.05 O.D.). SD and saline animals exhibited basal levels (0.20 ± 0.03 and 0.16 ± 0.02, respectively). Additionally, the REB+E group showed a reversal of the effects observed by SD on ethanol-induced gastric oxidative stress, as there were no difference ($P>0.05$) in NP-SH (342.4 ± 38.7 mg/g tissue) and rGSH (7.3 ± 0.8 mg/g tissue), but not in 4-HNE levels (0.15 ± 0.01 O.D.; $P>0.05$), compared to the ethanol group (262.2 ± 22.2 mg/g tissue, 6.8 ± 1.8 mg/g tissue and 0.22 ± 0.02 O.D., respectively). REB animals maintained basal levels (654.8 ± 57.1 mg/g tissue; 19.2 ± 0.68 mg/g tissue; 0.11 ± 0.01, respectively). Ethanol increased ($P<0.05$) gastric vascular permeability (32.2 ± 1.8 mg/animal) compared to the saline group (14.25 ± 1.2 mg/animal). However, this effect was reversed in SD+E animals (21.8 ± 1.3 mg/animal). Conclusion: Our data indicate that sleep deprivation exerts a protective effect on gastric mucosa in an animal model of ethanol-induced injury. This effect was characterized by a reduction in oxidative stress and prevention of increased vascular permeability. The mechanisms underlying this gastroprotective effect have yet to be fully elucidated, warranting further studies. Support: CNPq and FACEPE. Protocol: Protocol No. 0022/2024</p>



Title	Iota-carrageenan from <i>Solieria filiformis</i> modulates oxidative and inflammatory responses for gastrointestinal protection against naproxen-induced injury
Authors	LUCAS HENRIQUE MARQUES RODRIGUES, JOÃO LUCAS SILVA PINHEIRO, WILLER MALTA DE SOUSA, FRANCISCO FELIPE BEZERRA, VICTÓRIA MARTINS RODRIGUES DOS SANTOS, LORENA DUARTE DA SILVA, SAMARA RODRIGUES BONFIM DAMASCENO OLIVEIRA, RUDY DIAVILA BINGANA, ANDRÉ LUIZ DOS REIS BARBOSA, MARCELLUS HENRIQUE LOIOLA PONTE SOUZA, ANA LÚCIA PONTE FREITAS, RENAN OLIVEIRA SILVA DAMASCENO
Affiliations	Department of Physiology and Pharmacology, UFPE, Department of Biochemistry and Molecular Biology, UFC, Department of Physiology and Pharmacology, UFC, Biotechnology and Biodiversity Center Research, UFDPAr
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Naproxen is a nonsteroidal anti-inflammatory drug (NSAID) widely used in clinical practice. However, its nonspecific inhibition of COX reduces gastrointestinal prostaglandins synthesis via COX-1, leading to the development of lesions. Thus, marine algae have emerged as a natural source of bioactive compounds with gastrointestinal cytoprotective activity that can possibly mitigate the toxicity promoted by NSAIDs. Objective: To evaluate the protective effect and therapeutic safety of an iota-carrageenan from <i>S. filiformis</i> (IC-Sf), a red marine alga, against naproxen-induced gastrointestinal injury. Methods: Male Wistar albino rats (6-8 weeks old, 150-200g; Protocol No. 58/2019) received naproxen (80 mg/kg, p.o.) or saline (control) twice daily for two days, while other groups received IC-Sf (10, 30 or 90 mg/kg, p.o.) 1h before naproxen. In the second day, 4h after naproxen administration, the macroscopic analysis was performed, the animals were euthanized, and stomach and small intestine samples were collected for evaluation of oxidative stress and inflammatory markers. In another protocol, male Balb/c mice (6-8 weeks old, 25-30g) received IC-Sf (30 mg/kg, p.o.) or saline to evaluate gastric secretion and gastrointestinal motor functions. The acute toxicity was analyzed in mice using a single dose of IC-Sf (2000 mg/kg, p.o.) and behavior, body mass, biochemical markers and macroscopic and histopathological evaluation of key organs were performed. Results: IC-Sf reduced ($p < 0.05$) naproxen-induced macroscopic gastric (8.5 ± 1.9 mm vs 18.1 ± 1.7 mm) and intestinal (8.8 ± 1.74 vs 20.6 ± 0.4 score) injury in rats, with maximum effect at 30 mg/kg. Compared to naproxen group, IC-Sf prevented ($p < 0.05$) NP-SH consumption in the stomach (373.3 ± 9.9 $\mu\text{g/g}$ vs 301.1 ± 27.4 $\mu\text{g/g}$) and intestine (68.9 ± 23.3 $\mu\text{g/g}$ vs 16.3 ± 4.1 $\mu\text{g/g}$), and reduced ($p < 0.05$) MDA levels in the both segments (75.3 ± 12.2 $\mu\text{g/g}$ vs 121.1 ± 6.3 $\mu\text{g/g}$ and 85.0 ± 8.2 $\mu\text{g/g}$ vs 214.5 ± 58.8 $\mu\text{g/g}$, respectively). The control had baseline levels of NP-SH and MDA in the stomach (495.4 ± 15.1 $\mu\text{g/g}$ and 75.7 ± 11.2 $\mu\text{g/g}$, respectively) and intestine (149.0 ± 16.6 $\mu\text{g/g}$ and 105.8 ± 17.8 $\mu\text{g/g}$, respectively). About inflammatory response, IC-Sf suppressed ($p < 0.05$) gastric levels of MPO (4.1 ± 1.3 U/mg vs 13.3 ± 2.2 U/mg), TNF-α (430.4 ± 121.2 pg/mL vs 779.9 ± 115.9 pg/mL) and IL-1β (652.8 ± 79.2 pg/mL vs 1162.6 ± 233.1 pg/mL), compared to the naproxen group, and attenuated ($p < 0.05$) MPO (28.2 ± 6.1 U/mg vs 47.2 ± 4.6 U/mg) and IL-1β (1055.1 ± 231.9 pg/mL vs 1108.4 ± 69.6 pg/mL) levels in the intestine, but not TNF-α (1055.1 ± 231.9 pg/mL vs 1227.6 ± 273.6 pg/mL). Baseline values of gastric and intestinal MPO (0.9 ± 0.3 U/mg and 5.7 ± 0.9 U/mg), TNF-α (257.5 ± 68.1 pg/mL and 329.3 ± 87.2 pg/mL) and IL-1β (502.6 ± 140.0 pg/mL and 469.3 ± 46.3 pg/mL) were evidenced in the control, respectively. IC-Sf did not alter gastric secretion, emptying or intestinal transit. Toxicological analysis showed that IC-Sf did not alter corporal mass gain or organ weight, while histopathological and biochemical analysis also did not reveal significant differences between the IC-Sf and control groups. Conclusion: IC-Sf had protective effect against naproxen-induced gastrointestinal injury via reduction of oxidative stress and inflammation, in addition to not altering gastrointestinal physiological functions and did not present acute toxic effects. Support: CNPq and FACEPE Protocol: Protocol No. 58/2019</p>



Title	VAGUS NERVE NEURAL CIRCUIT REGULATES BILE ACID SECRETION IN THE LIVER
Authors	JOÃO SÉRGIO DA FONSECA GUIMARÃES, CAMILA DE FÁTIMA CARVALHO BRITO, ROBERTA CRISTELLI FONSECA, LUCAS RODRIGUES-RIBEIRO, ISADORA ZHONG LIANG FERREIRA FENG, MAÍSA ANTUNES, GUSTAVO BATISTA MENEZES, THIAGO VERANO-BRAGA, MARIA DE FÁTIMA LEITE, ANDRÉ GUSTAVO OLIVEIRA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Departamento de Morfologia, UFMG
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The bile is a complex secretion produced by the hepatocytes in the liver, involved in fat emulsification, essential for fat digestion and absorption; in the excretion of toxic substances and in intestinal immunity. Classically the genesis of the initial bile secretion is a mechanical and osmotic process dependent on a myriad of membrane transporters. Albeit a vital process for the organism, the regulation of bile secretion is not clearly elucidated. It is known that the secretion is influenced by humoral and neuronal factors. Objective: We investigated the role of the vagus nerve mediated neural circuit, the main innervation pathway for the gastrointestinal tract, in the regulation of bile secretion. Methods: We used 8 weeks old C57Bl6 mice that were divided in 2 groups (n=5/group per experiment): sham and vagotomy (VNX). Then, we performed liver proteomics and confocal intravital microscopy to address in vivo bile secretion dynamics. Raw mass spectra were analyzed using the MaxQuant software. Proteins were identified by searching the experimental spectra against the murine UniProt FASTA sequence database. Differences were analyzed using one-way ANOVA test considering $p < 0.05$. Differences in bile secretion in vivo were analyzed using Student's t test and considering $p < 0.05$. Results: Following VNX, mice displayed alterations in the hepatic proteomic landscape when compared to sham animals. We identified 453 differentially expressed proteins out of the 2121 proteins. A functional enrichment analysis using the KEGG database revealed an enrichment of proteins (Abcb4, Abcc3, Atp1a1, Atp1b1, Ephx1, Prkacb, Slc22a1 and Slco1a1) in the bile acid secretion pathway. Therefore, we asked whether these changes would impact the physiology of this pathway. For this purpose, we developed a new technique to monitor bile secretion in vivo and in real time by using indocyanine green and liver intravital microscopy. We were able to monitor all the phases of the intrahepatic process of bile secretion: sinusoid capillaries captation (phase 0), the metabolic phases (phases I and II) and the apical secretion phase (phase III). We observed that bile secretion was impaired in animals following VNX, as the amplitude of fluorescence signal was reduced in this group when compared to sham animals (mean intensity of Sham's hepatocytes = 0.5331433; sd =0.07309349 and mean intensity of VNX's hepatocytes= 0.4854003; sd=0.04076579; p-value = 9.985e-11). Also, there was a temporal delay (sham=751.3982 seconds ; sd=174.4501 seconds and VNX= 811.4255; sd=156.4756; p-value =0.0005458) in which maximal signal occurred in VNX hepatocytes. Conclusion: Our results suggest that the vagus nerve plays an important role in bile secretion regulation. Support: FAPEMIG, CAPES, CNPq Protocol: CEUA/UFMG 280/2018.</p>



Title	Exploring the impact of the extracellular matrix on Hepatic Stellate Cell behaviour using 3D Acellular Liver Scaffolds
Authors	GABRIEL REIS PINTO, ALEXANDRE CERQUEIRA DA SILVA FILHO, EVELLYN NUNES GOULART DA SILVA PEREIRA, ANISSA DALIRY, KRISTA ROMBOUTS, REGINA COELI DOS SANTOS GOLDENBERG, MARLON LEMOS DIAS
Affiliations	CPMP, Centro de Pesquisa em Medicina de Precisão, UFRJ, Institute for Liver & Digestive Health, UCL, Instituto Oswaldo Cruz, FIOCRUZ
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Acellular liver scaffolds (ALS) are powerful tools to overcome organ shortage problems. To date, it is unknown whether transplanted ALS are affected by cirrhotic livers, either becoming cirrhotic themselves or instead remaining as a robust template for healthy cell growth after transplantation (tx). Objective: Since Hepatic Stellate Cells (HSCs) play a key role in fibrogenic processes, the aim of this study was to analyse whether the change in the ECM impacts HSC behaviour (pro-fibrotic reverses into a more quiescent state?). Methods: To address this, in vivo and in vitro experiments using human 3D ALS were performed. For in vitro experiments, primary human HSC (250k) were cultured in cirrhotic ALS for 14 days. HSC were then extracted from cirrhotic ALS and reseeded in healthy ALS for 14 days. Histological analysis (H&E), cell viability, RT-PCR (Col1alfa1, PDGFR, ACTA2, and CYTGB), and western blot analysis were performed (n=4). For in vivo analysis, decellularized livers obtained from Wistar rats (CEUA/CCS-UFRJ 097/20) were transplanted into cirrhotic recipient rats. Cirrhotic recipient rats (n=5) received 5% ethanol in drinking water and i.p injections of carbon tetrachloride (1 ml/Kg) for 8 weeks, underwent hepatectomy (10%) and partial ALS orthotopic tx. H&E staining, immunohistochemistry (alfa-SMA), and microcirculation analysis were performed. Results: RT-PCR and western blot analysis from in vitro experiments revealed that the fibrotic HSC reverses to a more quiescent state when HSC are extracted from cirrhotic and subsequently seeded and cultured in healthy ALS. Results from in vivo analysis showed that HSC migrated from the recipient cirrhotic liver to healthy ALS after tx. Histological and microcirculation analyses revealed that HSC underwent remodeling, transitioning into a more quiescent state 30 days after tx. Conclusion: Our results showed that the ECM affected HSC behaviour, reversing from a profibrotic to a quiescent state. 3D ALS were a robust template for healthy cell growth stimulation. Support: CNPq, Capes, FAPERJ, INCT-REGENERA, Ministério da Saúde. Protocol: CEUA/CCS-UFRJ 097/20</p>



Title	A LC-MS Method for the Quantification of Bile Acids in Serum Samples. Case studies with patients of autoimmune hepatitis and liver reperfusion
Authors	JÚLIA MELISSA MARQUES, ISADORA ZHONG LIANG FERREIRA FENG, CLAUDIA ALVES COUTO, HADASSA RAMOS, TERESA CRISTINA FERRARI, LUCIANA COSTA FARIA, ANDRÉ GUSTAVO OLIVEIRA, FERNANDO FABRIZ SODRÉ, JARLEI FIAMONCINI, M. FÁTIMA LEITE
Affiliations	Fisiologia e Biofísica, UFMG, Gastroenterologia, UFMG, Alimentos e Nutrição Experimental, USP, Química Analítica e Ambiental, UnB
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The mortality rate due to liver diseases is high worldwide and keeps increasing partially because of the lack of non-invasive diagnosis methods for some of the pathologies. Bile acids (BA) are small molecules produced by the hepatocytes, primarily intended to emulsify and facilitate the absorption of lipids. They can also be found in the bloodstream and quantified to evaluate liver function. Objective: In the current study we implemented a LC-MS method to characterize the profile of circulating BA that could be used for the diagnosis of liver diseases. Methods: We selected blood samples from the biorepository of Hospital das Clínicas-UFMG, including two clinical cases: a 10-month follow-up of a patient with autoimmune hepatitis, and a case of liver transplant, with blood samples collected before and after reperfusion (COEP 0393.0.203.00-10). Serum from these patients was processed and analyzed by mass spectrometry to establish the circulating BA profile. Analyses were performed using an Agilent 1290 Infinity II liquid chromatograph coupled to an Agilent 6470 triple quadrupole mass spectrometer. Chromatographic separation was performed at 45°C using a Poroshell 120 EC-C18 reversed-phase column (3x100 mm, 2.7 µm, Agilent, Santa Clara, USA). The mobile phases used were ultrapure water (Arium Mini, Sartorius) with 0.1% formic acid and 20 mM ammonium acetate (solvent A) and acetone with 0.1% formic acid (solvent B). Mass spectrometric analyses were performed in positive mode using multiple reaction monitoring (MRM). Results: The method was established for the quantitation of 14 BA, with linearity ranging between 0.05 – 500 nM and limit of detection at 0.5 nM for most targets. It was observed a decrease in BA circulating levels with the course of autoimmune hepatitis, without remarkable changes in the percentual participation of the different BA groups in the circulating BA pool. For the case of liver reperfusion, it was observed a sharp decline in the circulating levels of BA, particularly unconjugated BA, followed by a trend to increase the concentration of BA in serum, 24 hours after reperfusion. Conclusion: We described a method for BA quantification in serum, with good reproducibility, linearity and a relative short run (compared to other methods). The analysis of the two clinical cases indicates the applicability of the method and the potential of using BA to monitor liver function. Further studies are ongoing to properly characterize the effects of autoimmune hepatitis and liver reperfusion in the circulating levels of BA. Support: CNPq, FAPEMIG, CAPES, INCT, Rede-FAPEMIG Protocol: 0393.0.203.00-10</p>

Title	Calcium channel expression in hepatic scaffolds transplanted into cirrhotic livers
Authors	MARIANA NERY FERREIRA, MARIA ALESSANDRA FERREIRA MARTINS, MARLON LEMOS DIAS, REGINA COELI DOS SANTOS GOLDENBERG, ALEXANDRE ANDRADE CERQUEIRA, PAULA VIEIRA TEIXEIRA VIDIGAL, MATHEUS DE FREITAS ITABORAHY, MARIA DE FÁTIMA LEITE
Affiliations	Fisiologia e Biofísica, UFMG, Fisiologia e Biofísica Celular, UFRJ, Departamento de Anatomia Patológica e Medicina Legal, UFMG
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Transplantation (Tx) is the only definitive treatment for liver failure. In this context, the use of Acellular Liver Scaffolds (ALS), which are created by removing cells from liver tissue through decellularization, represent a potential source to overcome organ shortage problems. However, there is currently limited understanding of how ALS function and interact with the body after Tx. Since calcium plays a significant role in both regeneration and liver metabolism, it is crucial to understand its signaling mechanisms. Objective: The objective of this study was to evaluate the intracellular calcium channels expression pattern in ALS transplanted into cirrhotic livers. Methods: For decellularization, livers procured from Wistar rats (n=5) (CEUA/UFRJ 097/20) were perfused through the portal vein at 3 ml/min with water for 2 h followed by 1% Triton X-100 for 2 hours and SDS 1% for 18h. After that, livers were washed with distilled water for 1 day and then submitted to DNA quantification and histology analysis (H&E). Cirrhotic recipient rats (n=5) previously received 5% of ethanol in drinking water and intraperitoneal injections of carbon tetrachloride (1 ml/Kg) every other day for 8 weeks. Then, they were submitted to median lobe hepatectomy (10%) and subsequently to partial ALS orthotopic Tx. Recipients rat serum biochemical analyzes (albumin (ALB) and alanine aminotransferase (ALT)) were measured before and 7-, 15- and 30-days post-Tx. H&E, and immunohistochemistry (IHC) analyzes (Inositol 1,4,5-triphosphate receptor isoform 3, ITPR3) were performed to evaluate ALS 7-, 15- and 30-days post-Tx. Results: ALS macroscopy, H&E staining, and DNA quantification analyzes showed that the decellularization process removed all cell content. Serum biochemical parameters (ALB, ALT) analysis indicated that the presence of the transplanted ALS normalized the ALB and ALT serum biochemical parameters after Tx. Histological findings revealed an extensive ALS recellularization 7-, 15- and 30-days post-Tx. IHC analyses showed a transitory ITPR3 expression in the recipient cirrhotic liver after ALS Tx. A significant ITPR3 higher expression was detected after 7 days post-Tx, followed by a decreasing 15- and 30-days post-Tx (7 day vs. 30 days; P=0.0022). As a perspective, ITPR3 gene expression will be analyzed by qPCR in both recipient and AHA. Conclusion: This preliminary data suggests that the AHA Tx may impact ITPR3 expression on cirrhotic recipient rats contributing to liver homeostasis and regeneration after Tx. Support: FAPERJ e CNPq Protocol: 097/20</p>

Title	MODERATE-INTENSITY EXERCISE MODULATES GASTROINTESTINAL MOTILITY AND AUTONOMIC BALANCE IN RATS WITH ILEITIS
Authors	BRENDA LOIS BARROS DOS SANTOS, ALDA CÁSSIA ALVES DA SILVA, JULIANA SOARES SEVERO, MAISA CAMPÊLO DE SOUSA, FRANCISCO ASSIS DOS SANTOS MOREIRA, LUCAS ESTEVÃO DE SOUSA, HERON SILVA SOARES, ANTÔNIO KLINGEM FREITAS,-, MOISÉS TOLENTINO BENTO DA SILVA
Affiliations	Programa de pós graduação em Ciências Farmacêuticas, Universidade Federal do Piauí, Universidade do Porto, Portugal, ICBAS U.Porto, Programa de pós graduação Farmacologia, Universidade Federal do Piauí, Núcleo de plantas medicinais, Universidade Federal do Piauí, Programa de pós graduação Farmacologia, UFC, Departamento de Biofísica e Fisiologia, Universidade Federal do Piauí
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ileitis is an inflammatory bowel disease (IBD) that affects a significant portion of the world's population. Its causes include neuroimmune, inflammatory, and autonomic imbalances. Physical exercise has been considered a beneficial strategy for managing CD symptoms. However, at the moment, the effect of physical exercise on autonomic changes in gastrointestinal disease remains unknown. Objective: Here, we investigate the impact of physical exercise on gastrointestinal changes, oxidative stress, body composition, and autonomic disorders in rats with ileitis. Methods: Male Wistar rats (n= ~10/group), weighing 260-300g, divided into groups: control; ileitis; and exercise+ileitis. The ileitis was induced with 2,4,6-trinitrobenzene sulfonic acid (TNBS) (40mM, 1mL) intraleally and the control group received only 1mL of 9% saline solution intraleally. The exercise+ileitis group received TNBS after 5 weeks of the swimming trainer (1h/day/4 weeks, 5% of body weight). Results: After 7 days of the ileitis induction, we don't observe the difference in body weight and food intake between all groups. In body composition, a significant increase (P<0.05) in total water was observed in the ileitis group, which was prevented by exercise (216.8±11.4 vs. 79.9±5.9mL) in the control group. Additionally, there was a significant increase (P<0.05) in fat-free mass in the ileitis group compared to the Exercise+ileitis group (296.20±15.63 vs. 145.20±6.02g). Regarding gastrointestinal parameters, the ileitis group showed greater retention in the duodenum (P<0.05) (46.3±2.5 vs. 24.9±1.7%) and less intestinal retention (P<0.05) in the jejunum (34.2±2.3 vs. 47.3± 1.4%) and ileum (14.08±0.88 vs. 34.15±2.38%) compared to the control group. In the Exercise+ileitis group there was a significant decrease (P<0.05) in gastric retention (11.2±1.9 vs. 35.1±1.0%), intestinal retention in the duodenum (24.96±1.66 vs. 46.3±2.56%) and increased retention in the ileum (40.3±3.7 vs. 14.0±0.8%) compared to the ileitis group. The ileitis group in stress parameters showed a significant increase (P<0.05) in MDA (4.81±0.62 vs. 2.2±0.1Kg) and a decrease (P<0.05) in GSH (17.5±0.4 vs. 22.06±1.7 NPSH/mg) compared to control. The Exercise+ileitis group showed a significant increase (P<0.05) in NOx (288.1±9.62 vs. 220.5±4.8 µM), decreased (P<0.05) MDA (2.9 ±0.1 vs. 4.8±0.6 nmol MDA/g tissue) and increased (P<0.05) SOD (2.0±0.1 vs. 1.2±0.1 USOD/mg of tissue) compared to the ileitis group. On the electrocardiogram (ECG), Exercise+ileitis decreased (P<0.05) the heart rate (HR) compared to the ileitis group (342 ± 5.23 vs. 368.6 ± 8.31bpm). In heart rate variability (HRV) parameters, the LF component decreased significantly (P<0.05) in the Exercise+ileitis group compared to the ileitis group (19.85 ± 0.82 vs. 31.32 ± 3.99nu). The LF/HF ratio showed a significant reduction (P<0.05) in both the ileitis (0.38 ± 0.05%) and Exercise+ileitis (0.29 ± 0.01%) groups compared to the control (0.82 ± 0.14%). Conclusion: This study suggests that ileitis causes systemic changes both at the gastrointestinal level and autonomic balance. Physical exercise can prevent these changes, improving GI motility, balancing anti- and pro-oxidant biomarkers and restoring autonomic balance. Support: Capes Protocol: Federal University of Piauí nu</p>

Title	POLYCYSTIC OVARY SYNDROME INDUCES GASTROINTESTINAL DYSMOTILITY AND AUTONOMIC IMBALANCE IN RATS. ROLE OF THE PHYSICAL EXERCISE, PYRIDOSTIGMINE AND ATENOLOL
Authors	JULIANA SOARES SEVERO, ALDA CÁSSIA ALVES DA SILVA, BRENDA LOIS BARROS DOS SANTOS, WENNA LÚCIA LIMA SANTOS, YASMIN DE ANDRADE GOMES, ARMÊNIO AGUIAR DOS SANTOS, MOISÉS TOLENTINO BENTO DA SILVA
Affiliations	Immuno Physiology and Pharmacology, University of Porto – Porto, Portugal., Physiology and Pharmacology, UFC, Pharmacology, UFPI, Biophysics and Physiology, UFPI, Pharmaceutical Sciences, UFPI
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Polycystic ovarian syndrome (PCOS) is an endocrine dysfunction with reproductive and metabolic complications. In a previous study from our research group, we showed that PCOS modifies body composition and nutritional parameters and induces changes in oxidative stress in white and brown adipose tissue. Objective: Here, we investigated the role of the physical, pyridostigmine and atenolol on the gastrointestinal and cardiovascular disorders in rats with PCOS. Methods: Female rats, (190-220g) were divided into: Control (CO), PCOS, PCOS+Pyrido, PCOS+Atenolol and PCOS+Exercise. The exercise protocol was swimming (5% of b.w, 1h/day/21 days). After 21 days we assessed GI motility, heart rate variability (HRV), and electrocardiogram (ECG) in all groups. PCOS was induced by letrozole (1 mg/kg p.o) for 21 days consecutive. The physical exercise, atenolol (20mg/kg, p.o) and Pyridostigmine, treatment (22mg/kg, s.c) started simultaneously with letrozole treatment on day 0. Results: PCOS reduced the % of gastric emptying ($p < 0.05$) compared to CO (51.8 ± 0.6 vs 61.3 ± 2.3%), while the PCOS+Exercise (59.3 ± 1.8 vs 51.8 ± 0.6%) prevented this reduction compared to PCOS. PCOS+Pyrido (65.6 ± 2.8 vs 51.8 ± 0.6%) and PCOS+Atenolol (76.2 ± 4.7 vs 51.8 ± 0.6%) increased ($p < 0.05$) the % of gastric emptying compared to PCOS. Regarding the % of intestinal retention, the PCOS reduced ($p < 0.05$) in the duodenum portion (16.3 ± 1.1 vs 25.7 ± 2.2%) compared to CO. PCOS+Exercise was able to increase ($p < 0.05$) the portion of the duodenum (23.9 ± 1.1 vs 16.37 ± 1.1%) and ileum (18.1 ± 2.3 vs 11.7 ± 1.3%) compared to the PCOS group. The PCOS+Pyrido and Atenolol increased the % of intestinal retention ($p < 0.05$) in the portions of the duodenum (40.9 ± 1.8 / 40.6 ± 2.7 vs 16.3 ± 1.1%), jejunum (37.6 ± 0.8 / 38.3 ± 4.6 vs 27.2 ± 1.8%), and ileum (21.3 ± 2.3 / 21.0 ± 4.0 vs 11.7 ± 1.3%), compared to the PCOS group. The PCOS increased ($p < 0.05$) LF (45.9 ± 1.9 vs 36.1 ± 2.7nu), decreased ($p < 0.05$) HF (50.6 ± 1.8 vs 59.6 ± 2.4nu), compared to CO. The PCOS+Exercise reduced LF ($p < 0.05$) (30.4 ± 1.8 vs 45.9 ± 1.9nu) and increased HF ($p < 0.05$) (57.0 ± 2.2 vs 50.6 ± 1.8nu). The Pyrido reduced LF (32.6 ± 2.0 vs 45.9 ± 1.9nu), increased HF (58.9 ± 1.49 vs 50.6 ± 1.8nu) and also the LF/HF ratio (1.2 ± 0 vs 0.72 ± 0nu). The Atenolol reduced HF (47.2 ± 2.4 vs 50.6 ± 1.8nu) and increased the LF/HF ratio (1.3 ± 0.1 vs 0.7 ± 0.8nu) compared to the PCOS group. The PCOS+Exercise and PCOS+Atenolol increased ($p < 0.05$) the R-R' Interval compared to the PCOS (0.16 ± 0 / 0.16 ± 0 vs 0.14 ± 0s). Regarding heartbeats, there was an increase ($p < 0.05$) in frequency in the PCOS compared to CO (421.8 ± 13.9 vs 372.7 ± 13.7bpm) and a reduction in the PCOS+Exercise (348.3 ± 8.3 vs 421.8 ± 13.9bpm), PCOS+Pyrido (374.6 ± 8.2 vs 421.8 ± 13.9bpm), PCOS+Atenolol (366.9 ± 6 vs 421.8 ± 13.9bpm) compared to the PCOS. There was an increase ($p < 0.05$) in the QRS interval in the PCOS group compared to the CO (0.01 ± 0 vs 0.015 ± 0s). The PCOS+Exercise (0.01 ± 0 vs 0.017 ± 0s), PCOS+Pyrido (0.015 ± 0 vs 0.017 ± 0s) and PCOS+Atenolol (0.015 ± 0 vs 0.017 ± 0s) group had reduced QRS interval compared to the PCOS group. There was an increase in the QTc interval ($p < 0.05$) in the PCOS group compared to the CO (0.059 ± 0 vs 0.052 ± 0s). The PCOS+Exercise (0.053 ± 0 vs 0.059 ± 0s), PCOS+Pyrido (0.053 ± 0 vs 0.059 ± 0s) and PCOS+Atenolol (0.051 ± 0 vs 0.059 ± 0s) group had reduced QTc interval compared to the PCOS group. Conclusion: Polycystic ovary syndrome induces gastrointestinal disorders and changes in autonomic parameters. We suggest parasympathetic modulation by physical exercise, acetylcholinesterase inhibitor (pyridostigmine), or β1-adrenergic receptor blocker (atenolol) may improve these disorders. Support: CAPES. University of Porto. Protocol: Committee for the Use of Anima</p>

Title	HEPATOCTES DIFFERENTIATED FROM INDUCED PLURIPOTENCY STEM CELLS FROM PATIENTS WITH MASLD AND MASH
Authors	JULIA HELENA OLIVEIRA DE BARROS, DÉBORA ALVES COMUNE, ALEXANDRE CERQUEIRA SILVA FILHO, GUILHERME DA MOTTA FERREIRA REZENDE, NATHALIA FERREIRA FERRARI DE SALES, MARLON LEMOS DIAS, TAIS HANAE KASAI-BRUNSWICK, REGINA COELI DOS SANTOS GOLDENBERG
Affiliations	Precision Medicine Research Center, UFRJ, Liver Hemodynamics Laboratory, UFRJ, National Center for Structural Biology and Bioimaging, UFRJ
Session	3-Fisiologia Gastrointestinal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) is the most common cause of chronic liver disease worldwide. Changes in liver fat metabolism significantly contribute to the development of liver diseases, supporting the association of the disease with metabolic dysfunction. Recent studies indicate that genetic factors, such as PNPLA3 gene polymorphism, associated with dietary habits, diabetes and other related variables to contribute to the pathogenesis of MASLD. In some individuals, MASLD may progress to metabolic dysfunction-associated steatohepatitis (MASH), characterized by intense fat deposition in hepatocytes, inflammation, cellular injury with or without fibrosis. However, the reasons why patients with the same degree of MASLD have different outcomes are unknown. Therefore, precision medicine presents itself as an alternative to unravel the mechanisms involved in disease progression, including the use of induced pluripotent stem cells (iPSCs), which hold great potential in disease modeling.</p> <p>Objective: To generate hepatocytes from iPSCs of patients with MASLD and MASH to investigate MASLD progression. Methods: Patients (n=7) were recruited at the hepatology department of Clementino Fraga Filho University Hospital (HUCFF) and stratified based on the findings of elastography by FibroScan®. Peripheral blood samples were collected, and patients' biochemical profiles were evaluated through hepatogram and lipidogram analyses. The PNPLA3 single nucleotide polymorphism (rs738409 C>G) will be detected by Sanger sequencing to confirm the presence of the genetic risk factor. Peripheral blood mononuclear cells were isolated for subsequent iPSC reprogramming using the CytoTuneTmPS 2.0 Sendai Reprogramming Kit. Cells will be characterized at markers of pluripotency by flow cytometry and RT-PCR. After iPSC generation, these cells will be differentiated into hepatocytes (iHEP) and phenotypically characterized. Results: The project included men and women aged 47 to 77 years. Groups were structured in alignment with the elastography assessments with either: (I) absent/mild fibrosis diagnosis, levels 0 and 1, with n=4, including 3 women and 1 man, or (II) advanced fibrosis diagnosis, levels 3 and 4, with n=4, including 3 women and 1 man. Healthy individuals in the same age range were recruited as controls, with n=2, including 1 woman and 1 man. Biochemical profile analysis showed no significant differences between control, group I and group II in lipidogram profile, including total cholesterol, LDL, HDL, TG and VLDL, neither in hepatogram profile, including total bilirubin, alkaline phosphatase, AST, albumin, and GGT, except for elevated ALT enzyme levels in group II (mean: 28.75) compared to the control (mean: 12.00) (p<0.05). After reprogramming the cells, we noticed that the iPSCs displayed specific features, including the formation of dense, opaque, and spherical colonies, which suggested a successful reprogramming process. Conclusion: This project will enable the study of differentiated hepatocytes derived from MASLD and MASH patients without the need for a biopsy to access primary liver cells. Additionally, this model of iHEP can be a powerful tool to study MASLD progression, which, in the future, by matching iPSC-derived hepatocyte with omics analyses, might be able to explore the molecular landscape behind disease etiology. Support: FAPERJ, CNPq and Capes Protocol: 16079319.0.0000.5257</p>



Title	Revisiting concepts in human physiology to understand the mechanisms of illness in the most prevalent diseases in primary care: report of teaching experience in the teaching of Family and Community Medicine at the Federal University of Norte do Tocantins
Authors	JOSUE MOURA TELLES, WAGNER DOS SANTOS MARIANO
Affiliations	
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Human physiology explores the biological processes and mechanisms by which the body functions and regulates its functions. Knowing these mechanisms is essential to understanding how diseases occur and how they manifest themselves in primary care patients. For example, understanding how hypertension structurally affects the heart and blood vessels allows doctors to identify risk factors and manipulate these conditions. The professor who teaches Family and Community Medicine has the responsibility not only to teach the theoretical foundations of medical practice in primary care, but also to connect these concepts with other equally important knowledge and subjects in the medical curriculum, such as Human Physiology. Understanding Human Physiology leads students to a deeper understanding of the mechanisms of illness. This approach not only enriches student learning, but also prepares them to address public health challenges in our region. Objective: Report the teaching experience in teaching classes that involve the relationship and importance of Human Physiology for understanding Family and Community Medicine; understanding which is relevant is understanding the mechanisms of illness in the natural history of chronic diseases for their adequate management in primary care. Methods: This work is an experience report, based on the teacher's impressions during the semester. Results: By revisiting physiology concepts, such as the functioning of the cardiovascular system, glucose regulation and lung function, students begin to understand how small changes in these systems can lead to diverse clinical manifestations. For example, we discussed how increased peripheral resistance can lead to hypertension and its complications, or how dysfunction of pancreatic beta cells can result in uncontrolled glycemic control and complications of diabetes. Additionally, we explore how environmental, socioeconomic, and behavioral factors interact with physiology to influence the development and progression of these diseases. This includes discussions about diet, physical activity, smoking and access to healthcare, fundamental aspects in the Family and Community Medicine approach. A concrete example of this integrated approach was our analysis of the increasing prevalence of chronic respiratory diseases in our region, often exacerbated by specific environmental conditions. By understanding the physiological mechanisms underlying lung function, students were able to not only better identify at-risk patients, but also propose more effective prevention and management strategies. The role of human physiology in training in Family and Community Medicine goes beyond simple theoretical understanding; it is essential to empowering future doctors to be agents of change in their communities. Conclusion: By understanding how physiological systems interact with environmental and social factors to influence health and illness, students are better prepared to provide integrated, patient-centered and prevention-oriented care. In summary, the connection between human physiology and Family and Community Medicine not only strengthens the educational curriculum, but also prepares health professionals to face the complex challenges of clinical practice in primary care. This focus not only educates, but empowers students to be leaders in promoting health and preventing disease in their communities, which is essential to the advancement of public health in our region. Support: UFNT Protocol: N.A.</p>



Title	IMPACTO DO IMC E DA PRESSÃO ARTERIAL SISTÓLICA NO DESEMPENHO COGNITIVO DE MULHERES NA PERIMENOPAUSA: UM ESTUDO TRANSVERSAL
Authors	ANA LIVIA PINHEIRO CANTARIM, ARTHUR POLVEIRO SILVA, MATEUS MARTINS MOREIRA, GABRIEL PEINADO COSTA, ÁTILA, CAMILA DE MORAES
Affiliations	Grupo de Estudo e Pesquisa em Exercício Físico e Condições Especiais de Saúde, USP
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Durante o envelhecimento reprodutivo ocorrem processos neuroendócrinos com repercussões em múltiplos sistemas, incluindo o sistema nervoso central. Apesar de sintomas cognitivos serem comumente relatados, a maioria das mulheres passa por esse período sem manifestações de comprometimento cognitivo. Porém, o acometimento por fatores de risco cardiometabólicos como níveis elevados de pressão arterial (PA) e obesidade podem influenciar negativamente a função cognitiva.</p> <p>Objective: Verificar a relação entre índice de massa corporal, pressão arterial sistólica e declínio cognitivo em mulheres pré e pós menopausa. Methods: Estudo transversal, com participantes de um projeto de extensão universitária. O estado nutricional foi verificado por meio do Índice de Massa Corporal (IMC), calculado a partir da razão entre massa corporal (kg) e estatura (m²); a medida da pressão arterial braquial foi realizada utilizando o aparelho digital da marca OMRON (modelo HEM-7113). Foram classificadas como normotensão valores de pressão arterial sistólica (PAS) inferiores a 130 mmHg e pressão arterial diastólica (PAD) inferiores a 85 mmHg; o desempenho cognitivo no domínio da memória foi avaliado a partir do Exame Cognitivo de Addenbroke e a classificação do estágio reprodutivo foi realizada de acordo com as recomendações do STRAW+10, sendo Pré-menopausa (presença de ciclos menstruais nos últimos 12 meses) e Pós-menopausa (Amenorreia igual ou superior a 12 meses). A relação entre os preditores e o desempenho no domínio da memória foi verificada por meio de um modelo de regressão linear múltipla, no qual o modelo final foi escolhido por meio do Critério de Informação de Akaike (AIC). Results: Foram incluídas 40 participantes do sexo feminino, com idade média de 51±6 anos e 13,8±2,5 anos de escolaridade. Foram classificadas como pré-menopausa 37,5% das participantes e 62,5% como pós-menopausa. O IMC médio das participantes foi 32,1±5,2, sendo que 25,6% foi classificada como sobrepeso e 66,7% como obesidade. A proporção de mulheres com níveis pressóricos classificados como pré-hipertensão ou hipertensão foi de 25,6%. A média da pontuação no domínio de memória foi de 22,5±2,12. A análise resultou em um modelo significativo, apresentando um AIC de 150 [F(3)= 8,39; p<0,001; R²= 425]. O IMC ($\beta = 0,1817$; t=-3,31; p<0,006) e a PAS ($\beta = -0,0452$; t=-2,31; p=0,027) foram preditores do desempenho no domínio de memória, representando 42% de sua variabilidade. Conclusion: Conclui-se que a PAS e o IMC são preditores do desempenho no domínio da memória nesta amostra de mulheres pré e pós menopausa. Os resultados reforçam a importância de ações para a prevenção da hipertensão arterial e do excesso de peso visto que além dos agravos à saúde já conhecidos, estas condições também podem influenciar negativamente o desempenho da memória em mulheres na perimenopausa. Support: Pró-Reitoria de Pesquisa e Inovação USP (bolsa PUB-Pesquisa) e CAPES (Código de Financiamento 001) Protocol: CAAE: 59091922.6.0000.5659</p>

Title	Aldosterone actions on the urinary bladder of female Wistar rats.
Authors	DANILO BARBOZA TOSI, BÁRBARA DO VALE, PATRIK ARONSSON, EDUARDO M. CAFARCHIO, MONICA AKEMI SATO
Affiliations	Departamento de Morfologia e Fisiologia, Centro Universitário FMABC, Department of Pharmacology, University of Gothenburgh
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Previous studies in amphibians have shown that aldosterone can increase the expression of amiloride-sensitive sodium channels in the urinary bladder epithelial cells. In rabbits, aldosterone could also stimulate the activity of epithelial sodium channels in the bladder and this effect would be potentiated by cAMP, but attenuated by phosphodiesterase inhibitors, suggesting that this effect is caused by a non-genomic action of aldosterone. Nevertheless, it is unknown whether aldosterone acts or not on the urinary bladder of rats. Objective: In this study, we aimed to investigate the possible actions of aldosterone on intravesical pressure and cardiovascular parameters in anesthetized Wistar rats. Methods: Female Wistar rats (~250 g) were isoflurane anesthetized (2% in 100% O₂) and submitted to the catheterization of the femoral artery and vein (PE-10 connected to PE-50, Clay Adams, NJ) for pulsatile arterial pressure (PAP), mean arterial pressure (MAP) and heart rate recordings (HR) and infusion of drugs, respectively. The urinary bladder was cannulated for intravesical pressure (IP) measurement. All the physiological variables were recorded in a data acquisition system (Power Lab, ADInstruments). After the baseline PAP, MAP, HR and IP recordings for 15 min, aldosterone 10 µg/kg or spironolactone 50 µg/kg or saline (vehicle) was administered intravenously (bolus injection) or topically (in situ) onto the urinary bladder (UB) and all the parameters were recorded for additional 30 min. At the end of the experiments, rats were euthanized with i.v. sodium thiopental (100 mg/kg). All procedures of this study were approved by the Animals Ethics Committee (CEUA-FMABC#10/2022). Data are as mean±SEM and were submitted to paired Student's t-test (p<0.05). Results: The intravenous injection of aldosterone (n=6) evoked a significant increase in IP (125±12%, p=0.0003) and decrease in MAP (-26±5 mmHg, p=0.007) compared to baseline, whereas caused no change in HR (-4±3 bpm). The in situ administration of aldosterone on the UB (n=6) also increased the IP (37±9%, p=0.002), however, no changes were observed in MAP (-5±11 mmHg) and HR (-8±14 bpm). Spironolactone administered intravenously (n=6) significantly increased IP (119±15%, p=0.0004) and yielded no changes in MAP (2±2 mmHg) and HR (5±2 bpm) compared to baseline values. The in situ administration of spironolactone onto the UB (n=6) significantly increased the IP (48±11%) and induced no changes in MAP (-15±9 mmHg) and HR (15±11 bpm). No significant changes were elicited by i.v. or in situ saline on IP, MAP and HR. Conclusion: The findings suggest that aldosterone can exert an action directly on the urinary bladder, increasing the intravesical pressure, whereas in the dose used intravenously can evoke a hypotensive response in isoflurane anesthetized rats. Spironolactone likely acts as an inverse agonist at the dose used in this study. Both effects evoked by aldosterone and spironolactone are likely non-genomic actions. Support: FAPESP, PIBIC-CNPq and Centro Universitário FMABC. Protocol: N.A.</p>

Title	Ureaplasma parvum infection could alter the oxidative stress state and contribute to miscarriage.
Authors	FERNANDA KAROLINE ALMEIDA FREIRE, LARA FABIANA LUZ MALHEIRO, THIAGO MACEDO LOPES, LILIANY DE SOUZA BRITO AMARAL, ANDERSON SANTOS SOUZA, LUCAS MIRANDA MARQUES, CALINE NOVAIS TEIXEIRA OLIVEIRA, GUILHERME BARRETO CAMPOS
Affiliations	Programa de pós graduação multicêntrico em ciências fisiológicas, UFBA, UNIVERSIDADE FEDERAL DA BAHIA/IMS CAT
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: During pregnancy, the physiological production of reactive oxygen species (ROS) plays a role in developmental processes. The abnormal overproduction of ROS can disrupt these processes, leading to spontaneous abortion, a phenomenon influenced by various factors, including genital infections. Objective: This study aimed to investigate whether <i>Ureaplasma parvum</i> infection (UPi) disrupts oxidative stress markers in the context of spontaneous abortion. Methods: Eighty-nine women with a history of spontaneous abortion (abortion group) and 20 women who had a full-term delivery (delivery group) were included. The groups were subdivided into full-term delivery without UPi (P), full-term delivery with UPi (P+UPi), spontaneous abortion without UPi (A), and spontaneous abortion with UPi (A+UPi). Placental tissue samples were obtained aseptically. We analyzed the activity of antioxidant enzymes (SOD, CAT, and GPx), lipid peroxidation markers (TBARS), protein carbonylation, and nitrite. Additional experiments included measure the cofactors, inductively coupled plasma optical emission spectrometry (ICP-OES) was used., gene expression, and immunohistochemistry analyses of NRF2 and 8-OHDG. Results: Results were considered statistically significant when ($p < 0.05$). The results indicated that TBARS levels were reduced in the A+UPi group compared to the A group (0.2309 ± 0.3170; 0.1083 ± 0.0050), while protein carbonylation and nitrite levels were elevated, respectively (2.704 ± 0.5783; 3.873 ± 1.535), (1.566 ± 0.4899; 2.577 ± 0.5547). SOD was elevated in the A+UPi group compared to the A group (2.341 ± 0.2216; 2.563 ± 0.2470); consequently, this group had reduced CAT levels compared to the A group (0.4644 ± 0.1060; 0.3584 ± 0.0963). GPx levels (0.2309 ± 0.1227; 0.1083 ± 0.0195), the SOD/CAT ratio (6.806 ± 1.530; 6.442 ± 0.6813), and the SOD/GPx ratio (5.958 ± 0.6059; 28.83 ± 7.729) were reduced by the infection when comparing the A group with the A+UPi group. Gene expression analysis revealed that the P+UPi group reduced the expression of CAT (2.376 ± 0.7960; 1.002 ± 0.2587) and NRF2 (1.169 ± 0.1963; 0.9971 ± 0.0460) when compared to the P group, while there was no difference between the abortion groups. Conversely, the A+UPi group increased the Cu/Zn-SOD/CAT (1.390 ± 0.2013; 1.844 ± 0.3344) and Mn-SOD/CAT (1.422 ± 0.1800; 1.793 ± 0.2883) ratios and reduced the Cu/Zn-SOD/GPx (1.709 ± 0.2618; 2.187 ± 0.3387) and Mn-SOD/GPx (2.930 ± 0.5604; 1.284 ± 0.4010) ratios when compared to the A group. In PCA, samples from the abortion groups with and without infection were related and highlighted by higher concentrations of manganese, copper, and zinc. In immunohistochemistry, NRF2 staining levels showed differences when comparing the P group with the A+UPi group (10.21 ± 0.7042; 7.814 ± 0.7031), and the P+UPi group compared to the A group (7.814 ± 0.7037; 4.440 ± 0.3892), in 8-OHDG when comparing the A group with A+UPi (2.603 ± 1.248; 0.9422 ± 0.5479), and the A group compared to the P group (6.252 ± 1.248; 0.9422 ± 1.194), with staining being lower in the A+UPi group. Conclusion: These findings underscore significant alterations in redox status, including oxidative/nitroxidative damage and notable variability in antioxidant capacity associated with UP infection. Overall, our data suggests that <i>Ureaplasma parvum</i> may exacerbate oxidative stress, thereby increasing the risk of spontaneous abortion. Support: Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB) Protocol: 1.764.332.</p>

Title	Assessment of the Toxicological Effects of Tricyclic PAHs on Embryonic Development of Danio rerio
Authors	CAROLINA BRIOSCHI DELPUPO, DANIELA MARIA PAMPANIN, NATALIA MARTINS FEITOSA
Affiliations	CCS, UFRJ
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Polycyclic aromatic hydrocarbons (PAHs) are organic pollutants produced naturally or anthropogenically, composed of two or more aromatic rings. These compounds began to be studied due to their carcinogenic and mutagenic capacity in humans. Low molecular weight PAHs, with up to three rings, easily adhere to atmospheric molecules and water due to their ease of degradation. In 1991, the Agency for Toxic Substances and Disease Registry (ATSDR) in the United States classified phenanthrene and fluorene as compounds that pose health risks. It is already known that these compounds can cause abnormal behavior and anxiety in rats, liver damage and oxidative stress in fish, and act as endocrine disruptors (ED). Dibenzothiophene is a common pollutant found in fuels and also has ED effects. Within cells, PAHs promote the expression of the <i>cyp1a</i> gene, a precursor of the enzyme from the cytochrome P450 family, which metabolizes these compounds. Moreover, PAHs can cause dysfunctions in the endocrine, reproductive, and immune systems. To assess the effects of these PAHs, we opted to use <i>Danio rerio</i> embryos as the model organism due to the ease of visualization during embryonic development, low maintenance cost, and over 70% similarity in the genes encoding proteins with humans, allowing us to compare the effects in these animals with humans. Objective: To evaluate the effects of dibenzothiophene, fluorene, and phenanthrene PAHs separately and in combination on <i>Danio rerio</i> embryos and to analyze the expression of endocrine and inflammatory biomarkers. Methods: Fish embryo acute toxicity tests (FET) were conducted with PAHs at environmentally relevant concentrations. Subsequently, RNA extraction, cDNA synthesis, and qPCR were performed to evaluate biomarker expression. Results: No phenotypic alterations were observed in embryos exposed to PAHs, and biomarker analyses are ongoing. Conclusion: Normally, endocrine disorders do not cause significant morphological changes, thus making the detailed assessment of the environmental and health impacts resulting from PAH exposure highly relevant. Support: Faperj Protocol: 059/21</p>

Title	Expressão de Tryptophanil-tRNA sintetase (WARS) e indoleamina 2,3-dioxigenase-1 (IDO1) na predição do estadiamento do câncer de bexiga
Authors	ALINE ÁUREA DE SOUZA SANTOS, DOUGLAS EDGARD LEMES, JOSÉ PONTES JUNIOR, HUMBERTO DELLÊ
Affiliations	Pós graduação em ciências, Medicina, UNINOVE, Urologia, FMUSP
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O câncer de bexiga (CB) é uma das neoplasias mais comuns no mundo. Assim como outros tipos, o CB pode produzir a enzima indoleamina 2,3-dioxigenase-1 (IDO1), que, ao modular o sistema imune, protege o tumor, favorecendo sua progressão. Quando a IDO1 está presente, ela degrada o triptofano do microambiente, produzindo os catabólitos da quinurenina. Esta situação bloqueia a resposta imune local, porém não afeta a própria célula produtora de IDO1. Os mecanismos para essa resistência permanecem desconhecidos, porém há evidência de que estoques são gerados pela enzima triptofanil RNAt sintetase (WARS), que carrega tRNA com o aminoácido, garantindo a síntese proteica e o ciclo celular. Objective: O objetivo do estudo foi verificar se a expressão de IDO1 e WARS está associada ao estadiamento do CB.</p> <p>Methods: Foram incluídos no estudo espécimes de CB extraídos de 165 pacientes, sendo 88 portadores de CB não-músculo invasivo (CBNMI) e 77 portadores de CB músculo invasivo (CBMI). Projeto aprovado no comitê de ética (49446515.0.0000.5511). A expressão de IDO1 e WARS foi avaliada por imuno-histoquímica, tanto em células neoplásicas como em células inflamatórias. Análise de correlação (Spearman) e curva ROC foram utilizadas. Results: Resultados preliminares: Embora não tenha sido detectada correlação entre IDO1 e Wars, a expressão de ambas proteínas foi eficaz na predição do CBNMI. Conclusion: Conclusão preliminar: É possível que as enzimas IDO1 e WARS tenham papel na fisiopatologia do CB e poder preditivo no estadiamento da doença. O estudo está em andamento para maiores esclarecimentos. Support: Financiamento: FAPESP 2022/15575-8 Protocol: 49446515.0.0000.5511</p>

Title	THE SARS-COV2 SPIKE PROTEIN INCREASES THE EXPRESSION OF MasR, AND AT1R MEDIATED BY AT1R AND MasR ACTIVATION ON HUMAN BRONCHIAL SMOOTH MUSCLE CELLS
Authors	JULIANE STEPHANIE MENDONÇA RODRIGUES, SANDRA HELENA PENHA DE OLIVEIRA
Affiliations	Departamento de Ciências Básicas, UNESP
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Coronavirus 2 (SARS-CoV-2) is a virus capable of developing severe acute respiratory syndrome and is responsible for the COVID-19 disease that emerged at the end of 2019 and became a pandemic in 2020. SARS-CoV-2 has several critical structural proteins, such as the envelope protein (E), the membrane protein (M), the nucleocapsid protein (N), and the spike glycoprotein (Sp). The S protein regulates and binds to the angiotensin-converting enzyme 2 (ACE2) surface receptor and is a critical step for virus entry. The renin-angiotensin system (RAS) is a peptide cascade that orchestrates essential processes of human pathophysiology. RAS exerts its primary effects through the binding of angiotensin II (Ang II) with its receptors AT1 and AT2. ACE2 is an enzyme that catalyzes the cleavage of Ang II into Ang (1-7), a heptapeptide that acts on its MAS receptor. Objective: The aim of this study was to investigate whether recombinant SARS-CoV-2 spike protein and Ang II stimulate human bronchial smooth muscle cells (BSMC) to express ACE2, MasR, and AT1R mRNA. Methods: The recombinant Sp was tested at different concentrations (10 ng, 50 ng, 100 ng, and 500 ng/mL) and was used to stimulate human BSMC (5x10⁴ cells/well). Ang II (100 ng/mL) was also used to stimulate BSMC alone or 1h before Sp stimulation. Cells were pre-treated with RAS inhibitors such as Captopril (capto, 1 µM) and Losartan (losart, 2 µM) 1 h before, and A-779 (100 nM) 2h before the Sp and/or Ang II stimulation and the ACE2, MasR, and AT1R expressions were evaluated 3 and 12 h after by qRT-PCR. Results: At concentrations of 10 ng and 50 ng of Sp, did not induce any ACE2, MasR, and AT1R expression in any of the times evaluated, and at 100 ng of Sp, they induced an increased MasR expression at 3, 12, and 24 h after. But for AT1R and ACE2 expression, Sp induced an increase only 3 h after stimulation. After the dose-response and time-response experiment, we decided to choose the concentration of 100 ng/mL of Sp evaluated at 3 and 12h. The Ang II (100 ng/mL) only induced an increase in MasR expression. Ang II potentiated the MasR expression induced by Sp (100 ng/mL) at 12 h. The results showed that human BSMC constitutively expressed MasR, ACE2, and AT1R. Pretreatment with losart and A-779, but not capto, decreased the AT1R expression induced by Sp at 3 h, and losart but not capture nor A-779 decreases AT1R expression caused by Ang II plus Sp. The MasR expression was pretreated with capto, but not losart nor A-779 was potentiated at 3 h. At 12 h, the MasR expression induced by Ang II plus Sp was decreased by capto, losart, and A-779. The pretreatment with capto, but not losart nor A-779, increased the ACE2 expression induced by Ang II plus Sp. Conclusion: In conclusion, human BSMC stimulated by Sp increased the mRNA expression of ACE2, MasR, and AT1R. Ang II increased the ACE2 and MasR but not AT1R expression. The increased expression of MasR induced by Ang II plus Sp is dependent on Ace production, AT1R, and MasR activation. The increased AT1R expression induced by Sp is dependent on AT1R and MasR activation, and induced by Ang II plus Sp is dependent on AT1R activation. Taken together, these results suggest that the increase in MasR and AT1R expression is dependent on the action of the Sp in this receptor in BMSCs. And ACE2 expression induced by Sp can be inhibited by the production of ACE. Support: CNPq, CAPES e FAPESP Protocol: N.A.</p>

Title	INVESTIGAÇÃO DO EFEITO DO CANABIDIOL SOBRE A ATIVAÇÃO DE CÉLULAS DA GLIA EM MODELO DE NOCICEPÇÃO INDUZIDO POR PACLITAXEL
Authors	RAFAELA SILVA DOS SANTOS, GIOVANE GALDINO DE SOUZA
Affiliations	CEBIOEX, Unifal MG
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ao longo da vida, a dor tanto de característica aguda quanto crônica, é uma das razões para a maior frequência de visitas médicas e um dos motivos mais comuns para o uso de medicamentos, além de ser uma das principais causas de incapacidade no trabalho. Estudos têm demonstrado que a dor causa ativação das células da glia, com aumento da expressão do Tool-like receptors (TRL4). Os TLR4 reconhecem ligantes endógenos e exógenos DAMPS (padrões moleculares associados ao dano) e PAMPS (padrões moleculares associados a patógenos) não só envolvidos com a infecção ou lesão, mas também com outros processos fisiopatológicos como a dor. Assim várias estratégias de tratamento têm sido desenvolvidas para controlar esse sintoma, como o tratamento com canabidiol (CBD), um fitocanabinóide. Desse modo, sabendo que o CBD é uma importante estratégia de tratamento para o controle da dor e tendo em vista seu amplo benefício para pacientes com câncer, o seu uso para o controle da dor neuropática induzida pelo tratamento quimioterápico pode ser de grande valia. Os receptores canabinóides do tipo 2 (CB2), expressos em tecidos periféricos e células inflamatórias, parecem estar envolvidos na antinocicepção induzido pelo CBD. Além disso, estudos tem demonstrado que tais receptores também estejam expressos no Sistema Nervoso Central (SNC), incluindo as células gliais. Objective: O presente estudo tem como objetivo a investigação do efeito do CBD na dor neuropática induzida por paclitaxel (PTX). Methods: Foram utilizados camundongos Swiss, pesando entre 25 a 30g. O limiar nociceptivo foi avaliado pelo teste de filamentos de Von frey. O modelo de dor neuropática foi induzido pela injeção intraperitoneal de PTX. Para verificar os níveis de citocinas pró-inflamatórias, IL-1β e TNF-α foi realizado o ensaio de ELISA. Foram utilizadas as drogas, AM630, para investigar a participação de receptores CB2, a dosagem de anandamida (AEA) e 2-araquidonoilglicerol (2-AG), para avaliar a participação de endocanabinóides, a minociclina e o fluorocitrato, para investigar o envolvimento da micróglia e do astrócito e o LPS-RS para verificar a participação do receptor TRL4. Também foi realizado o ensaio de wester blot para averiguar o efeito do CBD sobre os níveis da expressão do receptor CB2, IBA-1, GFAP e TRL4, além da imunofluorescência para avaliar a co-localização dos receptores CB2/TRL4 no corno da raiz dorsal da medula espinhal. Results: Após 4 dias de tratamento com PTX, os animais apresentaram uma alodínia mecânica e esta foi revertida pelo CBD. O AM630 inibiu a antinocicepção induzida pelo CBD no modelo nociceptivo. O CBD aumentou os níveis de AEA e 2-AG na medula espinhal, a minociclina, o fluorocitrato eo LPS-RS bloquearam a nocicepção no modelo estudado. Os resultados do ensaio de ELISA demonstraram que o CBD reduziu os níveis de TNF-α e IL-1β. O CBD aumentou a expressão do CB2 no modelo de nocicepção induzido pelo PTX e reduziu os níveis de IBA-1 e TRL4. Conclusion: Concluímos que o CBD reduz a nocicepção induzida por PTX, o sistema endocanabinóide participa desse efeito e as células da glia parecem estar envolvidas na gênese e manutenção da dor, pela ativação do TRL4, com consequente liberação de citocinas pró-inflamatórias TNF-α e IL-1β. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais Protocol: 13/2017</p>

Title	T Lymphocyte Profile in Women with Fibromyalgia: a cross-sectional observational study
Authors	NICOLE PEREIRA FRANÇA, ANDRÉ LUIZ SILVA SANTOS, MONALISA MARTINS MONTALVÃO, JOSYMARA SALES LÍRIO, BRENDA OLIVEIRA DOS SANTOS, MONIQUE OLIVEIRA DOS SANTOS, JILENO FERREIRA SANTOS, CRISTIANE BANI CORREA, JOSIMARI MELO DESANTANA
Affiliations	Departamento de Fisioterapia, UFS, Departamento de Ciências Fisiológicas, UFS, Departamento de Ciências da Saúde, UFS
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Fibromyalgia (FM) is a chronic syndrome characterized by widespread musculoskeletal pain, commonly associated with mental and physical fatigue, allodynia, cognitive alterations, and psychosocial disturbances. Recent studies have demonstrated that the immune system is capable of modulating pain processing and may be involved in the development and maintenance of FM. Thus, alterations in the frequency and polarization of CD4+ T cells can be observed in FM, impacting the functionality of the immune system. However, the mechanism mediating responses related to adaptive immune dysregulation is still unknown. Therefore, investigating how the presence of T cells, especially CD4+ and CD8+ T lymphocytes, may be involved in the development and maintenance of pain is necessary for a better understanding of the pathophysiological mechanisms present in FM. Objective: The aim of this study was to analyze the levels of CD4+ and CD8+ T lymphocytes in women with fibromyalgia. Methods: This is a cross-sectional observational study. The project was approved by the Research Ethics Committee of the Federal University of Sergipe (CAAE 73736223.7.0000.5546), and research participants signed the Informed Consent Form. The study included women aged between 18 and 60 years diagnosed with fibromyalgia. CD4+ and CD8+ T lymphocyte outcomes were evaluated using peripheral blood collected from participants and stored in tubes containing EDTA, which was then centrifuged on Fycoll-Hypaque gradient. Mononuclear cells were plated at a quantity of 1×10^6 cells per well and incubated with 50 μl of Fc blocking solution for 20 minutes at 4°C and then incubated with anti-human antibodies for 30 minutes. For the phenotypic evaluation of T cells, antibodies CD3, CD4, CD8, CD45RA, and CCR7 were used. After incubation, samples were fixed in 2% formaldehyde and analyzed in a flow cytometer. FlowJo 10.9 software was used for phenotype analysis. Values were expressed as mean \pm standard deviation. Results: Fourteen participants were evaluated, with a mean age of 6.44 ± 5.47. In the CD4+ T cell profile, a percentage of (46.96 ± 7.67) was observed, with the naive T cell phenotype (TN) being the most expressive (55.81 ± 21.20), followed by the T effector memory (TEM) phenotype, with 15.54 ± 14.21. Conversely, the lowest expression levels were demonstrated in the central memory T (TCM) and TEM reexpressing CD45RA (TEMRA) phenotypes, with 15.41 ± 12.95 and 13.24 ± 12.29, respectively. Regarding the population of CD8+ T cells (8.84 ± 4.71) analyzed, the TN and TEMRA subpopulations showed higher prevalence $(49.51 \pm 18.36$ and 32.29 ± 9.39, respectively), while the TEM and TCM subpopulations showed lower expression levels $(16.94 \pm 17.11$ and 1.17 ± 1.39, respectively). Conclusion: Women with fibromyalgia exhibit an overlap of CD4+ T lymphocytes compared to circulating CD8+ T lymphocytes. Additionally, higher expression of TEMRA in the distribution of CD8+ T lymphocytes may be related to the process of immunosenescence in people with fibromyalgia. Support: Coordination for the Improvement of Higher Education Personnel (CAPES); National Council for Scientific and Technological Development (CNPq). Protocol: 73736223.7.0000.5546</p>

Title	Effects of concurrent and functional training on memory T cell subpopulations in women with fibromyalgia: a randomized clinical trial pilot
Authors	JOSYMARA SALES LÍRIO, ANDRÉ LUÍZ SILVA SANTOS, MONALISA MARTINS MONTALVÃO, LARA COSTA MOURA, FLÁVIA DIANA SANTOS FIGUEREDO, ANTÔNIO GOMES DE RESENDE NETO, JILENO FERREIRA SANTOS, CRISTIANE BANI CORREA, JOSIMARI MELO DESANTANA
Affiliations	Departamento de Fisioterapia, UFS, Departamento de Ciências da saúde, UFS, Departamento de Ciências Fisiológicas, UFS, Departamento de Educação Física, UNESA
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Fibromyalgia syndrome (FMS) is a condition of widespread chronic musculoskeletal pain associated with fatigue and psychosocial disturbances. Evidence suggests that mast cells and T cells may be involved in the development and maintenance of chronic pain. In chronic pain conditions, there may be a reduction in the number of cytotoxic CD8+ T lymphocytes and an increase in CD4+ T cells producing inflammatory cytokines. Given this, physical exercise may be crucial for improving the immune profile in people with chronic pain. There are still no studies investigating the repercussions of concurrent training (CT) and functional training (FT) on CD4+ and CD8+ T lymphocytes in people with FMS. Objective: To analyze the effects of concurrent and functional training on CD8+ and CD4+ T lymphocyte levels in women with fibromyalgia. Methods: This is a pilot study of a randomized clinical trial. The project was approved by the Research Ethics Committee of the Federal University of Sergipe (CAAE 73736223.7.0000.5546), and research participants signed the Informed Consent Form. The study included women between 18 and 60 years old, diagnosed with fibromyalgia. Ten participants were allocated and randomized into CT or FT groups. CD4+ and CD8+ T lymphocyte outcomes were evaluated using peripheral blood mononuclear cells. For phenotypic evaluation of T cells, antibodies CD3, CD4, CD8, CD45RA, and CCR7 were used. Samples were analyzed using a flow cytometer. FlowJo 10.9 software was used for phenotype analysis. Values were expressed as mean percentages and were considered statistically significant when $p < 0.05$. Shapiro-Wilk test, two-way ANOVA, and Tukey were used. GraphPad Prism 8.0 was used for data analysis. Results: An increase in the percentage of CD8+ T cells was observed in both CT and FT groups when comparing pre (CT: 4.88%; FT: 10.19%) and post (CT: 17.80%, $p = 0.0029$; FT: 20.97%, $p = 0.0024$) moments, while there was no difference in the percentage of CD4+ T cells in both groups (CT: $p = 0.8795$; FT: $p = 0.9628$). In comparison between the CT and FT groups, there was no statistical difference in the percentage of CD8+ T cells and CD4+ T cells. Regarding the frequency of memory T cells, no difference was observed in the percentage of terminally differentiated effector memory CD4+ T cells repressing CD45RA (TEMRA) (CT: -4.41%, $p = 0.9703$; FT: -14.15%, $p = 0.3393$) and CD8+ TEMRA cells (CT: +13.25%, $p = 0.3753$; FT: -16.93%, $p = 0.0819$) in both training protocols. Conversely, an increase in the percentage of effector memory (TEM) CD4+ T cells was observed only in the CT group (-30.78%, $p = 0.0484$), while CD8+ showed no difference (CT: -9.86%, $p = 0.7719$; FT: +3.08%, $p = 0.9822$). Additionally, both FT and CT showed no difference in the percentage of central memory (TCM) CD4+ (CT: -0.10%, $p > 0.9999$; FT: +8.34%, $p = 0.4405$) and CD8+ T cells (CT: -0.71%, $p = 0.8254$; FT: +0.22%, $p = 0.9863$). In CT and FT groups, there was no difference in the percentage of naive (TN) CD4+ (CT: +35.26%, $p = 0.1419$; FT: +22.10%, $p = 0.3279$) and CD8+ (CT: +23.85%, $p = 0.2804$; FT: +13.62%, $p = 0.5728$) cells. Conclusion: Both concurrent training and functional training were able to promote an increase in the frequency of CD8+ T cells in women with fibromyalgia. Additionally, both training modalities seem to not promote alterations in T cell memory subpopulations. However, physical training may promote an increase in the immune defense system in people with fibromyalgia, regardless of the modality. Support: Coordination for the Improvement of Higher Education Personnel (CAPES); National Council for Scientific and Technological Development (CNPq). Protocol: 73736223.7.0000.5546</p>

Title	Anti-inflammatory and antinociceptive activities and toxicological potential of <i>Commiphora leptophloeos</i> (Mart.) JB Gillet bark extracts using in vivo and in vitro assays.
Authors	SARAH ROCHA LIMA BRAGA, LORENA LÔBO BRITO MORBECK, TALITA SANTOS COSTA, REGIANE YATSUDA
Affiliations	Programa de Pós Graduação Multicêntrico em Ciências Fisiológicas, UFBA
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: <i>Commiphora leptophloeos</i> (Mart.) J.B. Gillet, is a thorny tree, popularly known as female umburana. In Brazil, it is found where the vegetation is exposed to adverse climate and soil conditions, typical characteristics of the Sertão. Due to its medicinal properties, it is traditionally used in local communities in the Brazilian Northeast as a fortifier, wound healer, antitussive, and in the treatment of bronchitis, gastritis, ulcers, and urinary disorders. Objective: The study aimed to evaluate the medicinal potential of <i>Commiphora leptophloeos</i> as an anti-inflammatory, antinociceptive, and toxicological potential. Methods: For in vivo nociceptive and inflammatory assays, adult male Balb/c mice, weighing approximately 25g, were used. The test groups were composed of a Control Group (Vehicle) and Treatment Group (Ethanol extract of <i>C. leptophloeos</i>), the concentrations of the extract used were 50, 100 and 200mg/kg, except in the Assessment of Possible Antinociceptive Mechanisms, in which we only used the concentration of 100mg/kg, which was considered most effective in our preliminary tests. The antinociceptive effect was evaluated by the following tests: abdominal writhing induced by 0.6% acetic acid; evaluation of possible antinociceptive mechanisms; intraplantar injection of 1.5% formalin; and the von Frey paw pressure test. To evaluate the anti-inflammatory effect, were applied the tests: neutrophil recruitment to the peritoneal cavity; evaluation of nitric oxide production by determining nitrite levels; and assessment of vascular permeability (Evans blue). Toxicity was determined through lethality test against <i>A. salina</i> and by evaluating cytotoxicity using the MTT assay in a breast adenocarcinoma cell line (MDA-MB-231). Results: In the assays applied to evaluate antinociceptive activity, all tested concentrations (50, 100, and 200 mg/kg) showed significant reduction compared to the vehicle ($p < 0.05$). In the assessment of antinociceptive mechanisms, the plant extract (100 mg/kg) demonstrated possible involvement of the cholinergic and nitric oxide systems in the antinociceptive effect ($p < 0.05$). The <i>C. leptophloeos</i> extract was also effective in reducing neutrophil infiltration, nitric oxide production, and vascular permeability at all tested concentrations (50, 100, and 200 mg/kg) ($p < 0.05$). In the toxicity investigation, the extract was found to be highly toxic against <i>A. salina</i>, and in the evaluation of cytotoxicity by the MTT assay, the concentrations of 50 and 100 $\mu\text{g/mL}$ significantly reduced the cell viability of breast adenocarcinoma cells ($p < 0.05$) in 52 and 53% respectively. Conclusion: The results suggest that <i>C. leptophloeos</i> is a promising natural source for the identification of new bioactive compounds and therapeutic agents, given its anti-inflammatory potential, antinociceptive cholinergic agonist and participation in the nitric oxide system, as well as possible antitumor action, characterizing it as a promising species for use in phytotherapy. Support: Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB) and Conselho Nacional de Desenvolvimento Científico (CNPq) Protocol: 080/2020</p>

Title	A funcionalidade muscular e a adiposidade visceral, mas não a massa muscular, influenciam o desempenho cognitivo nos domínios de atenção e orientação em adultos
Authors	MATHEUS MARTINS MOREIRA, ARTHUR POLVEIRO DA SILVA, ANA LIVIA PINHEIRO CANTARIM, GABRIEL PEINADO COSTA, ÁTILA ALEXANDRE TRAPE, CAMILA DE MORAES
Affiliations	Educação Física, Usp
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O comprometimento cognitivo está associado ao aumento da mortalidade e redução da qualidade de vida. Tratando-se do domínio “atenção e orientação”, a sua avaliação se torna mais relevante, visto que a integridade de ambos são imprescindíveis para a realização das atividades do cotidiano, desde as simples às complexas. Nesse contexto, alguns estudos têm mostrado relação entre esses domínios cognitivos e parâmetros antropométricos. Objective: Verificar a relação entre o desempenho no bloco cognitivo da atenção e orientação com a massa muscular, a força muscular e o perímetro de cintura. Methods: Estudo transversal com amostra composta por 31 pessoas, sendo 67,7% (N= 21) do sexo feminino, com idade de 30 a 68 anos ($50,1 \pm 10,3$), participantes do Programa de Atividade Física para Adultos da Escola de Educação Física e Esportes de Ribeirão Preto, São Paulo. O desempenho cognitivo nos domínios de atenção e orientação foi obtido pelo Addenbrooke’s Cognitive Examination, Revised (ACE-R). O perímetro de cintura foi obtido utilizando uma fita antropométrica, tendo a cicatriz umbilical como ponto de referência. A força muscular foi determinada pelo teste de preensão manual, utilizando o dinamômetro hidráulico, classificando em força muscular reduzida e preservada. A massa muscular foi obtida através do DEXA utilizando dados da Massa Magra Apendicular, ajustada pela altura ($MMA/altura^2$). Dados analisados por regressão linear generalizada, distribuição gama, nível de significância de 5% e dados descritos pelo coeficiente beta [IC95%] da diferença média entre níveis. Results: Os participantes com força de preensão manual abaixo do esperado (PDA) apresentaram menor desempenho no domínio de atenção e orientação quando comparados aos participantes com força de preensão manual dentro do esperado (PDE) ($PDE-PDA = 1,4310 [0,2999; 2,25792]$). O modelo apresentou a circunferência de cintura como um preditor para o desempenho no domínio de atenção e orientação ($\beta = -0,0479 [-0,0789; -0,0140]$). Não foi verificada relação entre sexo, massa magra apendicular e o desempenho nos domínios de atenção e orientação. A força muscular e perímetro de cintura indicam respectivamente 18% ($p=0,044$) e 25% ($p=0,015$) da variabilidade da atenção e orientação. Já os valores da $MMA/altura^2$ ($p=0,149$) não apresentaram significância estatística. Conclusion: A funcionalidade muscular, e não a quantidade de massa muscular, têm relação com o desempenho nos domínios atenção e orientação. Além disso, um maior perímetro abdominal, indicador do depósito de gordura visceral, também afeta negativamente o desempenho nos domínios avaliados. Support: CAPES (Código de Financiamento 001) Protocol: 58595122.0.0000.5659</p>

Title	AVALIAÇÃO DA PARTICIPAÇÃO DO RECEPTOR TRANSIENTE DO POTENCIAL VANILÓIDE 1, RECEPTOR TOLL LIKE 4 EM CÉLULAS GLIAIS TALÂMICAS DURANTE A DOR NEUROPÁTICA
Authors	JOÃO PAULO PRADO, LÍVIA MARIA SILVESTRE ELISEI, GIOVANE GALDINO DE SOUZA
Affiliations	CBIOEX, Unifal, MG
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: As células gliais estão envolvidas em diversas dores crônicas, incluindo a dor neuropática. Elas potencializam as descargas neuronais aumentando a expressão de receptores que ativam cascatas de sinalização intracelulares, liberando citocinas pró-inflamatórias. Objective: Investigar a participação das células gliais frente a ativação dos receptores TLR4 (receptor Toll like 4) e TRPV1 (receptor transiente do potencial vanilóide 1) e da via MAPK p38 (mapquinase p38)/NFκB (fator nuclear kappa B) no tálamo de camundongos Methods: Foram utilizados camundongos C57BL6 machos e a injúria por constrição crônica realizada para induzir alodinia mecânica. A avaliação da coordenação motora de animais neuropáticos após tratamento com inibidores farmacológicos foi realizada no 14º dia de neuropatia por meio do teste rota rod. Examinamos a participação das células da glia, dos receptores TLR4 e TRPV1, MAPK p38 e do NFκB na manutenção da alodinia mecânica no tálamo de animais com 14 dias de neuropatia. O tálamo foi extraído a fim de analisar a expressão e síntese proteica de marcadores gliais, Iba1 (molécula adaptadora ionizada de ligação ao cálcio 1), TMEM119 (proteína transmembrana 119) e GFAP (proteína glial fibrilar ácida), dos receptores TLR4 e TRPV1 e da via MAPK p38 utilizando a técnica de Western Blot e RT-PCR, bem como, os níveis de citocinas TNFα e IL1β por meio do ELISA. A ativação do TLR4 em células da glia em animais neuropáticos também foi examinada no tálamo por meio da imunofluorescência. Results: As microinjeções administradas no tálamo ventrobasal contralateral à lesão por CCI, reduziram significativamente a alodinia mecânica sem alterações motoras. A expressão e síntese proteica aumentada para Iba1/TMEM119, GFAP e TLR4 foram demonstradas no tálamo ventrobasal, após 14 dias de CCI, com aumento dos níveis de TNFα, corroborando com a co-localização entre marcadores gliais e o TLR4. Conclusion: Concluímos que as células da glia tem determinante participação na neuromodulação da dor neuropática à nível talâmico por meio da ativação do receptor TLR4, permitindo o NFκB a transcrição gênica para a produção de TNFα a qual contribui para o estado persistente de dor. Support: Fundação de Amparo à Pesquisa de Minas Gerais Protocol: 19/2019</p>

Title	Analysis of Cannabidiol Treatment in an Animal Model of Autism Caused by Prenatal Exposure to Valproic Acid
Authors	RUBIA APARECIDA FERNANDES, MATHEUS SILVA DE OLIVEIRA, VICTOR RODRIGUES SANTOS
Affiliations	Moforlogia, UFMG
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by challenges in social interaction and communication, along with restricted and repetitive behavioral patterns. ASD has a prevalence of approximately 1% worldwide, but there is currently no effective cure or treatment for the disorder. Valproate (VPA) when administered during the embryonic period, can induce autism-like behaviors in rodents, making it a suitable animal model for ASD research. The mechanisms underlying VPA-induced autism-like behaviors are associated with dysregulation in the endocannabinoid system (ES) and neuroinflammation. Cannabidiol (CBD) is a non-psychotropic phytocannabinoid found in <i>Cannabis sativa</i>. It acts on the central nervous system by modulating the ES and exhibits neuroprotective and anti-inflammatory properties in certain conditions. Objective: The objective of this study is to assess the impact of CBD treatment on an animal model of ASD induced by embryonic exposure to VPA. By conducting this research, we aim to investigate the potential therapeutic effects of CBD in alleviating the ASD-like behaviors observed in this specific model. Methods: The study utilized female Wistar rats and their pups for the experiments. All procedures and animal care adhered to the Ethics Committee on the Use of Animals (CEUA) guidelines, following protocol: 66/2024. To establish the animal model, pregnant female rats received either VPA at 500 mg/kg or saline via the intraperitoneal (IP) route on embryonic day 12.5. CBD treatment at a dosage of 30 mg/kg was administered to the pregnant rats on gestational day 12.5, also through IP administration. In the assessment of neurodevelopmental abnormalities various behavioral tests were conducted on postnatal days (PND) 9 to 19, including weight analysis, eye-opening assessment from PND 13 to 17, posture reflex, and olfactory discrimination on PND 9. To evaluate social interaction and preference, the three-chamber test was performed on PND 30. Lastly, on PND 31, the Activity Cage test was conducted to observe compulsive self-grooming behaviors. All the tests were analyzed using the Anymaze program. Results: The neurodevelopmental behavioral tests revealed differences between the VPA-exposed group and the vehicle group, indicating the adverse effects of VPA on behavior. However, the group treated with CBD in combination with VPA showed a reversal of the altered behaviors caused by VPA exposure. Controlled tests from PND 30 onwards also exhibited notable distinctions between the VPA-exposed group and the CBD+VPA group, the latter showing a greater preference for social novelty in the three-chamber test (VPA 29.8±16.2, CBD+VPA 60.44±18.37, $p < 0.05$). It is worth mentioning that the offspring of the CBD+VPA group exhibited a curled tail, which is a common characteristic observed in animals exposed to VPA during the embryonic period. These findings suggest that CBD has the potential to alleviate some behavioral impairments of VPA on neurodevelopmental behaviors associated with ASD; it may not completely reverse all physical manifestations associated with VPA exposure. Conclusion: CBD shows potential as a therapeutic intervention for autism-like behaviors induced by VPA. Further studies are necessary to investigate the mechanisms through which CBD acts to reverse the effects of VPA. Support: Fundação de Amparo à Pesquisa do Estado de Minas Gerais (APQ-02238-23) Protocol: 66/2024</p>

Title	Structural Characterization of Tick Evasins Proteins from Rhipicephalus microplus
Authors	RENATO BERNABÉ, HELGA GOMES, GLÓRIA BRAZ, ITABAJARA VAZ JR, CARLOS LOGULLO, JORGE MORAES
Affiliations	Departamento de Química, UFRJ, Centro de Biotecnologia,, UFRGS, Bioquímica de Artrópodes Hematófagos, UFRJ, Laboratório Integrado de Bioquímica Hatisaburo Masuda, UFRJ
Session	12-Outros
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Ticks are ectoparasites that feed blood of humans and animals and are known to be disease vectors. The economic impact of ticks on livestock systems is significant. Ticks secrete in their saliva a group of proteins belonging to a family called Evasins. These Evasins modulate the host's immune system, allowing the tick to parasitize long enough to feed. This modulation is due to its binding to host immune components called chemokines. Our work has already obtained transcriptome sequences from the tick Rhipicephalus microplus. Objective: In this study we intend to: build structural models of Evasins using transcriptome sequences; validate structures using Ramachandran graphs; perform docking between evasins and chemokines; express Evasin EVABm1A, on a plasmid with induced expression, which showed majority expression in the transcriptome. Methods: Evasin sequences obtained from the transcriptome of the tick Rhipicephalus microplus, chemokine sequences obtained from the Protein Data Bank (PDB). Sequences were submitted to the AlphaFold2 molecular modeling server. The predicted models from molecular modeling server were submitted to the Ramachandran MolProbity and Procheck validation servers; the validated models were hydrogenated on the PDB2PQR server to perform molecular docking on the ClusPro server. To express Evasin EVABm14B, the GeneScript website was used to design the construct by inserting the evasin sequence into the pET28a+ plasmid for expression in E. coli bacteria and into the pPICZalphaA plasmid for expression in Pichia pastoris yeast. Results: It shows the identification of 15 Evasinas, 12 belonging to Class A, 1 to Class B and 2 unclassified. The Evasinas had their structures modeled and validities. The docking assay was carried out between evasins and their probable binding chemokines, showing a high degree of interaction. Furthermore, Evasin EVABm14B was expressed in a plasmid under IPTG induction, for future purification and inhibition tests to control tick infestation, tests with anticoagulant and possible anti-inflammatory agent. Conclusion: Purified Evasins could possibly be used in an inflammatory process to inhibit chemokines involved in certain clinical situations, due to their biotechnological potential. Support: UFRJ, CNPq, FAPERJ, INCT Protocol: N.A.</p>

Title	AVALIAÇÕES COMPORTAMENTAIS EM MODELO DE SINTOMAS NÃO-MOTORES DE DOENÇA DE PARKINSON
Authors	ISABELA BORGES HUBNER, BEATRIZ LAGE ARAUJO SCHWEIZER, MATEUS PRATES, CLARA GOMES, MARIA CLARA DE ASSIS, STEPHANIE SENNA COTTA QUEIROZ DE OLIVEIRA, WANESSA ALMEIDA LUNA, FERNANDO PADOVAN-NETO, CLEITON LOPES AGUIAR
Affiliations	Fisiologia e Biofísica, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A Doença de Parkinson (DP) é caracterizada classicamente pela degeneração de neurônios de neurônios dopaminérgicos nigroestriatais, responsáveis pelo controle motor fino do corpo. Pacientes com DP apresentam sintomas motores, como bradicinesia, tremor, déficits posturais e acinesia. No entanto, a DP também está associada a sintomas não motores, cujos mecanismos ainda são pouco compreendidos. Dentre estes sintomas, são comumente observados prejuízos cognitivos, distúrbios de sono, ansiedade e depressão. Sendo assim, a partir de um modelo experimental com infusão de 6-hidroxidopamina (6-OHDA) em ratos Wistar, investigamos se os sintomas não motores apresentados na DP. Objective: Testar se a lesão bilateral parcial da via nigroestriatal por 6-OHDA seria suficiente para reproduzir alguns dos sintomas não-motores observados na DP. Methods: Foram utilizados ratos Wistar adultos machos, com 250g. O grupo experimental foi submetido a infusão de 6-OHDA bilateralmente no estriado dorsolateral, enquanto o grupo controle teve infusão apenas de veículo. Três e quatro semanas após a infusão, os animais foram submetidos aos testes de marcha (footprint), campo aberto, preferência à sacarose e interação social. Ademais, cerca de 12 meses após a infusão, todos os testes foram repetidos para analisar a progressão dos sintomas de DP. Também realizamos o teste de rotarod para complementar nossas avaliações motoras. Os dados desses experimentos estão em fase de análise. Todos os procedimentos realizados foram aprovados pelo comitê de ética (CEUA PP 0154/2022). Results: Em relação ao teste de footprint, não foram observadas diferenças significativas entre os grupos para o comprimento das passadas entre os membros posteriores ($p=0,82$) e anteriores ($p=0,81$). Também não observamos diferenças significativas quanto à largura das passadas dos membros anteriores ($p=0,87$) e posteriores ($p=0,11$). Na 4ª semana, os resultados continuaram não significativos, $p=0,63$ e $p=0,61$ em comprimento de passada, e $p=0,72$ e $p>0,99$ em largura. O campo aberto, realizado na 3ª semana, não evidenciou diferença significativa entre os grupos quanto à distância total percorrida ($p=0,089$) e velocidade média ($p=0,091$). Também não observamos diferenças para os mesmos parâmetros na 4ª semana. No teste de preferência à sacarose, o grupo 6-OHDA mostrou menor preferência à sacarose na 1ª semana ($p=0,013$). Entretanto, na 3ª semana, não observamos diferença significativa entre os grupos ($p=0,12$). Por fim, no teste de interação social, os animais 6-OHDA interagiram significativamente menos com outro animal comparado ao grupo controle ($p=0,005$). Conclusion: A lesão parcial bilateral da via nigroestriatal produzida por infusão de 6-OHDA não produziu alterações motoras proeminentes, mas foi suficiente para produzir um estado transiente de anedonia e um prejuízo importante de interação social. Esses achados colaboram para a validação deste modelo animal de sintomas não motores da DP e abrem caminho para avaliações dos seus mecanismos subjacentes por meio de registros eletrofisiológicos e análises neuroquímicas. Support: ISN-CDG program, ISN-CAEN-1B program, FAPEMIG, Parkinson's Foundation, PRPq Protocol: (CEUA PP 0154/2022).</p>

Title	Modulation of recruitment from primary to secondary epileptic focus with different patterns of electrical stimulation in Wistar Audiogenic Rats
Authors	EVANDRO VALENTIM DE LIMA, FLÁVIO AFONSO GONÇALVES MOURÃO, MARCIO FLAVIO DUTRA MORAES, LEONARDO DE OLIVEIRA GUARNIERI
Affiliations	Fisiologia e Farmacologia, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy, though often seen as a syndrome with diverse causes and symptoms, consistently involves the spread of the epileptic focus to other regions in the brain. The Wistar Audiogenic Rat is an epilepsy animal model that has seizures when submitted to a 110dB sound. When this protocol is repeated over several days, the primary epileptic focus situated in the inferior colliculus begins to recruit a secondary one, the basolateral amygdala (BLA) in a phenomenon named Audiogenic Kindling. In the brain, inhibitory feedback loops are known to generate rhythmic neural activity. These rhythms create periods of heightened probability for neuronal firing, establishing an optimal structural basis for coordinated neural activity. Previous studies from our laboratory have shown that WARs have enhanced activation of the primary auditory pathway using steady state responses (ASSR). In order to investigate the mechanisms behind secondarily recruited epileptic foci, this work tests the hypothesis that the degree of coupling of amygdaloid activation to ASSR modulation frequency may facilitate or impair acoustic-limbic circuitry. Objective: Investigate if the amplitude-modulated ASSR degree of coupling with electrical stimulation of the amygdaloid complex modifies the pattern of audiogenic seizures. Methods: Female Wistar (n=10) and WAR (n=31) rats (age:8-10 weeks; weight:250-300g), were subjected to 3 consecutive days of continuous sound stimulation at 110dB for 1 minute each day. Following this stimulation, they were then divided into 3 groups: Wistar, WAR Low Audiogenic Response (WAR LAR) (WAR < 0.61 in Mesencephalic seizure severity indexes), and WAR High Audiogenic Response (WAR HAR)(≥ 0.61). All animals were then subjected to stereotaxic surgery for bilateral electrode implantation in the BLA. After one-week later, each group was further subdivided into three subgroups: Sham, synchronic stimulation (sync) (constant interpulse intervals of 250 ms synchronized with the peak of modulatory frequency), and non-synchronic (non-sync)(randomized interpulse intervals at an average of 4Hz). The experiment consisted of 3 consecutive days of sound stimulation at 110dB, modulated at 4Hz, with ES patterns corresponding to their respective groups (100μs duration pulse at 50 μA). Sound and ES stimuli were sustained for one minute. Results: In both WAR LAR (p=0,0303; F(1,13)=5,908) and WAR HAR (p=0,0022; F(1,12)=15,10) the modulated sound changed the severity of the mesencephalic seizures. Furthermore, the synchronic stimulation group of WAR LAR presented a statistical difference when compared with non-synchronic during the modulated sound (p=0,0114). It was also observed that synchronous stimulation in the WAR LAR group led to an increase in the severity of the seizures (Sham: 0.25(0, 0.36); WAR LAR Sync 0.85(0, 1)), while in the WAR HAR, there was a reduction in the severity of the seizures for both synchronous and non-synchronous sound modulation stimuli (Sham: 0.85(0, 1); WAR HAR non-sync 0 (0, 1); WAR HAR sync 0.18 (0, 1)). No limbic seizures were observed in these groups, with all remaining at 0 on the Racine scale. Conclusion: The modulated sound is capable of changing the severity of the mesencephalic seizures in WAR and combined with a synchronic electric stimulation in the BLA of LAR group can increase the seizures severity. In addition, randomized ES, probably `decoupling` acoustic-limbic integration, reduced seizure severity in both LAR and HAR groups. Support: We thank CAPES, CNPQ and FAPEMIG for supporting our research. Protocol: 147/2021</p>





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14 a 17 de Setembro de 2024
Hotel Glória Caxambu Resort & Convention

Title	Analysis of the anxiolytic profile and cognitive capacity of female Wistar rats at different ages during the periostropause phase
Authors	THAINÁ DAGUANE ESPERANÇA, MARIA EDUARDA RODRIGUES MARIN, BEATRIZ PROCÓPIO STRINGHETTA-VILLAR, DÉBORA PRAZIAS CAVALCANTE, LUANA GALANTE DOURADINHO, ISABELLA RIBEIRO PRADELA, JÚLIA ZANUTO DOURADINHO, FERNANDA BARBOSA LIMA, RITA CÁSSIA MENEGATI DORNELLES
Affiliations	Departamento de Ciências Básicas, UNESP, Universidade Estadual Paulista "Júlio de Mesquita Filho", Departamento de Ciências Fisiológicas, UFSC, Universidade Federal de Santa Catarina
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Aging, a process that all living beings experience, results from cellular functional decline. Perimenopause, a transitional phase in reproductive senescence exclusive to women, is characterized by various neurological symptoms and fluctuations in ovarian hormones. These hormonal changes, occurring during this critical period, can influence cognitive functions. Laboratory models using senescent female rodents are effective for studying human perimenopause. Understanding and identifying this critical period is essential for developing future interventions to positively impact female physiology. Objective: To analyze the anxiolytic profile and changes in recognition memory at different ages during the perimenopausal phase in rats. Methods: Female Wistar rats (n=24) with an average weight of 350 g and of different ages (15 months, 17 months, and 21 months) were included in the study (CEUA nº 0585-2021). The rats exhibited irregular estrous cycles (persistent diestrus). Ethological and temporal analyses were conducted using the open field test (OF) and the elevated plus maze (EPM). Short-term (STM) and long-term (LTM) memory retention were assessed using the object recognition test (OR), in addition to measuring the duration and frequency of object exploration. Data were expressed as mean ± SEM, with a significance level set at 5% (p<0.05). Results: Rats aged 21 months spent more time at the periphery of the apparatus during the OF test compared to rats aged 15 months (p<0.0001) and 17 months (p=0.0035). These 21-month-old rats also showed lower performance in terms of time spent in the center (p=0.0028 vs. 15Mo; p=0.0009 vs. 17Mo) and frequency of center entries (p=0.0234 vs. 15Mo; p<0.0001 vs. 17Mo). The number of quadrants covered in the center (p=0.0248 vs. 15Mo; p=0.0006 vs. 17Mo) and periphery (p=0.0363 vs. 15Mo; p=0.0079 vs. 17Mo) was also lower in the 21-month-old rats. In the EPM test, which analyzes the anxiolytic profile, the 21-month-old rats spent less time in the open arms compared to the 15-month-old rats (p=0.0492). The 17-month-old rats exhibited more rearing behavior (p=0.0009 vs. 15Mo; p<0.0001 vs. 21Mo) and greater immersion (p=0.0130 vs. 15Mo; p=0.0004 vs. 21Mo). In the OR task, during the training, 15-month-old rats explored the objects more than the 17-month-old (p=0.0007) and 21-month-old rats (p<0.0001). There were no significant differences between the groups in STM and LTM. However, the exploration time between familiar and new objects increased both with age (p=0.0056 and p=0.0197) and with the introduction of new objects (p<0.0001 and p=0.0005). The frequency of exploration also increased with age (p=0.0056) and with the introduction of new objects (p=0.0031 and p=0.0045, respectively). Conclusion: A characteristic anxiogenic profile was observed in animals at 21 months of age, a phase close to estropause. While the other age groups exhibited similar behaviors in many respects, they showed differences in specific situations, particularly the 17-month-old group, which alternated between an anxiolytic and anxiogenic profile. The same variability was seen in their exploratory capabilities. This indicates a possible critical window that should be studied for interventions aimed at reestablishing mechanisms prior to the transition phase. Such interventions could serve as preventive measures against neuropsychological and neurodegenerative disorders. Support: Coordination for the Improvement of Higher Education Personnel, CAPES (Code 001) Protocol: CEUA process nº 0585-2021</p>



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14 a 17 de Setembro de 2024
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Title	ANALYSIS OF ESTRADIOL IMMUNOMARKING IN THE HIPPOCAMPUS OF WISTAR FEMALES DURING REPRODUCTIVE SENESCENCE
Authors	LUANA GALANTE DOURADINHO, DÉBORA PRAZIAS CAVALCANTE, BEATRIZ PROCÓPIO STRINGHETTA VILLAR, THAINÁ DAGUANE ESPERANÇA, ISABELLA RIBEIRO PRADELA, JÚLIA ZANUTO DOURADINHO, ALLICE SANTOS CRUZ VERAS, RITA CÁSSIA MENEGATI DORNELLES
Affiliations	Departamento de Ciências Básicas, UNESP FOA
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The transition from adulthood to old age in women results from significant biological changes, characterizing reproductive senescence and aging. This period increases vulnerability to several health conditions, as neurodegenerative disorders, which can cause cognitive and memory decline. Objective: In this study, possible changes in the hippocampus of female rodents were investigated in different periods of reproductive life, from the cyclical period to the acyclical period. Methods: All procedures were approved by the Animal Use Ethics Committee (CEUA n° 760/2022). The study was carried out with multiparous females (<i>Rattus norvegicus albinus</i>; n=27), aged 9 months (regular estrous cycle, n= 9), 16 months old (with irregular estrous cycle, n= 9) and 24 months old (acyclic, n= 9), kept in a temperature-controlled room an inverted light-dark cycle. The hippocampi of decapitated animals were isolated for noradrenaline (NA) analysis by high-performance liquid chromatography with electrochemical detection (HPLC-EC) (n=6) and to citrate synthase enzyme (CS) activity analysis (n=6). Histological analysis were performed in each region of the hippocampus (DG: dentate gyrus; CA1; CA3) to quantify Nissl-positive cells after staining with cresyl violet. Immunolabeling for estrogen receptor beta (ERβ) was performed in the CA1 and DG regions (n=5). Data from manual cell counting, HPLC-EC, and CS analyses were subjected to ANOVA and Tukey's post-test. Results: The count of Nissl-positive cells in the three regions of the hippocampus was higher in cyclic rats aged 9 months. In contrast, the number of cells with Nissl bodies was significantly lower in the CA1 region of rats aged 16 months (p<0.0005) and 24 months (p<0.0001). Additionally, the reduction was more pronounced in female rats aged 24 months compared to those aged 16 months (p=0.0023). A significant reduction in the number of neural cells stained in the CA3 and GD regions was observed in acyclic rats aged 24 months (p<0.005) and in rats with an irregular estrous cycle at 16 months (p<0.05). Using the Immunostaining Pattern Score, differences in immunostaining was found between ages in the CA1 and GD regions of the hippocampus. Rats aged 16 months (p<0.0001; p<0.0016) and 24 months (p<0.0007; p<0.0020) had fewer cells immunostained with ERβ compared to 9-month-old rats. The determination of NA in the hippocampus did not show a statistically significant difference. However, 9-month-old rats exhibited greater CS enzymatic activity compared to 16-month-old rats (p=0.009), and 24-month-old rats showed higher activity than 16-month-old rats (p=0.003). Conclusion: These results indicate that during senescence, there is a reduction in the number of estrogen receptors, viable neural cells, and changes in noradrenaline levels. These effects are more pronounced in rats transitioning from cyclicity to reproductive acyclicity at 16 months, identifying this period as a 'critical window.' This transition involves complex pathway activations and deactivations in the female organism. Therefore, further basic and clinical research is needed to better understand how these neural changes can influence health and responses to therapeutic medications. Support: FAPESP Protocol: CEUA n° 760/2022</p>



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Title	Influences of prenatal exposure to valproic acid on rat behavior and hippocampus: animal model for autism
Authors	ISABELLA RIBEIRO PRADELA, DÉBORA PRAZIAS CAVALCANTE, THAINÁ DAGUANE ESPERANÇA, LUANA GALANTE DOURADINHO, BEATRIZ PROCÓPIO STRINGUETTA-VILLAR, JÚLIA ZANUTO DOURADINHO, RITA CASSIA MENEGATI DORNELLES
Affiliations	Laboratório de Fisiologia endócrina e envelhecimento, Universidade Estadual Paulista Júlio de Mesquita Filho, Unesp
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Autism spectrum disorder (ASD) is a neurobehavioral disorder characterized by delayed development of skills to varying degrees. Individuals with ASD often exhibit sensory and cognitive impairments, including deficits in executive functioning, spatial reasoning, and working memory. Structural and functional abnormalities in the hippocampus have been implicated in the cognitive and affective deficits observed in individuals with ASD. Animal studies have shown that valproic acid (VPA) affects brain development, leading to autism-like behaviors in rodents. Although VPA is used to treat epilepsy and bipolar disorder, its use during pregnancy raises significant concerns. Objective: To analyze the behavior of offspring exposed to a pro-oxidative environment triggered by VPA in utero. Methods: This study involved the offspring of 4 female rats and 2 male rats, all 3 months old. After collecting the estrous phase cycles, the animals were paired, with the first day of pregnancy confirmed by the presence of sperm in the estrous cycle collection (CEUA process FOA nº 510-2023). On day 12.5 of gestation, 2 rats received VPA (Santa Cruz; 600 mg/kg/ip – VPA Group) and 2 rats received saline solution (Saline Solution Group). Thirty puppies, male and female, participated in the study: 18 puppies from the saline group (Salina/M; Salina/F) and 12 puppies from the VPA group (VPA/M and VPA/F). Eye opening time, social aggregation test (PN16), object recognition test (PN30) and open field test (PN35) were analyzed. Data were expressed as mean ± SEM. The level of rejection of the null hypothesis was set at 5% ($p < 0.05$). Results: The eye-opening in the VPA groups occurred, on average, on the 14th day ($p < 0.05$), while the saline group opened their eyes on the 12th day after birth ($p < 0.05$). In social aggregation, time was taken into account, every 1 minute the VPA group demonstrated greater regularity in aggregation activity compared to the saline group. ($p = 0.0001$). In the open field test, the VPA/M group spent more time in the periphery compared to the saline/M group ($p = 0.0414$). Additionally, the saline/F group entered the center more frequently than the VPA/F group ($p = 0.0137$). No statistical differences were found in other analyses, including time spent in the center and the thigmotaxis index. In the ethological analysis of the open field test, the VPA/F group exhibited a lower frequency of grooming behavior compared to the saline/F group ($p = 0.0367$). There was no statistical difference in rearing. In the object recognition test, the VPA/F group showed greater exploration during the sample phase than the saline/F group ($p = 0.0016$). Similarly, the VPA/M group had greater exploration compared to the saline/M group ($p = 0.0121$). Significant differences in exploration were observed between the VPA groups (M and F) and the saline groups (M and F) ($p = 0.0230$). No statistical difference was noted in the choice phase analysis. Conclusion: The results showed an anxiogenic profile in the VPA group in relation to the saline group, suggesting behaviors, in rodents, similar to autism. In this study, we found that a single exposure to VPA in utero at 12.5 days of pregnancy leads to behavioral changes, emphasizing the critical nature of the exposure time window and its impact on neurodevelopment. We highlight the importance of understanding how exposure to VPA influences neurodevelopment and its link to cognitive function and the risk of autism. Support: Institutional Scientific Initiation Scholarship Program (PIBIC) Protocol: CEUA process FOA nº 510-2023</p>

Title	Neuroprotective effects of supplementation with flaxseed oil and/or α-lipoic acid in the hippocampus of rats in a model of orofacial dyskinesia induced by haloperidol
Authors	FRANCISCA TAYNÁ DA SILVA GOMES, KARINA MAIA PAIVA, RODRIGO FREIRE OLIVEIRA, PALOMA KATLHEEN MOURA MELO, LAVÍNNYA YÁSKARA DE AQUINO MATOSO, ALEXIA MIRANDA MORAIS, PAULO LEONARDO ARAUJO DE GOIS MORAIS, CIBELE DOS SANTOS BORGES, JOSÉ RODOLFO LOPES DE PAIVA CAVALCANTI
Affiliations	Departamento de Ciências Biomédicas, Universidade do Estado do Rio Grande do Norte, UERN, Departamento de Biociências, Universidade Federal Rural do Semi Árido, UFRSA
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Tardive dyskinesia is a motor syndrome primarily caused is the blockade of dopaminergic D2 receptors, linked to the nigrostriatal pathway. Research into substances with antioxidant action has intensified, such as the use of linseed oil (<i>Linum usitatissimum</i> L.) and α-lipoic acid, with emphasis on its neuroprotective action, in important neuroplastic regions such as the hippocampus. Objective: To quantify the behavioral activity of anxiety and memory/learning in rats treated with haloperidol and supplemented with antioxidant substances. Methods: The work was approved by the Animal Experimentation Ethics Committee (CEEA) of the State University of Rio Grande do Norte (UERN) with protocol number 002/2021. Eighty male Wistar rats were used, with an average age range of 3 to 8 months old, weighing between 250-350 g, randomly arranged in 5 experimental groups with 16 animals per group: I) control negative (no supplemental diet or haloperidol); II) administration of haloperidol; III) administration of haloperidol with a supplemental lipoic acid diet (HALAL); IV) administration of haloperidol with a supplementary diet of linseed oil (HALOL) and V) administration of haloperidol with a supplementary diet of lipoic acid and linseed oil (HALOLAL). For behavioral assessments of anxiety and memory/learning, open field, elevated plus maze, Y maze, object recognition and perforated plate tests were carried out. For statistical analysis, multiple comparison of parameters Analysis of Variance (ANOVA) One Way with Tukey post-test was used. Data were expressed as mean \pm standard error of the mean (SEM) and the level of significance adopted was defined as $p < 0.05$. Results: In the elevated plus maze, the HALOLAL group had a longer stay in the open arms compared to the haloperidol group [$F(4,40)=3$, $p < 0.05$], the HALOL group [$F(4,40)=3$, $p < 0.05$] and the negative control [$F(4,40)=3$, $p < 0.05$]. In the open field, the HALAL group showed greater exploration compared to the haloperidol group [$F(4,40)=0.0324$, $p=0.035$] and in the perforated plate test the HALOLAL group showed greater exploration compared to the haloperidol group [$F(4,40)=4$, $p=0.0044$]. In the Y-maze test, the HALAL group demonstrated better working memory performance when compared to the negative control [$F(4,40)=5.582$, $p < 0.05$] and haloperidol [$F(4,40)=5.582$, $p < 0.05$]. In the short-term memory test, the HALAL group showed an increase in the recognition rate of the new object in relation to the haloperidol group [$F(4,40)=2$ $p < 0.05$], while in the assessment of long-term memory, the HALOL group presented a higher index in relation to the negative control [$F(4,35)=4$, $p=.0006$], haloperidol [$F(4,35)=4$, $p=.0273$] and HALAL [$F(4,35)=4$, $p=.0098$]. Conclusion: Our findings show that there was an increase in working memory capacity, as well as short- and long-term memory in the α-lipoic acid and flaxseed oil supplemented groups, respectively. Furthermore, an anxiolytic effect associated with the synergy of the substances was observed, evidenced in the elevated plus maze and perforated plate tests. Our results will proceed to molecular and immunohistochemical stages in order to identify potential morphological and/or neurochemical changes. Support: Grant granted by the National Council for Scientific and Technological Development (CNPq). Protocol: Protocol number 002/2021.</p>

Title	Evaluation of facilitatory and inhibitory pain pathways in women with fibromyalgia: a cross-sectional observational study
Authors	LARA COSTA MOURA, ANDRÉ LUÍZ SILVA SANTOS, NICOLE PEREIRA FRANÇA, ISABELA VICTORIA BATISTA DE JESUS, ANNE LETÍCIA ARLINDO ALMEIDA, FLÁVIA DIANA SANTOS FIGUEREDO, MONIQUE OLIVEIRA DOS SANTOS, THAÍS ALVES BARRETO PEREIRA, JOSIMARI MELO DESANTANA
Affiliations	Departamento de Fisioterapia, UFS, Departamento de Ciências da Saúde, UFS, Departamento de Ciências Fisiológicas, UFS, Departamento de Fisioterapia, UNIT
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Fibromyalgia is a syndrome characterized by chronic musculoskeletal pain associated with symptoms such as sleep disturbances and anxiety. Chronic pain can promote dysregulation at the level of the central nervous system, resulting in increased release of excitatory neuromodulators such as glutamate and substance P, and reduction of inhibitory ones, in the rostral ventromedial medulla, such as opioids and gamma-aminobutyric acid. Therefore, neurophysiological clinical knowledge of pain in women with fibromyalgia is necessary for a better understanding of its mechanisms. Objective: To evaluate the facilitatory and inhibitory neural pathways of pain in women with fibromyalgia. Methods: This is a cross-sectional observational study. The project was approved by the Research Ethics Committee of the Federal University of Sergipe (CAAE 73736223.7.0000.5546) and research participants signed the Informed Consent Form. The study included women between 18 and 60 years old, diagnosed with fibromyalgia. Outcomes were assessed using temporal summation and conditioned pain modulation tests to infer the level of facilitation and inhibition of pain pathways, respectively. Values were expressed as mean \pm standard deviation. Shapiro-Wilk normality test was used, followed by one-way ANOVA variance test and Tukey's post-test. GraphPad Prism 8.0 software was used. Values were considered statistically significant when $p < 0.05$. Results: Thirty-seven women were evaluated with a mean age of $42,76 \pm 9,54$. Based on the numerical pain scale, the sample had an average pain score of 6.63 ± 1.80 at the time of evaluation. In temporal summation, an increase in pain intensity at each sequential time was observed, showing significant differences between 1' and 10' ($p < 0.0001$), 10' and 20' ($p < 0.0001$), and 20' and 30' ($p = 0.0179$), suggesting an increase in the facilitatory pathway. While in conditioned pain modulation, a significant difference was observed between the pressure pain threshold measured before and during the test ($p = 0.0338$), whereas there was no difference between the pressure pain threshold during and 5 minutes after the test ($p = 0.88$), showing a reduction in the activity of the inhibitory pain pathway. Conclusion: Women with fibromyalgia present impairment of both facilitatory and inhibitory pain pathways, showing increased temporal summation and reduced conditioned pain modulation. Therefore, this condition may favor the increase of postsynaptic potentials, resulting in the sign amplification and increased pain intensity in fibromyalgia as detected in the clinical setting. Support: Coordination for the Improvement of Higher Education Personnel (CAPES); National Council for Scientific and Technological Development (CNPq). Protocol: 73736223.7.0000.5546</p>

Title	Defensive behavioral reactions evoked by threat pictures in students with and without violence trauma
Authors	SARA DOMICIANO DE JESUS GASPAR, BIANCA AFONSO SOARES DA SILVA, THAYANE FERREIRA DA COSTA FERNANDES, LIANA CATARINA LIMA PORTUGAL, LETICIA DE OLIVEIRA, MIRTES GARCIA PEREIRA, ELIANE VOLCHAN, ORLANDO FERNANDES JUNIOR, ISABELA VILLARINHO DE PAULA LOBO
Affiliations	Psicobiologia, UFRJ, , UERJ, Fisiologia, UFF, , UFRJ
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: After the perception of a threat, a sequence of defensive motivational behaviors is triggered in a process described as the `defensive cascade`. The progression of these defensive reactions is according to some characteristics, such as the proximity of the threat. Objective: Investigate differences in behavioral responses in participants with violence trauma versus without through a task with visual stimuli depicting guns where the direction of the gun in relation to the observer modulates the availability of escape.</p> <p>Methods: Sixty-nine participants (46 women, mean age= 25.83) viewed 80 photos (40 threat stimuli: 20 “directed-toward” (guns directed toward the observer) and 20 and “directed-away” (guns directed away from the observer), interleaved with 40 controls (people with non-lethal objects, 20 “directed-toward”, 20 “directed-away”). While viewing the pictures, the participants were asked to judge the valence of the pictures (unpleasant or neutral) by pressing their finger on the answer keys as quickly and as correctly as possible and the reaction time (RT), in milliseconds (ms), were collected. The sample was split into participants: a) people with the worst trauma related to urban, sexual or domestic violence; b) people without violence trauma being the worst trauma. The mean of the median RTs per participant in each condition was calculated and a Generalized Estimating Equations (GEE) model with Gamma with log link was conducted, with the factors direction, valence and group. The local Research Ethics Committee approved the experiment (CAEE: 92088518.8.0000.5699). Results: There was an effect of direction on RTs, where there was an acceleration for “directed-toward” images (645.47 ± 13.77) compared to “directed-away” images (676.24 ± 16.06) (GEE model, $p=0.002$, Bonferroni post hoc, $p= 0.002$). An effect of valence was also observed, with a lower RT for threat images (636.69 ± 14.63) than for neutral images (685.56 ± 14.93) (GEE model, $p<0.001$, Bonferroni post hoc, $p<0.0001$). Furthermore, there was an interaction between valence and trauma, in which the trauma group was faster at performing the task for the violent images (623.45 ± 21.42) compared to the neutral ones (698.75 ± 23.82) (GEE model, $p= 0.003$, Bonferroni post hoc, $p<0.0001$).</p> <p>Conclusion: The direction and valence of the stimulus influences defensive behavior. So, for the “directed-toward” and threat images generated an acceleration in RT, probably by evoking the second stage of the defensive cascade, a motor preparation related to fight-or-flight responses. Whereas for the “directed-away” images, a delay in RT associated with the first defensive behavior described in the defensive cascade, freezing, was observed. It was also seen that trauma is effective in modulating behavioral patterns of defense, where only the group with trauma showed acceleration for threat images. Support: CAPES, CNPq, FAPERJ. Protocol: 92088518.8.0000.5699</p>



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Title	RETINAL DEGENERATION AND CENTRAL BIOLOGICAL CLOCK ALTERATIONS INDUCED BY GLAUCOMA DISRUPT DAILY RHYTHM REGULATION IN THE HPA AXIS IN MICE
Authors	PIETRA SOUZA BARSANELE, LEONARDO VINICIUS DE ASSIS, ELIZ MARIA DE OLIVEIRA FURTADO, JULIANO JEFFERSON DA SILVA, JOSÉ CIPOLLA NETO, MARISTELA DE OLIVEIRA POLETINI, MARIA NATHÁLIA MORAES
Affiliations	Departamento de Ciências Biológicas, UNIFESP, Departamento de Fisiologia, USP, Departamento de Fisiologia e Biofísica, USP, Departamento de Fisiologia e Biofísica, UFMG, Department of Natural Sciences, University of Lübeck
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Glaucoma, a chronic optic neuropathy, causes degeneration of retinal ganglion cells, which are crucial for transmitting temporal signals to synchronize biological rhythms in the suprachiasmatic nucleus (SCN). The synchronization of the SCN by the environmental light-dark cycle establishes a unified time zone across organs via body temperature, hormone secretion (e.g., corticosterone) and other factors. We have demonstrated that glaucoma mice showed disrupted circadian oscillation in the transcription of light-responsive genes <i>Per1</i> and <i>Vip</i> in the SCN. Moreover, we observed a shift in the peak expression of <i>Avp</i>, which plays a crucial role in the efferent projection of the SCN to other brain regions. Objective: As the SCN temporally modulates corticosterone secretion through the hypothalamic-pituitary-adrenal axis (HPA), we investigated the impact of retinal neurodegeneration on the molecular clock machinery and the components of the HPA axis in mice with glaucoma. Methods: Twelve-month-old male control (DBA/2J GPNMB+) and advanced glaucoma mice (DBA/2J) were maintained on a 12L:12D cycle at a 24 (± 1) °C with food and water ad libitum. The pituitary and adrenal glands were removed every 4 hours for 24 hours and processed for gene expression analysis (N= 4-10 to each time point). Differences between groups were compared by Two-way ANOVA followed by Bonferroni post-test. Rhythmic parameters were performed by CircaCompare analysis. Results: We identified that the core clock genes <i>Per1</i>, <i>Per2</i>, and <i>Bmal1</i> display circadian oscillation in the pituitary gland in both groups. However, in mice with glaucoma, <i>Per1</i> and <i>Bmal1</i> showed a significant increase in mesor ($p < 0.0001$ for both genes) and amplitude ($p = 0.02$ and $p = 0.003$, respectively) compared to the control group. Additionally, <i>Per1</i> and <i>Bmal1</i> exhibited a phase advance of about 3 and 1 hour, respectively ($p = 0.04$ and $p = 0.01$). Rhythmic mRNA of <i>Crh-r1</i> was observed in both groups, but we noted a 12-hour phase delay ($p < 0.0001$) in the peak expression with a reduction in mesor ($p = 0.01$) in the glaucoma compared to the control mice. Control group showed a temporal oscillation of <i>Pomc</i> ($p < 0.0001$) that was lost in the glaucoma group. In the adrenal gland, we found a 3-hour phase delay ($p = 0.001$) in the peak expression of <i>Per2</i> compared to the control group, resulting in a shift of the peak from ZT13 to ZT16. <i>Bmal1</i> expression displayed a 1-hour phase delay ($p = 0.04$) in the glaucoma group compared to the control group. Glaucoma leads to a loss of oscillatory profile of <i>Mc2-r</i> mRNA ($p = 0.240$), while the control mice showed a rhythmic oscillation pattern ($p = 0.01$). Both groups exhibit rhythmicity in the expression of <i>Star</i>, but we notice an increase in <i>Star</i> expression at ZT12 ($p = 0.01$) in glaucoma group compared to the control. Conclusion: We describe changes in the molecular mechanisms of the HPA axis induced by retinal neurodegeneration in glaucoma. This neuronal degeneration defined the HPA axis transcript signature, with altered expression of genes involved in the circadian regulation of corticosterone secretion such as <i>Chr-r1</i>, <i>Mc2-r</i> and <i>Star</i>. Our study provides evidence of modifications in the HPA axis that could explain the alterations in corticosterone secretion observed in patients with glaucoma. Understanding the systemic effects of glaucoma can provide insights for developing targeted therapeutic interventions to address hormonal imbalances resulting from chronodisruption associated with glaucoma. Support: CNPq and Fapesp (Process 2022/07969-6, 2017/26651-9). Protocol: CEUA nº 8143290819</p>



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Title	Cytoarchitectonic Characterization of the Globus Pallidus of the Marmoset (<i>Callithrix jacchus</i>) using Immunohistochemistry for Parvalbumin
Authors	LAVÍNYYA YÁSKARA DE AQUINO MATOSO, FRANCISCA TAYNÁ DA SILVA GOMES, PALOMA KATLHEEN MOURA MELO, ALEXIA MIRANDA MORAIS, RODRIGO FREIRE OLIVEIRA, EXPEDITO SILVA DO NASCIMENTO JÚNIOR, PAULO LEONARDO ARAÚJO DE GOIS MORAIS, JOSÉ RODOLFO LOPES DE PAIVA CAVALCANTI
Affiliations	Departamento de Ciências Biomédicas, Universidade do Estado do Rio Grande do Norte, UERN, Centro de Biociências, UFRN
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The globus pallidus (GP) is a nuclear complex, divided into its lateral (GPI) and medial (GPm) portions, is an essential structure of the basal ganglia, playing a central role in the regulation of voluntary movement. Information about the morphophysiology of these nuclei is necessary to better understand how they have differentiated among various species and how their specificities can contribute to the expression of different behavioral repertoires. In this context, calcium-binding proteins such as parvalbumin (PV) are important markers for characterizing different populations of interneurons, as their distribution in GP interneurons may reflect significant functional variations, helping to clarify the mechanisms of movement regulation and possible alterations associated with motor disorders. Objective: Characterize the cytoarchitecture of the GP in the common marmoset (<i>Callithrix jacchus</i>) using immunohistochemical techniques, with the aim of identifying and describing the distribution, morphology, and density of interneurons marked by parvalbumin (PV). Methods: Six young adult male marmosets, aged 4 to 7 years and weighing between 200 and 400 grams, were used. Sections were subjected to immunohistochemistry for PV. For the sample collection, the animals underwent pre-anesthesia (atropine + tramadol), anesthesia (xylazine + ketamine), transcardiac perfusion, and brain removal. After removal, the brains were sectioned and the sections were subjected to immunohistochemistry against PV. The sections were then mounted on histological slides which, after osmium intensification, were evaluated using a microscope, with digital images documented. All procedures followed strict ethical and technical standards. Ethical approval protocol (002/2021, CEAA/UERN). Results: In general, PV immunohistochemical expression allowed for the structural delineation of the GP nuclear complex, especially in terms of differentiating its two nuclei (GPI and GPm). It is important to mention that its structural organization is similar to that of other previously studied species. Additionally, it was possible to identify subpopulations of PV+ neurons (predominantly fusiform and ovoid) in both nuclei, but with distinct distributions. In the GPI, the predominance of interneurons is in the dorsolateral compartment. In the GPm, in addition to having a higher concentration of PV+ neurons, these appear to be diffusely distributed throughout the GP. Conclusion: Indeed, the cytoarchitecture of the components that make up the GP nuclear complex is very similar to what is known about other studied species. However, the differences found in the distribution of PV+ cells throughout each of the nuclei may be related to the function of each of these nuclei in the basal ganglia circuit. From this, the importance of studies related to the neurochemical and connectomic characterization of these nuclei arises, in order to elucidate potential nuclear subunits, especially in the GPI. Support: Grant granted by the Coordination for the Improvement of Higher Education Personnel (CAPES). Protocol: Protocol number 002/2021.</p>

Title	TRATAMENTO PERINATAL COM QUERCETINA MELHORA FORÇA MUSCULAR EM RATOS EXPOSTOS À PARALISIA CEREBRAL EXPERIMENTAL
Authors	ANA CRISTINA DA SILVA, PAULA BRIELLE PONTES, JAMERSON NASCIMENTO DA SILVA, EULALIA REBECA SILVA ARAÚJO, DIEGO CABRAL LACERDA, HENRIQUE GOUVEIA, ANA ELISA TOSCANO, RAUL MANHÃES DE CASTRO, ANA CRISTINA DA SILVA
Affiliations	Departamento de Nutrição, UFPE
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Lesões perinatais têm impactos duradouros no funcionamento dos sistemas fisiológicos, como neurotransmissão (incluindo precursores, neurotransmissores, receptores e células neurais ou não neurais), mas também desempenham um papel crucial na plasticidade fenotípica do músculo esquelético e atividade locomotora. Nesse contexto, distúrbios neurológicos podem resultar de agressões ambientais, como é o caso da paralisia cerebral (PC). Este estudo tem como objetivo investigar o efeito do tratamento neonatal com quercetina na atividade locomotora em ratos submetidos à PC experimental. Objective: Objetivo geral: Estudar o efeito do tratamento perinatal com quercetina sobre a atividade locomotora e força muscular em ratos submetidos a PC. Objetivos específicos: 1) A evolução do ganho de peso corporal dos filhotes até 21º dia pós natal; 2) o desenvolvimento da atividade locomotora durante a lactação. Methods: Após aprovação do CEUA (n 005/2022), 40 ratos wistar machos provenientes de 10 ratas primíparas com entre 80 e 120d de idade e peso entre 220 a 250g. Após a confirmação da gravidez, foi introduzido o modelo farmacológico de paralisia cerebral. Os grupos foram divididos da seguinte forma: 1- Controle + salina (CS, n=10); 2- Controle + quercetina (50mg/kg) (CQ, n=10), 3- PC + salina (PCS, n=10) e 4- PC + quercetina (PCQ, n=10). Os grupos com PC receberam 200 µg/kg de lipopolissacarídeo (LPS) (i.p.) do dia 17 até 21 da gestação. Ao nascer, a prole foi submetida a anoxia por 20 min. No P25 os animais passaram pelo GripStrenght para avaliar a força de preensão. Os resultados foram avaliados em número absoluto e também relativizados pelo peso corporal. Os dados foram avaliados por Anova 2Way + Bonferroni's post test. Results: os grupos PCS (189.15 ± 58.67) e PCQ (216.31 ± 50.95) apresentaram menor força absoluta que o grupo CQ (329,50 ± 29,72) (p<0,05). A força muscular relativa em PCS (2,73 ± 0,84) e PCQ (3,28 ± 0,89) também foram menores que o grupo CQ (5,13 ± 1,02) (p<0,05). Conclusion: A quercetina é eficaz na melhoria da força muscular em ratos expostos à PC experimental. Support: Facepe Protocol: 005/2022</p>



Title	PROTECTIVE EFFECT OF EXERCISE TRAINING AND CURCUMIN ON REDOX STATUS AND SIRT1 EXPRESSION IN THE HIPPOCAMPUS OF RATS WITH DIABETES IN AN EXPERIMENTAL MODEL OF POSTMENOPAUSE
Authors	BEATRIZ ANJOS DE OLIVEIRA, SUZETE CARVALHO LANDULFO LUZ, JULITA MARIA PEREIRA BORGES, GABRIELA FREITAS SILVA BITENCOURT, MARINA MORENA BRITO FARIAS, RAIARA DOS SANTOS PEREIRA, LARISSA CRUZ AMADO, LUCAS FARIAS BRITO, UESLEI SILVA SANTOS, FLÁVIO SILVA JESUS, LUANA PEREIRA OLIVEIRA, SABRINA JULIA SILVA, GABRIELA SANTOS LIBARINO, TELMA DE JESUS SOARES
Affiliations	Departamento de Biointeração, UFBA, Departamento de Ciência e Tecnologia, UESB
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Hippocampal impairment in the coexistence of type 1 diabetes mellitus (T1DM) includes oxidative stress pathways and defects in Sirtuin 1 (SIRT1) signaling. However, there are no studies evaluating the effect of exercise and curcumin treatment on redox status and SIRT1 expression in the hippocampus of female rats with T1DM during the period of decreased ovarian hormones. Objective: Therefore, this study evaluated the effects of moderate-intensity training and curcumin on redox status, SIRT1 immunostaining in the CA3 area and on the extension of CA3 area in the hippocampus of ovariectomized rats with T1DM. Methods: 24 eight-week-old female Wistar rats were divided into 4 groups (n=6/each): Ovariectomized Sedentary Diabetic (OSD), Ovariectomized Trained Diabetic (OTD), Ovariectomized Sedentary Diabetic + Curcumin (OSD+CUR) and Ovariectomized Trained Diabetic + Curcumin (OTD+CUR). The animals underwent bilateral ovariectomy and T1DM was induced by a single intravenous injection of STZ (40 mg/Kg). The trained groups performed a treadmill running protocol for 8 weeks and rats treated with curcumin received it orally by gavage (100 mg/Kg) for the same period. The experiments were approved by the Animal Experimentation Ethics Committee of the IMS/CAT/UFBA (Protocol No. 096/2021). Statistical analysis was performed using Anova Two-Way in the presence of normal data distribution. Data were expressed as Mean±SD and results with p-value <0.05 were considered statistically significant. Results: Our results demonstrated that the association of exercise and curcumin treatment decreased the levels of TBARS (µM/mg) in the hippocampus of animals from the OTD+CUR group (0.9513±0.3814) compared to the isolated treated groups, OTD (1.509±0.3123) and OSD+CUR (1.588±0.4180), p<0.05. Exercise and curcumin decreased total nitrites (µM/mg) levels in the hippocampus of OTD (8.230±1.516) and OSD+CUR groups (7.455±1.309), respectively, compared to OSD (15.350±1.948), p<0.001. Combined treatment reduced total nitrite levels in the hippocampus of OTD+CUR group (5.424±1.074) only in relation to OTD group (8.230±1.516), p<0.01. In addition, protein carbonylation levels (nmol/mg) were decreased by the independent treatments in the hippocampus of OTD (3.417±0.7135) and OSD+CUR (4.912±0.8362) groups compared to OSD (8.135±0.8634), p<0.001. Exercise and curcumin increased GSH-Px (U/mg) levels in the OTD (0.3745±0.4135) and OSD+CUR (0.2280±0.02759) groups compared to OSD (0.1072±0.04094), p<0.001. Combined treatment improved these levels in OTD+CUR (0.3328±0.03984) group only in relation to OSD+CUR (0.2280±0.02759), p<0.001. Additionally, hippocampus CA3 area showed an increase of SIRT1 immunostaining in the isolated treatments, OTD (6.717±1.141) and OSD+CUR (3.344±0.7209), p<0.001, in relation to OSD (1.786±0.7365). Combined treatment, OTD+CUR (8.394±0.8613, p<0.05), improved SIRT1 expression compared to individual treatments. Furthermore, the extension of CA3 area in OTD (148.7±5.836, p<0.001) and OSD+CUR (102.3±11.04, p<0.01) were improved in comparison with OSD (75.79±16.54). Conclusion: Our study demonstrated that the association between curcumin and training attenuated oxidative damage by reducing TBARS and increasing SIRT1 immunostaining in CA3 area. Curcumin and training, independently, improved GSH-Px levels, reduced protein carbonylation and total nitrites and increased CA3 area extension in the hippocampus of ovariectomized rats with T1DM. Support: Capes Protocol: Protocol No. 096/2021.</p>



Title	Cytoarchitectonic and immunohistochemical characterization of calcium-binding proteins from the primary motor cortex of the marmoset (<i>Callithrix jacchus</i>)
Authors	ALEXIA MIRANDA MORAIS, LUÍS MARCOS DE MEDEIROS GUERRA, PALOMA KATLHEEN MOURA MELO, LAVÍNNYA YÁSKARA DE AQUINO MATOSO, FRANCISCA TAYNÁ DA SILVA GOMES, RODRIGO FREIRE OLIVEIRA, EXPEDITO SILVA DO NASCIMENTO-JÚNIOR, PAULO LEONARDO ARAÚJO DE GÓIS MORAIS, JOSÉ RODOLFO LOPES DE PAIVA CAVALCANTI
Affiliations	Departamento de Ciências Biomédicas (DCB), UERN, Centro de Biociências (CB), UFRN
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The primary motor cortex (M1) contains specialized neurons that are responsible for planning and initiating voluntary movements. Calcium-binding proteins (CBPs) are the main buffers of intracellular calcium, acting in neuronal protection, modulation, and plasticity. Furthermore, they serve as important anatomical markers for distinct neuronal subpopulations, aiding in the understanding of neuronal locomotor networks. The Common Marmoset (<i>Callithrix jacchus</i>) is an animal model that has been gaining interest in neuroscience due to its suitability for studying the neural basis of voluntary motor control. The existence of parallels and differences in the cortical motor system of marmosets underscores the need for investigations involving architectural and functional analyses. Objective: To analyze the cytoarchitecture of neurons with CBPs (calbindin, CB and parvalbumin, PV) in the M1 of marmosets. Methods: Were used existing slides of six adult male animals, obtained from the Primatology Nucleus of the Federal University of Rio Grande do Norte (UFRN). The slides, belonging to the archive of the Neuroanatomy Laboratory of UFRN, were obtained by perfusion procedures, brain extraction, microtomy, Nissl staining, and immunohistochemistry for CB and PV. The cortical sections were examined with a high-resolution optical microscopy system and analyzed using indirect observation to describe the cortical layers and Imagej® for morphometric analysis. The research was approved by the Ethics Committee on Animal Experimentation of UERN (CEEA/UERN), opinion 006/20. Results: The immunohistochemical analyses for CB (CBir) and PV (PVir) revealed satisfactory markings of the cortical structure. M1 demonstrated a homogeneous agranular appearance, highlighting structures of layer V and indistinctness of layer IV. Analyzing the immunoreactivity by visual contrast, in CBir, the cortical layers presented a decreasing gradient of immunoreactivity, layers I to III presented greater immunoreactivity; while layers II, III, and V showed greater hyperreactivity to PV. CBir had greater cell density in layer II and the presence of halo cells in layer V, while in PVir layers II, III and V had greater cell density. Neurons had greater soma in layer V and PVir neurons were larger than CBir. Conclusion: The CBPs allowed the anatomical characterization of the M1, with immunohistochemistry differences between the cytoarchitecture and morphometry. Variations in laminar distribution suggest the existence of different functions in the cortical circuit, contributing to regional differences. Support: This research was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES) and the National Council for Scientific and Technological Development (CNPq). Protocol: No. 006/20</p>

Title	Resistance Training: A Promising Strategy to Mitigate Neuronal Decline During Reproductive Senescence in Females
Authors	BEATRIZ PROCÓPIO STRINGHETTA-VILLAR, LUANA GALANTE DOURADINHO, THAINA DAGUANE ESPERANÇA, DÉBORA PRAZIAS CAVALCANTE, ISABELLA RIBEIRO PRADELA, JULIA ZANUTO DOURADINHO, ANGELA CRISTINA DE NICOLA, ANTONIO HERNANDES CHAVES NETO, RITA CÁSSIA MENEGATI DORNELLES
Affiliations	DEPARTAMENTO DE CIENCIAS BÁSICA (LAB. FISILOGIA ENDÓCRINA E ENVELHECIMENTO), UNESP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The transition from fertility to infertility in females involves hormonal and metabolic changes that affect neurological aspects, propitiating to cognitive and functional declines. Rodents in periostropause also experience follicular decline, irregular cycles, fertility issues, and steroid hormone fluctuations.</p> <p>Objective: Considering this transition phase as an opportunity for preventive strategies against neurodegenerative diseases, we chose to evaluate resistance training (RT) as a non-pharmacological approach to mitigate cognitive and functional decline during periostropause. Methods: This study was carried out with thirty 17-month-old female Wistar rats (382.5 ± 13.1 g) whose estrous cycle irregularity was confirmed. The rats were distributed into untrained group (NT; n=15) and RT group (n=15) (CEUA 585/2021). The RT group performed stair climbing (3 times/week for 4 months) on alternate days. Functional and cognitive tests (ambulation and object recognition) were conducted at the beginning and end of the experimental period when the rats were 21 months old (378.1 ± 15.8 g). The hippocampi of the rats were analyzed for citrate synthase (CS) activity, Nissl-positive cell quantification using cresyl violet staining, and BDNF labeling via immunohistochemistry. A two-way ANOVA was used to compare performance in functional and cognitive tests, while histological parameters were compared using an unpaired Student's t-test. Data were expressed as mean \pm SEM, with a significance level of 5% ($p < 0.05$). Results: Results showed a significant interaction between RT and the age of the rats in both length ($p < 0.0001$) and width ($p = 0.0453$) of stride. This analysis showed that at 21 months, the NT group exhibited a decrease in stride length ($p = 0.0458$) and an increase in stride width ($p = 0.0479$) compared to their measurements at 17 months. The object recognition test indicated cognitive improvement in the RT group, with significant interactions between intervention and age across all three test stages (total exploration time, $p = 0.0001$; Test 1, $p = 0.0003$; Test 2, $p = 0.0014$). This improvement was notable compared to the NT group, which showed a decline in memory capacity ($p < 0.01$). Hippocampal cells from the RT group demonstrated increased citrate synthase activity ($p = 0.0331$) and more Nissl body staining in the CA1 ($p = 0.0001$), CA3 ($p = 0.03$), and DG ($p = 0.01$) regions. Furthermore, BDNF immunostaining was higher ($p < 0.0001$) in the RT group in the CA1 (71.00 ± 0.9), CA3 (10.00 ± 0.5), and DG (40.00 ± 0) regions when compared with the NT group. Conclusion: These results demonstrate that RT during periostropause leads to significant improvements in functional abilities, cognitive performance, and neuroplasticity in aging female rats. Specifically, RT was shown to protect memory, as assessed through short- and long-term recognition tests, possibly via the BDNF pathway, which was more dense in the hippocampus of the RT group. Conversely, memory was impaired in rats that did not undergo RT during periostropause. These findings have important implications for developing exercise-based interventions to promote cognitive health and prevent cognitive decline. Although further investigation is required to understand the specific mechanisms underlying these benefits, RT appears to be an effective non-pharmacological intervention to prevent and reduce cognitive decline and improve cognitive and motor health in aging females. Support: CAPES Protocol: 585/2021</p>



Title	AVALIAÇÃO DA PARTICIPAÇÃO ESPINAL DOS SISTEMAS ENDOCANABINOIDE E OPIOIDE NA ANTINOCICEPÇÃO INDUZIDA PELA TERAPIA POR ONDAS DE CHOQUE EM CAMUNDONGOS COM DOR PÓS OPERATÓRIA
Authors	LÍVIA MARIA RIBEIRO ROSÁRIO, IAGO HENRIQUE SILVA MALTA, GIOVANE GALDINO DE SOUZA
Affiliations	Laboratório de Neuroimunobiologia da Dor, UNIFAL/MG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Dor pós-operatória(DPO) afeta a vida e a funcionalidade da pessoa. Terapias não farmacológicas como ondas de choque(TOC) baixam dor musculoesquelética com menos efeitos adversos. Entretanto, pouco se sabe dos mecanismos antinociceptivos da TOC, mormente no sistema nervoso central.</p> <p>Objective: Estudou-se a nível espinal a ação de sistemas endocanabinoide(SEC) e opioide(SOP) no efeito antinociceptivo da TOC em camundongos com DPO. Methods: Camundongos C57BL/6 machos receberam cirurgia incisiva, retração de pele/músculo(IRPM) na coxa direita para indução de DPO. Testou-se o limiar nociceptivo mecânico dos animais por monofilamentos de von Frey. Cirurgia IRPM induziu DPO do 1º ao 28º dia pós-operatório. Animais fizeram 2 sessões no 14º/16º dias pós-operatório com 100,200 ou 400 pulsos da TOC, densidade de fluxo de energia 0,11mJ/mm², 10Hz, área de aplicação de 5mm na área medial da coxa direita, ou método sham. No 16º dia da segunda aplicação da TOC o limiar nociceptivo foi visto. Results: Doses de 100 e 200 caíram DPO por 60 minutos. Pré-aplicação de inibidores da recaptção de anandamida(AEA) VDM11(1,2 e 4µg) e da enzima monoacilglicerol lipase(MAGL) JZL184(0,5, 1 e 2µg) potencializaram e prolongaram a antinocicepção da TOC. Pré-aplicação de Naloxona(1,2 e 4µg), antagonista não seletivo dos receptores opioides, Cloccinamox(1,2 e 4µg), antagonista seletivo dos receptores opioides µ e Nor-binaltorfimina(1,25, 2,5 e 5µg), antagonista seletivo dos receptores opioides κ, mostraram antagonização dos receptores opioides, seletivamente ou não, baixaram de modo dose-dependente a antinocicepção da TOC. Avaliação no 16º dia dos níveis espinais de AEA e 2-araquidonoilglicerol(2-AG) por cromatografia líquida/espectrometria de massa apontou aumento só nos níveis 2-AG de animais tratados. Análise de Western Blot mostrou queda na expressão espinal de MAGL e enzima hidrolase de amidas de ácidos graxos(FAAH). Conclusion: Nota-se que a TOC reduz DPO, SEC e SOP podem participar do efeito antinociceptivo da terapia. Support: Fundação de Amparo à Pesquisa de Minas Gerais (FAPEMIG) Protocol: Comissão de Ética em Experimen</p>

Title	EFFECTS OF CONTEXTUAL INFORMATION ON SOCIAL MEMORY
Authors	ELISA MICHELSTAEDTER BROCHADO, CAIO MARTINS DE CASTRO, MATHEUS COSTA PASSOS, GRACE SCHENATTO PEREIRA
Affiliations	Fisiologia e Biofísica, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: In gregarious species, episodic memory formation often occurs within dynamic social contexts, where interactions between individuals and their environment shape recall processes. While the significance of contextual cues in episodic memory is well-established, their role in the processing of Social Memory (SM), essential for conspecific recognition, remains unexplored. Here, we propose that SM can be affected by changing the context of social encounters. Objective: To investigate the effects of contextual information on SM processes. Methods: Adult C57BL/6 male mice (25g) underwent an adapted social recognition task. Initially, mice were habituated to Context A (CtxA), which consisted of an acrylic white box (30x30x30cm), for 10 minutes. Subsequently, a 5-minute training (TR) session was conducted in CtxA, allowing interaction with a social stimulus (C57BL/6 juvenile mouse). SM was assessed 24 hours later in context B (CtxB), which displayed the same dimensions, but featured striped wall motifs and grid-patterned flooring, during reactivation (RE) session. Twenty-four hours after, during the test (TT) session, mice were re-exposed to CtxA and the same social stimulus for final evaluation. Control group was exposed to CtxA and the same social stimulus during TR, RE and TT. Throughout each session, the mice were allowed unrestricted exploration of the contexts. Data were analyzed by t-test, one- and two-way ANOVA, followed by Bonferroni test for multiple comparisons. Significance level was set at $p < 0.05$. Results: Behavioral results, quantified by the time spent interacting with a juvenile mouse in seconds, revealed distinct patterns in SM retention based on training and reactivation contexts. We found that experimental mice exhibited robust SM retention when trained in CtxA and reactivated in CtxB ($n=11$; $52,87 \pm 11,13$; $p=0,0010$), as well as when SM was acquired in CtxB and reactivated in CtxA ($n=11$; $34,24 \pm 8,980$; $p=0,0034$). Similarly, control group, which trained and reactivated in CtxA, displayed intact SM during RE ($n=11$; 45.94 ± 7.87, $p=0.0002$). However, when both TR and RE were conducted in CtxB, SM was impaired ($n=11$; $4,736 \pm 10,11$; $p=0,6495$). These findings suggest that SM acquisition and recall may be affected by context complexity, particularly when social stimuli are present, as CtxB features additional somatosensory and visual cues. To determine whether exploratory activity influences the effect of CtxB on SM, we compared locomotor activity in the absence of a social stimulus and found comparable activity across both contexts ($n=16$; 20.09 ± 64.98, $p=0.7595$). This finding suggests that the differences in SM retention are likely due to context complexity associated with social information processing rather than variations in overall exploratory activity. Conclusion: Our preliminary results suggest that SM can be formed and reactivated in distinct contexts and that contextual information complexity associated with the presence of a social stimulus can affect SM processes. Support: CNPq Protocol: CEUA: 20/2024</p>

Title	Enriched environment and andrographolide, but not memantine, increase adult neurogenesis and prolong contextual fear memory.
Authors	LAURA F. JAIMES, MATHEUS C. PASSOS, LARA M. Z. MANSK, CAIO M. DE CASTRO, JULIÁN T. F. VEGA, LEONARDO O. GUARNIERI, FLÁVIO A. G. MOURÃO, ALEXANDER BIRBRAIR, VICTOR SANTOS, MÁRCIO F.D. MORAES, GRACE S. PEREIRA
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Departamento de Morfologia, UFMG, Departamento de Dermatologia, University of Wisconsin Madison
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Adult neurogenesis levels can improve memory duration in conditions with compromised hippocampal function. However, it remains undetermined whether altering neurogenesis levels would impact the longevity of a physiological memory trace. Objective: We hypothesized that the mechanisms of pro-neurogenic treatments and the nature of the memory trace would be determinants for memories to persist. Methods: We exposed adult male C57Bl/6 mice to behavioral procedures that produce fear memories, which naturally diminish within 10 days. We then examined whether increasing adult neurogenesis could prevent the natural decay of these memories. We examined the hippocampus's reliance on these memories using context, sound, or smell as the conditioned stimuli. Memantine (MEM), andrographolide (AND), and an enriched environment (EE) were used to gain insight into the mechanisms involved in increasing neurogenesis and its effects on memory retention. Results: EE and AND, but not MEM, increased neurogenesis in the dentate gyrus of the dorsal hippocampus (dDG) measured as the number of cells expressing doublecortin. Interestingly, neither treatment altered the progenitor cell population in the dDG of Nestin-GFP mice. We also recorded the oscillations in hippocampal local field potentials (LFP) immediately and 7 days after the pharmacological treatments. Acute administration of MEM increased slow and fast gamma power in the DG and decreased theta oscillatory activity. Unlike MEM, AND induced a reduction in both slow and fast gamma. No differences between treatments were detected in the LFP recording 7 days later. Finally, we tested whether MEM, AND, and EE would extend the persistence of fear conditioning memory. ANDRO and EE increased memory persistence, but only for contextual fear conditioning (CFC), suggesting that increasing adult neurogenesis can also prolong memories that usually do not persist. Conclusion: Our study shows that different methods to increase adult neurogenesis have varying effects on DG neurophysiology. Moreover, it suggests that memories that rely on the hippocampus, such as contextual fear conditioning (CFC), may be more prone to alterations in adult neurogenesis compared to memories less dependent on this brain region, such as auditory and olfactory fear conditioning. Support: CAPES, CNPq, FAPEMIG Protocol: 247/2020</p>

Title	Effects of a gluten-rich diet on intestinal homeostasis, food intake, and anxiety-related behavior in rats
Authors	AMANDA NUNES COSTA, LETÍCIA HELENA DE OLIVEIRA CASSIMIRO, JOÃO GUALBERTO VIEIRA VILELA, JOÃO PAULO LIUTE SCARRAMAL, LUCAS PERILLO CAMPOS, MILIANE MARTINS DE ANDRADE FAGUNDES, GUSTAVO SILVEIRA BREGUEZ, KARINA BARBOSA DE QUEIROZ, SÍLVIA DE PAULA GOMES, SYLVANA IZAURA SALYBA RENDEIRO DE NORONHA, RODRIGO CUNHA ALVIM DE MENEZES, DEOCLÉCIO ALVES CHIANCA-JR, FERNANDA CACILDA DOS SANTOS SILVA
Affiliations	Laboratório de Fisiologia Cardiovascular, Departamento de Ciências Biológicas, UFOP, Laboratório de Nutrição Experimental, Departamento de Alimentos, UFOP, Laboratório Multiusuário de Pesquisa em Bioquímica Nutricional e Biologia Molecular, UFOP, Laboratório de Bioquímica e Biologia Molecular, Departamento de Ciências Biológicas, UFOP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Gluten, a protein complex found in wheat, is added to food products to improve texture and flavor, and increase their consumption. There is no recommended intake of gluten for healthy individuals, but for sensitive individuals, dietary exclusion is crucial to prevent intestinal and extra-intestinal damage, such as anxiety disorders. In these individuals, gluten promotes intestinal dysbiosis and reduces the levels of short-chain fatty acids (SCFAs), intestinal microbial metabolites, whose reduction contributes to intestinal oxidative stress (OS) and inflammation, and behavioral changes. Among them, butyrate, the main energy source for colonocytes, regulates the intestinal epithelial barrier integrity, appetite, satiety, and anxiety, playing a key role in the gut-brain axis signaling. The toxic effects of gluten have been described in sensitive individuals, but there is a gap in understanding its effects on the general population, prompting the investigation of the impact of gluten-rich diet on intestinal homeostasis and its interface with (feeding and defensive) behavioral phenotype. Objective: To evaluate the effects of gluten-rich diet on: 1) food intake; 2) anxiety-related behavior; 3) intestinal OS and 4) fecal SCFAs profile. Methods: Wistar rats (N= 25; 21 days; \pm 50g) were separated in Control (C: n=12) and Gluten groups (G: n=13) and respectively fed with NUVILAB diet and gluten-rich diet (90% NUVILAB+10% gluten). Food intake was measured weekly. At the end of the dietary protocol, anxiety-related behavior was assessed in the Elevated Plus Maze (EPM) test, followed by euthanasia and collection of feces and intestine for analysis of SCFAs concentration and intestinal OS. OS was assessed by catalase (CAT) antioxidant activity and protein carbonyl concentration (PCO), a marker of protein oxidative damage. Statistical analysis was conducted using GraphPad Prism 8, employing the Shapiro-Wilk test (normality), Grubbs test (outliers), unpaired t-test (parametric data), and Mann-Whitney test (non-parametric data). Parametric data were expressed as mean \pm standard deviation, and non-parametric data as median and interquartile range (M; Q3, Q1); $p < 0.05$ was used as a significant value. Results: There was an increase in food intake in the gluten group compared to the control group (G: 26 ± 6 vs. C: 16 ± 4 g; $p = 0.02$). There was a reduction in the number of entries in the EPM open arms (G: 1; 3, 0 vs. C: 3; 6, 2; $p = 0.03$) and reduced head dipping time at the edges of these arms (G: 13 ± 6 vs. C: 25 ± 14 s; $p = 0.04$) by the gluten group compared to the control group, suggesting that gluten-rich diet induces anxiety-like behavior. In addition, CAT was reduced in the duodenum (G: 8 ± 3 vs. C: 12 ± 3 U/mg of ptn; $p = 0.004$), and PCO was increased in the duodenum (G: $1.3; 1.8 - 0.8$ vs. C: $0.7; 1.2 - 0.6$ PCO/mg of ptn; $p = 0.025$) and colon (G: $1.8; 4.9 - 1.2$ vs. C: $1.1; 1.6 - 0.7$ PCO/mg of ptn; $p = 0.03$) of the gluten group, showing reduced antioxidant enzyme activity and increased oxidative damage in these gut portions. Regarding SCFAs, butyrate was reduced in gluten compared to control group (G: 2.0 ± 0.3 vs. C: 2.4 ± 0.3 mg/g of feces; $p = 0.04$). Conclusion: Our data suggest that chronic exposure to gluten-rich diet in rats compromises the gut-brain signaling mediated by butyrate, resulting in increased intestinal oxidative stress, food intake and anxiety. Support: CAPES, Fapemig (APQ-00823-21), CNPq and UFOP. Acknowledgments: CCA/UFOP, FINEP and FAPEMIG (APQ-02511-22). Protocol: (CEUA/UFOP: nº 9520180121)</p>



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Title	O re-agrupamento recupera o prejuízo de memória causado pelo isolamento social de maneira tempo-dependente.
Authors	CAIO M. DE CASTRO, LEONARDO O. GUARNIERI, JOÃO VITOR FERRY DE ARAÚJO RIBEIRO, MÁRCIO F.D.MORAES, GRACE SCHENATTO PEREIRA MORAES
Affiliations	Fisiologia e Biofísica, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Estímulos sociais são necessários para a manutenção da sobrevivência em espécies gregárias. Para estes casos, foi proposto recentemente o conceito de homeostasia social (HS), que sugere existir um sistema que detecta, controla e efetiva respostas de ajuste, quantitativo e qualitativo, das interações sociais. Sendo assim, a condição de isolamento social configura uma ameaça à HS, podendo alterar as respostas de retroalimentação e até mesmo impor um novo ponto de ajuste. Objective: No presente estudo, investigamos se o re-agrupamento é capaz de recuperar o desbalanço na HS causado pelo isolamento social. Methods: Camundongos machos CD1 adultos foram distribuídos em dois grupos: agrupados (AG) ou isolados (IS) por 7 dias. Investigamos o efeito do reagrupamento na memória social. Sendo que, os animais foram reagrupados por 3 ou 7 dias. A memória social foi avaliada pelo teste de reconhecimento social, que consiste na apresentação do mesmo juvenil ao animal adulto, por dois dias consecutivos. Results: O déficit de memória causado pelo IS foi recuperado com 7, mas não com 3 dias de re-agrupamento. Conclusion: Os nossos resultados sugerem que o comprometimento na memória social pode ser revertido pelo reagrupamento. Support: CNPq, CAPES, FAPEMIG Protocol: 26/2021</p>



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Title	Exploring the Therapeutic Potential of Cannabigerol (CBG) in Attenuating PTZ-Induced Seizures in Adult Mice: A Dose-Dependent Study
Authors	ANNA CAROLINA TAVARES DE OLIVEIRA, LILLIAN SOARES PINTO, JOSÉ ALEXANDRE DE SOUZA CRIPPA, FABRÍCIO ARAÚJO MOREIRA, VICTOR RODRIGUES SANTOS
Affiliations	Morfologia, UFMG, Farmacologia, UFMG, Neurociências e Ciências do Comportamento, USP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy is a multifaceted neurological disorder characterized by abnormal electrical activity in the brain, marked by a chronic predisposition to spontaneous seizures. This condition leads to a variety of pathophysiological consequences, affecting neurobiology, cognitive function, and psychosocial aspects. Recent years have witnessed a surge in interest regarding the therapeutic potential of cannabinoids, compounds derived from <i>Cannabis sativa</i> L. Among these cannabinoids, Cannabigerol (CBG) has attracted significant attention due to its promising anti-inflammatory, antibacterial, hypotensive, vasoconstrictive, and neuroprotective properties. Objective: The objective of this study is to investigate the efficacy of CBG in mitigating pentylenetetrazol (PTZ)-induced seizures in adult mice, with a focus on determining the dose-response relationship. Methods: A total of twenty-three adult mice (CEUA 42/2024) were assigned to different treatment groups: a control group receiving a vehicle solution (n=6) and experimental groups receiving CBG at doses of 10, 30, and 100 mg/kg (n=5, 5, 7, respectively), administered intraperitoneally. Following CBG administration, all mice were exposed to PTZ, a well-established convulsant, to induce seizures. A 30-minute interval was maintained between CBG administration and PTZ exposure. Seizure duration was meticulously recorded for 15 minutes using AnyMaze software, and the data were subsequently analyzed. Statistical analysis was conducted using the Kruskal-Wallis ANOVA test, chosen for its robustness in comparing multiple groups. Results: The control group exhibited a mean seizure latency of 2:28 minutes. In contrast, CBG doses of 10 mg/kg, 30 mg/kg, and 100 mg/kg resulted in latency times of 4:59, 2:35, and 1:46 minutes, respectively. The Kruskal-Wallis test indicated a significant difference in latency, with a p-value of 0.001. Regarding seizure duration, the control group experienced a mean duration of 5:07 minutes. Administration of CBG at concentrations of 10 mg/kg, 30 mg/kg, and 100 mg/kg resulted in seizure durations of 5:12, 4:12, and 5:22 minutes, respectively. The Kruskal-Wallis test for total seizure duration did not reveal significant differences, yielding a p-value of 0.421. Conclusion: This study provides compelling evidence for the potential therapeutic role of CBG in epilepsy management. A dose-dependent effect was observed, with lower doses of CBG effectively delaying seizure onset. This finding underscores the intricate relationship between CBG concentration and its antiepileptic effects, warranting further investigation to establish a precise dose-response relationship. Additionally, CBG, particularly at a dose of 30 mg/kg, demonstrated a notable reduction in seizure duration, despite the lack of statistical significance, highlighting the complexity of cannabinoid interactions in epilepsy. Recognizing the limitations of this study, including sample size and other variables influencing seizure activity, extensive additional research with larger cohorts is necessary to validate these preliminary findings. This study underscores the potential of CBG as an innovative intervention for mitigating seizures. However, rigorous investigations are essential to elucidate CBG's mechanisms of action, optimize treatment protocols, and establish clinical applicability for individuals with epilepsy. Future research holds the potential to revolutionize epilepsy management, offering new hope to those affected by this challenging condition. Support: This research was supported by FAPEMIG and CNPQ. Protocol: CEUA 42/2024</p>

Title	Oxytocin levels in the anterior olfactory nucleus plays a crucial role in mediating the impact of social isolation on social memory
Authors	CAIO MARTINS DE CASTRO, ELISA MICHELSTAEDTER BROCHADO, MATHEUS COSTA PASSOS, EDSON JUNIO OLIVEIRA PERES, GRACE SCHENATTO PEREIRA
Affiliations	Fisiologia, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Rodents rely on olfactory cues to identify each other. Therefore, it is essential to maintain a memory trace of each conspecific's identity to facilitate their interactions within the group. In adult mice, social isolation (SI) compromises the social memory recognition (SM) of conspecifics. However, the neural mechanisms that underlie the impact of social interaction on SM still require further investigation. Here we hypothesize that the deficit in SM caused by SI is due to a failure in oxytocin levels in a key area of the olfactory system, known as the anterior olfactory nucleus (AON). Objective: To investigate whether social isolation compromises social recognition memory by altering OXT levels in the AON. Methods: Adult male ICR-CD1 mice were group-housed (GH) or socially isolated (SI) for 7 days. To estimate oxytocin's (OXT) mRNA and protein levels we use qPCR and immunofluorescence, respectively. SM was tested using the social recognition task. For pharmacology experiments, mice underwent stereotaxic surgery to implant guide cannulas into the AON. SI mice received 0.01 ng/μL OXT, while GH mice received 12 μg/μL OXT receptor antagonist (L-368,899). The neural connection between the paraventricular nucleus (PVN) and AON was established by using the neuronal tracing Cholera Toxin B (CTB) and AAV-Syn-EYFP. Results: SI did not alter mRNA expression in the PVN for either OXT (GH: n=11, 1.16 ± 0.81; SI: n=8, 1.05 ± 0.79) or its receptor (GH: n=11, 1.33 ± 0.93; SI: n=8, 0.88 ± 0.38). Additionally, receptor expression remained unchanged in the AON (GH: n=1, 1.12 ± 0.57; SI: 1.46 ± 0.77). However, we observed reduced OXT+ neuron numbers in the PVN post-SI (GH: n=5, 238.3 ± 52.02; SI: n=6, 141 ± 46.58). OXT intra-AON improved memory deficits in SI mice when administered before retrieval (Saline: n = 8, TR: 40.81 ± 10.54, TT: 30.09 ± 18.59; OXT: n = 8, TR: 40.64 ± 11.54; TT: 26.09 ± 17.86), but not before or immediately after acquisition. Accordingly, L-368,899 intra-AON impaired SM retrieval of GH mice (Saline: n = 9, TR: 79.23 ± 31.55, TT: 34.38 ± 28.69; OXTR: n = 9, TR: 75.11 ± 28.51; TT: 65.17 ± 29.55). AON injection of CTB, which is a retrograde tracer, did not label PVN oxytocinergic neurons. However, we observed fluorescence labeling in the AON after injecting the anterograde tracer AVV-Syn-EYFP into the PVN. Conclusion: Our results show that SI impaired SM by compromising the OXY levels in the AON. We also suggest that PVN neurons innervate the AON. Support: CNPq, CAPES e FAPEMIG Protocol: CEUA:26/2021</p>

Title	The impacts on the neurodevelopment of the offspring and the pregnancy of Wistar rats submitted to an experimental Fibromyalgia model
Authors	ANA BEATRIZ DA SILVA OLIVEIRA, CAMILA EVELYN PERETE DE FREITAS, JOSIMARI MELO DE SANTANA, LEANDRO MARQUES DE SOUZA, PATRÍCIA RODRIGUES MARQUES DE SOUZA
Affiliations	Departamento de Fisiologia, UFS
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Fibromyalgia (FM) is a painful and chronic musculoskeletal syndrome, but whose etiology is still unknown, which mostly affects women in adulthood. The involvement of environmental, autoimmune, hormonal or genetic factors in its development is suspected. It is still necessary to clarify many gaps regarding the cause of the disease, the best treatments and mainly the impact of FM on future generations, since, as it is more prevalent in women of reproductive age, it is extremely important to assess the impact of this disease on the descendants of these women. Chronic Widespread Muscle Hyperalgesia (CWMH) induced by acidic saline does not generate tissue damage and persists for up to 4 weeks, resembling fibromyalgia in humans. Hyperalgesia is a powerful stressor and the fetal programming hypothesis states that adverse events occurring in the mother during pregnancy, such as chronic stress, imply changes in the health-disease pattern of her offspring. Objective: The aim of this study was to evaluate the impact of an experimental Fibromyalgia model, the CWMH, during pregnancy, as well as to characterize the response of neonatal reflexes and developmental milestones in the offspring. Methods: At 90 days of age and weighing an average of 230g, 18 Wistar female rats were divided into three groups: 1- Acid Saline (AS), 2- Neutral Saline (NS) and 3- Control (CTRL). Initially, the CWMH was induced in the SA group, followed by scheduled mating of all groups. The female rats were evaluated for behavior to ensure that the induction of hyperalgesia was effective. The evaluation of reflexes and developmental milestones in the offspring was blind carried out by two independent evaluators from postnatal day 01 to 21. Results: The hyperalgesia of the rats in the AS group showed a significant difference in the AS group with a reduction in the threshold post-induction, showing that the hyperalgesia was effective ($p=0.0004$). There was no hyperalgesia in the NS and CTRL groups, as expected ($p= 0.0846$, $p= 0.5339$, respectively). The results obtained demonstrate that CWMH does not prevent fertilization and copulation, as females from the AS group performed copulation on the first day of union with the male, showing pro-social behavior and greater receptivity to the male, than females of NS and CTRL groups. The AS group pregnancy lasted 22 days, while the NS and CTRL groups lasted 21 days. The AS group gave birth to 64 rats, the NS group gave birth to 42 rats, and the CTRL group gave birth to 44 rats. It was noted that 8 puppies died on the second postnatal day in the AS group. In terms of reflexes, the offspring of the AS group showed a delay (mean of +2 days) in the appearance of the following reflexes: palmar grasp, plantar grasp, righting, cliff avoidance, auditory startle and accelerated righting; when compared to the NS and CTRL groups. Conclusion: Our study shows that hyperalgesia favors copulation and does not interfere on pregnancy, but it does influence pregnancy, leading to higher neonatal mortality in the AS group. An impact on six sensorimotor reflexes was observed in the AS group, showing a significant difference, indicating that hyperalgesia affected the fetal neurodevelopment of the offspring. This is the first study to assess the impact of Fibromyalgia and its repercussions on the neurodevelopment of offspring in an experimental model. A topic of great importance, to begin to elucidate how current cases of this condition will impact future generations. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). Protocol: 8239041219</p>

Title	Oleylethanolamide Associated with Phosphatidylcholine Nanoparticle: Effect on Oxidative Stress in an Experimental Model of Alzheimer`s Disease
Authors	CAMILA MARIA COLTRI, CAROLINE STEFANI PLANK, MARIA JULIA TODERO, ELOISA CAROLINA FABRO DAI, GABRIELA CARDOSO POSTERARO, LEANNA CAMILA MACARINI, VANESSA MARIELI CEGLAREK, RAFAEL PORTO INEU, ODINEI HESS GONÇALVES, SARA CRISTINA SAGAE SHNEIDER
Affiliations	CCBS, UNIOESTE, CCMF, UNIOESTE, UTFPR, UTFPR, UFRGS, UFRGS
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Alzheimer`s disease (AD) is the most common cause of dementia. The neuropathological markers of AD include the deposition of Aβ peptide in the brain, which is related to oxidative stress, as its induction generates reactive oxygen species, resulting in neurodegenerative damage. Oleylethanolamide (OEA) has anti-inflammatory and antioxidant effects, which may be important for preventing or reducing these AD-associated changes. To optimize the administration of OEA, an endogenous lipid, we associated it with a nanoparticulate vehicle, Phosphatidylcholine. Objective: To evaluate the effect of OEA associated with phosphatidylcholine on plasma levels of oxidative stress markers in a mouse model of Alzheimer`s disease. Methods: Twenty-five adult male C57BL/6 mice, aged 100-112 days and weighing between 25-30g were divided in groups: CTL (animals receiving icv administration of saline solution, n=5), STZ (animals receiving icv administration of streptozotocin for AD induction, n=5), STZ+OEA (animals receiving icv administration of streptozotocin for AD induction and ip administration of OEA, n=5), and STZ+OEA NANO (animals receiving icv administration of streptozotocin for AD induction and ip administration of OEA associated with phosphatidylcholine nanoparticle, n=5). Streptozotocin (STZ) was administered intracerebroventricularly at a unilateral dose of 3μL with a concentration of 3mg/kg, and the CTL group received saline. 15 days after STZ administration, the animals were treated for 7 days with 20mg/kg of OEA ip. Plasma analyses were performed to determine the activity of glutathione peroxidase (GPx), glutathione S-transferase (GST), glutathione reductase (GR), and lipid peroxidation (LPO) detection using the thiobarbituric acid method. The Kruskal-Wallis test with Dunn`s post-hoc was used, considering a p-value < 0.05 for statistical analysis, in GraphPad Prism 9.3.0 software. Data were expressed as mean \pm SEM. Results: The analyses revealed a statistical trend in the activities of GPx (H=7.464, p=0.113), GST (H=9.253, p=0.0551), and LPO (H=4.999, p=0.2874) between the groups. However, for GR activity, there was a statistical difference between the STZ+OEA (169.6\pm42.49) and STZ+OEA NANO (58.63\pm9.650) groups with values of H=9.508 and p=0.0496. Conclusion: The data showed that the activity of the antioxidant enzymes GPx, GST, and GR was not significantly altered by the treatment. Additionally, the LPO levels, an indicator of oxidative damage, also did not show statistically significant differences between the treated and control groups. These results suggest that the treatment did not affect the oxidative stress markers in the evaluated experimental context. Support: UNIOESTE and Fundação Araucária. Protocol: Protocol N$^{\circ}$ 20-21</p>



Title	Behavioral expression as a nonlinear outcome: age- and sex-dependent effects of early immune activation and early weaning in mice
Authors	ELIFRANCES GALDINO DE OLIVEIRA, MAYARA VICTÓRIA DE SOUZA BARBOSA, DIÓGENES AFONSO DE LIMA, EDUARDO CARVALHO LIRA, SANDRA LOPES DE SOUZA, DAYANE APARECIDA GOMES
Affiliations	Departamento de Fisiologia e Farmacologia, UFPE, Departamento de Anatomia, UFPE
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Experiencing early life adversity (ELA) alters the physiological course of neurodevelopment and increases the risk of developing psychiatric disorders. Early immune activation and early weaning (EW) are two ELA that are considered risk factors for psychiatric disorders and are widely reported in low- and middle-income countries, but their combined effects are unknown. Objective: To analyze the effects of early immune activation and/or EW on spatial working memory, anxiety-like behavior, and depression-like behavior in male and female mice during adolescence and adulthood. Methods: To induce immune activation, male and female mice (<i>Mus musculus</i>, Swiss) were administered with LPS (100 µg/kg) or saline on postnatal day (PND) 14. In addition, animals were weaned on PND day 14 (early weaning, EW) or 21 (normal weaning, NW), resulting in 4 experimental groups for each sex: CTRL (NW+saline), LPS (NW+LPS), EW (EW+saline), and EW+LPS. The Y-maze test, open-field test (OFT), and tail-suspension test (TST) were performed during adolescence (40 to 42 PND) and adulthood (80 to 82 postnatal PND). Ethical approval protocol nº 112/2022.</p> <p>Results: Adolescent males: In the Y-maze test, the LPS showed a reduction in alternation ($p=0.01$; CTRL=60.7±1.4%; LPS=53.9±1.2%) compared to the CTRL; in the OFT, the LPS demonstrated a reduction in time in center ($p=0.0001$; CTRL=102.4±10.9 s; LPS=42.4±6.2 s) compared to the CTRL; in the TST, the EW ($p<0.0001$) and EW+LPS ($p=0.02$) showed increased immobility (CTRL=12.8±2.2 s; EW=73.9±10.6 s; EW+LPS=39.5±7.1 s) compared to the CTRL. Adolescent females: in the Y-maze test, the EW and EW+LPS exhibited increased alternation ($p<0.0005$; CTRL=52.5±1.6%; EW=63.3±1.7%; EW+LPS=62.8±1.7%) compared to the CTRL; in the OFT, the LPS, EW, and EW+LPS showed a reduction in time in center ($p<0.0005$; CTRL=76.8±7.2 s; LPS=43.31±4.5 s; EW=45.8±5.8 s; EW+LPS=42.6±5.8 s) compared to the CTRL; in the TST, the LPS, EW and EW+LPS showed increased immobility ($p<0.0001$; CTRL=5.0±2.1 s; LPS=59.1±3.3 s; EW=41.2±5.8 s; EW+LPS=36.5±4.8 s) compared to the CTRL. Adult males: there was no difference among the groups in the Y-maze test (CTRL=59.3±1.2%; LPS=60.7±1.6%; EW=56.9±2.5%; EW+LPS=56.9±2.3%); in the OFT, the LPS, EW and EW+LPS demonstrated a reduction in time in center ($p<0.05$; CTRL=93.8±11.8 s; LPS=53.9±4.6 s; EW=57.0±10.5 s; EW+LPS=45.5±2.8 s) compared to the CTRL; in the TST, the EW showed increased immobility ($p=0.0005$; CTRL=52.1±5.6 s; EW=112.3±15.7 s) compared to the CTRL. Adult females: there was no difference among the groups in the Y-maze test (CTRL=55.0±1.4%; LPS=55.5±1.1%; EW=59.20±1.4%; EW+LPS=59.0±1.5%); in the OFT, the EW+LPS exhibited a reduction in timer in center ($p=0.02$; CTRL=59.5±7.9 s; EW+LPS=27.8±4.9 s) compared to the CTRL; in the TST, the LPS showed a reduction in immobility ($p=0.01$; CTRL=55.3±9.9 s; LPS=111.0±12.2 s) compared to the CTRL. Conclusion: Adolescent LPS males showed memory deficits while EW and EW+LPS females showed memory improvement. Adult males and females showed no changes in memory. In males, increased anxiety-like behavior was found in adolescent LPS and adult LPS, EW and EW+LPS. In females, increased anxiety-like behavior was observed in adolescent LPS, EW and EW+LPS, but only adult EW+LPS showed increased anxiety. EW and EW+LPS induced depression-like behavior in adolescent males, but only EW in adults. Adolescent LPS, EW and EW+LPS females showed increased depression-like behavior and only LSP in adulthood.</p> <p>Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES; Finance Code 001) and Fundação de Amparo a Ciência e Tecnologia de Pernambuco (FACEPE, process BCT-0327-4.01/21) Protocol: 112/2022.</p>



Title	EFEITOS DO TRATAMENTO COM LOSARTAN SOBRE AS ALTERAÇÕES COMPORTAMENTAIS EM RATOS PÓS ACIDENTE VASCULAR CEREBRAL EXPERIMENTAL NO CÓRTEX INSULAR
Authors	MATHEUS HENRIQUE DA SILVA CRUZ, LILIANE RAMOS DOS SANTOS MACHADO, ANA CAROLINE VENTRIS GODOY, MARCO ANTÔNIO PELIKY FONTES
Affiliations	Fisiologia e Biofísica, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O Acidente Vascular Cerebral (AVC) é uma condição grave que está associado à diversas complicações funcionais. Recentemente descrevemos um modelo de AVC hemorrágico experimental no córtex insular (CI) de ratos que reproduz várias alterações observadas em humanos incluindo taquicardia, arritmias e alterações renais. Estas alterações cardiorenais são amenizadas pelo tratamento com o losartan, antagonista de receptores AT1 de angiotensina II (Ang II). Além de ações periféricas, estudos mostram que o losartan pode modular a ansiedade. Objective: Avaliar o efeito do losartan nas alterações comportamentais pós-AVC insular em ratos. Methods: Ratos Wistar machos, 300 a 350g (n=6) foram: 1) preparados para injeção unilateral de sangue autólogo (ICH) ou veículo (solução salina – Sal IC) no CI, 2) grupos separados receberam três dias de tratamento (dose diária i.p.) com losartan (los; 10 mg / kg; los + A779; dose 200µg/Kg; antagonista de receptores Mas) ou veículo (NaCl 0,9% 0,1 ml / 100g) e 3) submetidos aos testes de labirinto em cruz elevado, campo aberto, atividade locomotora e wire hang. Results: O teste de EPM mostrou que ICH resultou em aumento da ansiedade (SalCI = 8,67 ± 0,76 vs ICH-sal = 2,33 ± 0,42 entradas braço aberto; P< 0,05). O efeito ansiogênico da ICH foi abolido com o losartan (ICH-los 8,33 ± 0,71 entradas braço aberto; P<0,05). Os efeitos do losartan foram revertidos pelo A-779. O grupo ICH não mostrou nenhuma alteração significativa na atividade locomotora e força muscular. Conclusion: O bloqueio dos receptores AT1 pode amenizar o efeito ansiogênico pós-AVC insular sem produzir efeitos significativos somatomotores. Support: FAPEMIG APQ-01128-21; CNPq 308923/2021-9 Protocol: CEUA UFMG 112/2019</p>

Title	AgNOR ANALYSIS IN THE DORSOPOSTERIOR AREA OF THE <i>Leporinus macrocephalus</i> TELENCEPHALIC SUBJECTED TO THE INHIBITORY AVOIDANCE TASK
Authors	ANA CAROLINA RODRIGUES DE AZEVEDO DONADONI, RAFAEL TOSHIO FUJIOKA, AMANDA SOARES COURA, LILIAM MIDORI IDE
Affiliations	Departamento de Ciências Naturais (DCNAT), UFSJ
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The experimental model of inhibitory avoidance is widely used in memory studies as it enables rapid learning and relatively long-lasting memory. The neuronal plasticity study proceeded through morphometric analysis of brain sections processed histochemically with the silver impregnation technique in the argyrophilic organizing nucleolar regions (AgNORs). It is consensus that the dorsal and ventral portions of the everted telencephalon are homologous to the pallium and subpallium, respectively. The dorsal region of the telencephalon of teleosts has four main areas: dorsomedial, dorsodorsal, dorsolateral (DI), and dorsoposterior (Dp). Dp is a specialized part of DI (Dlp), or simply Dp, the main area in processing olfactory information, associated with olfactory memory, and possibly homologous to the olfactory cortex of tetrapods. Objective: In the present study, we used AgNOR neuro-histochemical staining to quantitatively determine learning-related morphological changes in the AgNOR of the dorsoposterior area of the piauçus <i>Leporinus macrocephalus</i> telencephalic pallium using an inhibitory avoidance protocol. Methods: Sixteen juvenile <i>L. macrocephalus</i> (Actinopterygii; Anostomidae), without distinction of sex, with a standard length of 10 to 15 cm, aged five to ten months, were subjected to the inhibitory avoidance task with mechanical-visual stimuli (EXP, n=8) or not (CTR, n=8). The brains of these animals were removed after euthanasia and fixed in 10% formalin. Transverse telencephalon sections were silver stained using the AgNOR technique for histomorphometric study after viewing under a light microscope using an oil immersion lens (1,000X magnification) scanning and Dp image capture. The behavioral and the histomorphometric data were analyzed using the Mann-Whitney test and the Welch t-test, respectively, with a significance level of 0.05 in all tests performed. The research protocol was examined and approved by CEUA/UFSJ (Protocol 023/2013). Results: <i>L. macrocephalus</i> showed a scototaxis behavioral pattern (Mann-Whitney test; P = 0.0137). However, there was no statistical difference in the number (111.4 ± 7.2; 112.6 ± 6.0; $t=0.35$, $df=12.98$) and size of AgNORs ($0.862 \pm 0.088 \text{ um}^2$; $1.014 \pm 0.182 \text{ um}^2$; $t=2.015$, $df=8.419$; $P=0.077$) in the experimental (n=8) and control (n=7) Dp groups. The relative area of AgNORs of neurons in the experimental group ($3.042 \pm 0.439 \%$) was also not statistically different from the control ($3.553 \pm 0.673 \%$; $t=1.715$, $df=10.10$). Conclusion: The experimental animals <i>Leporinus macrocephalus</i> do not show significant histomorphometric changes in AgNORs in the neurons of the dorsoposterior area of the telencephalon when subjected to an inhibitory avoidance task using mechanical-visual stimuli. Support: * PIBIC-Af/UFSJ Scholarship; UFSJ. Protocol: CEUA/UFSJ (Protocol 023/2013)</p>

Title	EFFECT OF FULL-SPECTRUM CANNABIDIOL OIL ON THE REDOX BALANCE OF RATS EXPOSED TO CRACK DURING THE GESTATIONAL PERIOD
Authors	MERCIA THAISA ARAÚJO COSTA HOMERO, AMANDA LARISSA DIAS PACHECO, FERNANDA MARIA ARAÚJO DE SOUZA, EDITE SANTOS SIQUEIRA, KELLYSSON BRUNO OLIVEIRA, BIANCA RODRIGUES MELO DA SILVAA, KEYLLA LAVÍNIA DA SILVA OLIVEIRA, FERNANDA DE SOUZA SILVA, IASMIM ISAÍRES NERI DOS SANTOS, BRUNA OLIVEIRA MONTEIRO PEIXOTO, ANA CATARINA R. LEITE, IGOR SANTANA DE MELO, OLAGIDE WAGNER DE CASTRO
Affiliations	LABORATÓRIO DE NEUROFARMACOLOGIA E FISIOLÓGIA INTEGRATIVA, UNIVERSIDADE FEDERAL DE ALAGOAS
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Full-spectrum cannabidiol (CBD) oil derived from Cannabis sativa is a promising therapeutic substance due to its anti-inflammatory and antioxidant properties, which offer potential protection against oxidative stress. Here, we evaluated the effect of CBD treatment on redox balance in offspring following gestational exposure to crack cocaine (PN-Crack) in Wistar rats (Ethical approval, CEUA #28/2021). Objective: To analyze the effects of full-spectrum cannabidiol oil on the redox balance on Wistar rats exposed to crack cocaine during the gestational period Methods: Pregnant rats (60-90 days old; n=20) were exposed to crack (200 mg) or ambient air daily from the 5th to the 21st day of gestation. The offspring (males n=40; females n=40) were treated orally with CBD (30 mg/kg) or 0.9% saline solution (VEH) for 14 days, forming four experimental groups (n=10). The brains were subsequently resected for redox balance evaluation. Results: Our results demonstrated that PN-Crack exposure increased SOD enzyme activity in both females and males compared to the unexposed group (CTRL+VEH) (F (1, 32) = 18.63; P = 0.0001). Oral CBD treatment in PN-Crack exposed animals (CRK+CBD) increased CAT activity in both females and males compared to the exposed group (CRK+VEH) (F (1, 32) = 13.30; P = 0.0009). In females, PN-Crack exposure (CRK+VEH) led to a decrease in GPX activity compared to the unexposed group (CTRL+VEH) (F (1, 32) = 9.30; P = 0.004). PN-Crack exposure (CRK+VEH) increased GSSG content in both sexes compared to the unexposed group (CTRL+VEH) (F (1, 32) = 8.23; P = 0.007), and CBD treatment blocked this effect (F (1, 32) = 10.10; P = 0.003). Furthermore, the GHS/GSSG ratio was reduced in both sexes after PN-Crack exposure (CRK+VEH) compared to the unexposed group (CTRL+VEH) (F (1, 32) = 32.41; P < 0.0001), and CBD treatment also inhibited this reduction (F (1, 32) = 24.13; P < 0.0001). In both sexes, PN-Crack exposure (CRK+VEH) significantly decreased total thiol levels compared to the unexposed group (CTRL+VEH) (F (1, 31) = 22.10; P < 0.0001), and CBD treatment blocked this decrease only in males (CRK+CBD) (t-test, t8 = 2.87; P = 0.02). PN-Crack exposure (CRK+VEH) increased MDA content in both sexes compared to the unexposed group (CTRL+VEH) (F (1, 32) = 30.5; P < 0.0001), and CBD treatment prevented this effect only in females (CRK+CBD) (F (1, 32) = 16.9; P = 0.0003). In PN-Crack exposed groups (CRK+VEH), LPO content in both sexes increased compared to the CTRL+VEH group (F (1, 32) = 22.68; P < 0.0001), and CBD treatment blocked this effect only in females (t-test, t8 = 2.63; P = 0.03). PN-Crack exposure (CRK+VEH) reduced AChE activity in both sexes compared to the unexposed group (CTRL+VEH) (F (1, 32) = 22.86; P < 0.0001), and CBD treatment inhibited this reduction only in males (t-test, t8 = 4.24; P = 0.003). Conclusion: Our results revealed that animals exposed to crack cocaine during the gestational period (PN-Crack) presented increased oxidative stress and redox imbalance, and that CBD treatment reversed many of these parameters in a sex-dependent manner, exhibiting a robust neuroprotective effect. Our findings suggest that CBD may represent a promising alternative therapy for improving the prognosis of children exposed to crack cocaine during gestation. Support: This project was supported by FAPEAL (nº E:60030.0000000161/2022 e nº E:60030.0000000328/2023), CNPq (406727/2021-0), and CAPES. Protocol: No 28 /2021</p>

Title	Deciphering the Anticonvulsant Code: Temporal Dynamics and Asynchronous Patterns in Basolateral Amygdala Electrical Stimulation for Seizure Control in the PTZ Model
Authors	ARTHUR RIBEIRO RODRIGUES, LEONARDO DE OLIVEIRAGUARNIERI, VINÍCIUS ROSA COTA, MÁRCIO FLÁVIO DUTRA MORAES
Affiliations	Neurosciência, UFMG, Departamento de Fisiologia e Biofísica, UFMG, Rehab Technologies Lab, Center for Convergent Technologies
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The rationalized development of neuromodulation protocols using electrical stimulation is a promising emerging therapeutic option for drug-resistant epilepsy. Our research has shown that distinct temporal patterns of electrical stimulation, varying only in their temporal regularity from periodic (fixed frequency) stimulus (PS) to temporally complex (NPS, power law of inter-pulse-intervals IPIs), is effective in either promoting or inhibiting epileptic seizures. This work further explores how stimulation patterns composed of binary-coded words, made up of 14 ms bins roughly dividing a theta-oscillation. Objective: This study aims to determine the effectiveness of non-periodic versus periodic ES patterns in reducing seizure frequency and severity in a PTZ-induced seizure model. Specifically, we compare the latency to seizure onset across different ES patterns and assess ES impact on neuronal activity in the basolateral amygdala. For the latter, we evaluate neuronal damage using Fluoro-Jade B staining and investigate C-Fos expression as a marker of neuronal activation. Methods: Male Wistar rats (age: 8-10 weeks; weight: 250-300g) from the Biological Sciences Institute's Bioterium Vivarium at UFMG were used, housed under controlled conditions following ethical guidelines. The experimental protocol was approved by the Animal Ethics Committee. Rats were divided into four groups, each subjected to different ES patterns via implanted bipolar stimulation electrodes in the basolateral amygdala: GE1 (fixed word 4-stimuli per second, FIXw non-periodic organized at 4 Hz), GE2 (PS fixed 250 ms inter-pulse intervals), GE3 (NPS non-periodic at 4 Hz with restricted randomization), and GE4 (multiple words 4-stimuli per second, MULTw non-periodic temporally disorganized at 4 Hz). One week after surgery and recovery, baseline seizure thresholds were determined. On the experiment day, rats were i.v. infused with a PTZ ramp (tail vein 10 mg/ml PTZ 1 ml/min) concomitant with ES protocols. Behavioral responses were recorded to assess latency to forelimb clonus and tonic-clonic seizures. After the experiments, surviving animals were euthanized and analyzed using Fluoro-Jade B staining and C-Fos expression to assess both neuronal damage and activation. Results: Significant differences in seizure onset latency were observed across the different ES patterns. Non-periodic, temporally disorganized ES (GE4) significantly increased latency to seizure onset compared to periodic ES (GE2), suggesting enhanced seizure suppression. Neuronal activity analysis in the basolateral amygdala revealed reduced activation in non-periodic groups, particularly GE4. Converting the PTZ threshold into the volume of drug injected into the animal, we have: Disorganized Words Stimulus: 2 ml (Mean: 1,75 ml), Organized Words Stimulus: 1ml (Mean: 1,1 ml), Periodic Stimulus: 0,5 ml (Mean: 0,55 ml), and Power Law Stimulus: 1,8 ml (Mean: 1,9 ml). The ANOVA p-value was 0.1049, and the total normalized standard deviation was 0.05. The c-Fos and FluoroJ data are still being analyzed. Conclusion: This research advances non-periodic ES as a novel therapeutic approach for seizure control. By elucidating the efficacy and mechanisms of this stimulation pattern, we aim to contribute to more effective personalized treatments for drug-resistant epilepsy, potentially improving patient quality of life and reducing the burden of uncontrolled seizures. Non-periodic, temporally disorganized ES offers significant therapeutic benefits in managing drug-resistant epilepsy. Support: This study was financed by the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: 19/2024</p>

Title	Early Auditory Deprivation Impairs Hippocampal-Dependent Memory but not LTP in the Schaffer-CA1 synapse.
Authors	MARIANE MARTINS MIGLIACCIO, DANIEL MENDES FILHO, RICARDO MAURICIO XAVIER LEÃO
Affiliations	Fisiologia, USP, Ciências da Saúde e Biológicas, UEG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The full maturation of neurons and auditory circuits occurs only after the opening of the auditory meatus and the onset of hearing. There are evidences that cognitive and motor functions depend on auditory sensory stimuli for their full development. But mechanisms linking hearing loss and superior brain functions are not fully elucidated. Objective: This study aims to evaluate the effects of early sound deprivation on memory and motor performance and on the induction of hippocampal long-term potentiation in male Swiss mice (32.5±2.5g). Methods: At 14 days of age, mice have their auditory meatus obstructed with silicone plugs, elevating the auditory thresholds. After 30 days of deprivation (p44), auditory thresholds were again measured by Auditory Brainstem Response (ABR). The animals were then euthanized for the dissection of brain tissue from which hippocampal slices are obtained. Extracellular recordings of dendritic regions of CA1 pyramidal neurons and induction of long-term potentiation (LTP) using the theta-burst stimulation (TBS) protocol were performed. Another group of animals underwent object recognition test. The animals' motor activity was evaluated in the Open Field, where the number of sections crossed, a measure indirectly representing the total distance traveled by the animal, and rearing, an exploratory behavior, were analyzed. Results: 30-day auditory deprivation increased auditory thresholds to 68.33±6.0 dB (n=6) compared to animals in the sham group (50 dB; n=6) (t-student p=0.01). The TBS protocol was effective in inducing LTP in all groups (control 2.1±0.3, n= 10 slices/7 animals; sham 5.2±2.3, n=10 slices/5 animals; plug: 1.7±0.1, n= 11 slices/6 animals). No significant differences were found between groups in the fEPSP slope after LTP induction (One-Way ANOVA F(2,26)=0.96). The amplitude of the afferent volley was similar both before and after LTP induction (control-0.41±0.05 mV; sham-0.43±0.09 mV; plug:-0.41±0.046 mV) and between groups (One-Way ANOVA F(2,28)=0.36). Object recognition test showed reduced discretionary capacity (t-student p=0.0001) the and Open Field tests revealed a decrease in the sections crossed (t-student p=0.0045), and rearing (t-student p<0.0001) in the PLUG group (n=10) compared to the sham group (n=10). Conclusion: Our results indicate that early auditory sensory deprivation induces deficits in motor activity and memory but did not interfere with LTP and excitatory transmission in the hippocampal Schaffer-CA1 pathway. Further experiments are under way to elucidate this lack of correlation, investigating other hippocampal pathways. Support: CAPES/PROEX Protocol: 1290/2024R1</p>

Title	OVERNUTRITION DURING DEVELOPMENT CAUSES ABNORMALITIES IN THE BIOCHEMICAL PROFILE, FOOD CONSUMPTION, MITOCHONDRIAL FUNCTION AND OXIDATIVE BALANCE IN THE HYPOTHALAMUS OF JUVENILE FEMALE RATS
Authors	THYAGO DE OLIVEIRA RODRIGUES, MARIA DANIELE TEIXEIRA BELTRÃO DE LEMOS, OSMAR HENRIQUE DOS SANTOS JÚNIOR, CLAUDIA JACQUES LAGRANHA
Affiliations	Centro acadêmico de Vitória, UFPE
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Overnutrition, characterized by excessive nutrient intake, can trigger an energy imbalance, paving the way for disorders like obesity. This condition might impact the developing offspring. Objective: Evaluate in the hypothalamus of female offspring, at 30 days of life, the effect of overnutrition during the lactation period on body parameters, behavioral parameters, blood profile, mitochondrial function, and oxidative balance. Methods: This study was approved by the ethics committee (protocol nº 0013/2023). Female offspring were divided according to the nutritional insult into normonourished-NS or overnourished-OS groups on the third day of life. At 30 days of life, rats were euthanized, and blood and hypothalamus were collected. Data were expressed as mean \pm SEM. The significance level was maintained at 5% ($p < 0.05$) for all analyses. Statistical analyses were performed using GraphPad Prism 8.0 software. Results: Our data showed that body weight was higher in the OS group than NS (NS: 81.00 ± 2.36; OS: 96.89 ± 2.62; $p=0.006$); this increase in weight was followed by an increase in the Lee index in the same group (NS: 283.9 ± 4.61; OS: 313.8 ± 4.27; $p=0.0002$). In the plasma of OS, we found an increase in glucose and total cholesterol levels (NS: 168.3 ± 3.07; OS: 198.9 ± 7.83; $p=0.007$) and (NS: 69.24 ± 0.90; OS: 81.36 ± 2.42; $p=0.007$). The OS group ate more cookies and labina (NS: 2.57 ± 0.07; OS: 4.78 ± 0.38; $p=0.001$) and (NS: 2.88 ± 0.002; OS: 3.18 ± 0.040; $p=0.001$). In addition, this group ate more in the light cycle (NS: 1.74 ± 0.04; OS: 2.20 ± 0.12; $p=0.015$). The citrate synthase and NAD levels in the hypothalamus decrease by overnutrition (NS: 2.85 ± 0.35; OS: 0.52 ± 0.15; $p=0.001$) and (NS: 2.61 ± 0.18; OS: 1.70 ± 0.07; $p=0.001$). ROS production was higher in the hypothalamus of OS (NS: 0.79 ± 0.03; OS: 0.93 ± 0.008; $p=0.028$). Protein oxidation was higher in OS (NS: 18.06 ± 2.96; OS: 37.37 ± 1.26; $p=0.004$). Interestingly, SOD activity was higher in the OS vs NS group (NS: 28.00 ± 5.22; OS: 52.64 ± 4.74; $p=0.026$). However, overnutrition reduced GST's antioxidant activity (NS: 0.04 ± 0.004; OS: 0.023 ± 0.001; $p=0.015$). GSH levels were reduced in the OS group (NS: 4.52 ± 0.28; OS: 3.54 ± 0.19; $p=0.038$); the REDOX status decreased in OS (NS: 498.4 ± 39.87; OS: 381.9 ± 32.06; $p=0.038$). Conclusion: Overnutrition during lactation affects the female offspring's global health and increases the risk of neurological disease due to the establishment of mitochondrial dysfunction and oxidative stress. Support: Fundação de Amparo a Ciência e Tecnologia de PE (FACEPE) e Fundação Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Protocol: Protocol nº 0013/2023</p>

Title	Age-dependent influence of PKR on opioid-induced analgesia: Insights from a mouse model of burning injury
Authors	TERENCE DUARTE, ANDREA MAIA CARVALHO, EMANUELA MASSAROTO, SÔNIA ZANON, GUILHERME DE ARAÚJO LUCAS
Affiliations	Fisiologia, USP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Double-stranded RNA-activated kinase (PKR) is essential in inflammation and immune dysfunction. Recent evidence has shown that PKR is activated in inflammatory pain, and plays a crucial role in mediating thermal hyperalgesia. In addition, PKR inhibition reduces opioid analgesia under inflammatory pain conditions in adult mice. However, opioid-mediated antinociception varies significantly depending on the developmental period after birth. More importantly, the analgesic effect of morphine depends on the origin of the inflammatory processes, such as incisional or burning injuries. Thus, the understanding of the interaction between PKR and opioids in the early stages of postnatal development may reveal new cellular and molecular mechanisms underlying pathological pain. Objective: To further understand the molecular mechanisms of PKR and opioids on inflammatory pain, we used a mouse model of burning injury to assess the roles of PKR in opioid-mediated analgesia across different ages. Methods: The burning pain model was used in C57Bl/6 mice of both sexes at P14, P28, and P70 age. The hindpaw of mice was lesioned by immersing the paw in water at 60°C for 8 seconds under isoflurane anesthesia. Animals were treated with different doses of morphine (1, 2, or 4mg/kg; s.c.) one hour and 72 hours after the thermal stimulus (by immersing the left hind paw in water at 49°C) and the time to withdraw the paw was measured. Animals with different ages (P14, P28, P70) (n=10/group) received a PKR inhibitor, imidazole-oxindole at a dose of 0.25 mg/kg (i.p.) 15 minutes before receiving the morphine injection (4 mg/kg, s.c.) after 72 hours of the thermal stimulus. After opioid administration, the latency period for paw withdrawal from the thermal stimulus was monitored at 30, 60, 90, and 120 minutes. The control group received saline (n=10/group). Results: The results show that morphine causes significant analgesia observed by reduced thermal hyperalgesia measured by paw withdrawal latency after thermal stimulation. Comparing the analgesic effect of morphine (area under the curve – AUC) in the acute (1h post-burning) and persistent (72h post-burning) phase of the inflammatory process, the development of drug tolerance was observed at doses of 2 and 4 mg/kg. In addition, PKR inhibitor at 0.25 mg/kg also induced significant analgesia. Corroborating the idea that PKR plays an important role in opioid receptors and TRPV1 crosstalking when PKR was pharmacologically inhibited, morphine analgesia was markedly reduced at all doses used. The saline injection did not change the mice’s response latency to thermal noxious stimulation. In the experiment with different ages, applying the thermal noxious stimulus led to a consistent withdrawal response with all three ages. Seventy-two hours after the burning lesion, PKR inhibition reduced morphine analgesia in all ages. However, with the ages of P14 and P28, this effect was more pronounced compared to the adult group (P70). Conclusion: Our results showed that PKR inhibition reduces morphine-induced analgesia in a burning model of inflammatory pain. These findings strongly support the idea of a potential interaction between PKR and TRPV1 in the presence of drugs used to treat inflammatory pain. This interaction may occur through direct or indirect processes and represents a crucial avenue for further exploration. Furthermore, the differences observed across age groups could unveil novel targets for the development of more effective analgesic drugs, particularly for the use of opioids in children and adolescents. Support: FAPESP 2022/14342-0; FAPESP 2-22/15306-7; FAPESP2023/16422-3 Protocol: 1056/2022R3</p>

Title	Early acoustic deprivation does not substantially affect the electrophysiological properties of fusiform neurons of the dorsal cochlear nucleus of mice.
Authors	ALAN EIDI SASAKI, MARIO HENRIQUE DEE OLIVEIRA, RICARDO MAURICIO XAVIER LEÃO
Affiliations	Fisiologia, USP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The auditory system is responsible for processing sound information received from the environment. The cochlear nuclei constitute the first processing center for auditory information in the central nervous system. The cochlear nucleus is divided into a dorsal part (DCN) and a ventral part (VCN), the latter subdivided into an anterior portion (AVCN), posterior portion (PVCN), and nerve root region (NR). Fusiform neurons (principal neurons) present in the DCN are responsible for integrating input signals to the DCN and projecting axons to the inferior colliculus. These neurons present active states (firing spontaneously) and silent states (not firing spontaneously). Recent work from our group (Benites et al., 2023) showed that the electrophysiological properties of fusiform neurons present several changes during post-natal development, with several changes happening after the establishment of hearing at p14, especially the maturation of the action potentials of these neurons, the appearance of spontaneously active neurons and the increase in the persistent sodium current, which is linked to the generation of spontaneous firing.</p> <p>Objective: Here we tested the hypothesis that auditory sensory establishment triggers the action potential maturation of fusiform neurons of the DCN of mice. for this we used a non-aggressive acoustic deprivation model using a silicon plug in the ear canal applied at p14 when the acoustic meatus opens, and the mice start to hear. Methods: All experimental procedures were approved by the Ethics Comittee for Animal Experimentation of FMRP-USP CEUA – 1289/2024R1. Female swiss mice (p14, 7 grams) are divided into 2 groups: sham (manipulated, no earplug) and plug (earplug applied at p14). At p21±2, 14 grams, sham and plug groups are tested for plug effectiveness using Auditory Brainstem Response (ABR). At this same age, all groups are euthanized for brainstem dissection and DCN slices and whole-cell patch clamp is performed for current- and voltage-clamp recordings. Results: Occlusion of the ear canal was effective in increasing the hearing thresholds in 20 dB, compared with the sham group (t=7,420, df=17, p<0,0001). Action potential parameters such as peak amplitude, threshold, afterhyperpolarization (AHP), decay time, max rise, halfwidth and latency were analyzed, but differences were only found in the AHP amplitude, from 19.57±3.969 mV (sham, n=6) to 25.17±4.992 mV (plug, n=7), (t=2.211, df=11 , p=0.0492). The frequency of firing of Action Potentials was similar in both groups. We found that most fusiform neurons from acoustically deprived animals were quiet (no action potentials fired), but a similar proportion was found in neurons from the sham group. Interestingly the magnitude of the sodium persistent current was similar in both groups. Conclusion: Even though ABR has confirmed the gel plug’s effectiveness in reducing the mice’s hearing, no significant alteration has been observed in most AP parameters, in the proportion of active and quiet neurons, and in the INaP development. Our results suggest that the post-hearing changes in the action potentials of DCN fusiform neurons do not depend on sensory input from the ears. Support: CAPES, PROEX Protocol: FMRP-USP CEUA – 1289/2024R1</p>



Title	THE MODULATORY EFFECT OF NOVELTY ON THE PERSISTENCE OF RECONSOLIDATED RECOGNITION MEMORY DEPENDS ON THE ACTIVATION OF AMPA RECEPTORS IN THE DORSAL HIPPOCAMPUS OF RATS
Authors	ANA CAROLINA DE SOUZA DA ROSA, KARINE RAMIRES LIMA, GABRIELA CRISTIANE MENDES GOMES, ANNA CECÍLIA PERRETTO VIEIRA DE SOUZA, GIULIA AZEVEDO MARTINEZ, BRUNO PEREIRA COURA, PÂMELA BILLIG MELLO CARPES
Affiliations	Laboratorio de Neuroquímica, UNIPAMPA
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Each time that we evoke a memory, its reconsolidation can occur. Reconsolidation promotes the temporary destabilization of the original information, making it susceptible to interference, which can strengthen or modify the memory trace. Exposure to novelty has been studied and used to improve recognition memory, and glutamatergic receptors are involved in this effect. Objective: Therefore, we investigated the involvement of NMDA and AMPA glutamatergic receptors in modulating novelty over the persistence of reconsolidated memory. Methods: This study was approved by the Ethics Committee/Unipampa (protocol 028/2022). Adult male Wistar rats (250-350g) were used and divided into 5 groups (n=14-31/group): (i) control+vehicle; (ii) control+NMDA; (iii) novelty+vehicle; (iv) novelty+AP5 (NMDA antagonist); (v) novelty+NBQX (AMPA antagonist). Initially, the animals underwent stereotaxic surgery to implant cannulas in the CA1 region of the hippocampus; after recovery, the Object Recognition (OR) task was performed. OR training session included the exposition to two new objects (A and B) to 5 minutes of free exploration; 24 hours later, a reactivation (recovery) session with a familiar object (A) and a new object (C) was performed. Immediately after reactivation, the novelty groups were exposed to a novelty for 5min. Vehicle or drugs (NMDA, AP5, NBQX) were infused in the hippocampus according to the group 5min after reactivation (for groups i and ii) and immediately after the novelty for the others. The OR memory test was performed 7 d later to assess memory persistence. In the test, each of the groups was subdivided into 3 groups, whose memory was tested with different sets of objects, being a new object (D) associated with: (I) one to which the animal was exposed only in training (B); (II) one to which it was exposed in training and reactivation (A): or, (III) one to which he was exposed only in reactivation (C). Exploration time was converted into % of total exploration time and compared with a theoretical mean of 50%. Differences were considered statistically significant when $P < 0.05$. Results: During the reactivation session, all animals explored the new object (c) for more than 50% of the total exploration time ($p < 0.0001$ for all groups). In the reconsolidated OR memory persistence test, group (i) explored around 50% of both objects in the 3 combinations tested ($p = 0.5184$ for A+D; $p = 0.0701$ for B+D; $p = 0.2783$ for C+D), demonstrating that the reactivation session alone is not capable of promoting the persistence of reconsolidated memory. Differently, animals in group (iii) showed persistence of memory for objects A and B ($p = 0.0156$ for A+D; $p = 0.0378$ for B+D), as well as persistence of consolidated memory for object C ($p = 0.0119$ for C+D). We also observed the persistence of memory for objects A and B ($p = 0.0177$ for A+D; $p = 0.0193$ for B+D) in group (ii). Furthermore, when we blocked hippocampal NMDA receptors in animals exposed to the novelty immediately after reactivation (iv), 7 days later we found that they continued to show persistence of memory for objects A and B ($p = 0.0120$ for A+D; $p = 0.0123$ for B+D). However, when we infused NBQX after novelty, we did not observe memory persistence in any tested combinations ($p = 0.0938$ for A+D; $p = 0.1310$ for B+D; $p = 0.4053$ for C+D). Conclusion: The data suggest that the effect of novelty on the persistence of reconsolidated OR memory does not depend on the activation of NMDA receptors but depends on the activation of hippocampal AMPA receptors. Support: CAPES, CNPq, Carrefour Protocol: 028/2022</p>





14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	Efeito imediato da música na aprendizagem motora em crianças neurotípicas: ECR
Authors	ANA FLAVIA FELICIONI DE OLIVEIRA, GRAZIELE FONSECA, LÍVIA MARIA RIBEIRO ROSÁRIO, MÔNICA CÁSSIA BERNARDO DE SOUZA, TALES ANDRADE PEREIRA, ADRIANA TERESA SILVA SANTOS, LUCIANA MARIA DOS REIS
Affiliations	Ciência da Reabilitação, UNIFAL
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introdução. A música é capaz de gerar interações auditivo-motoras no cérebro de quem a executa e também de quem a ouve, facilitando o aprendizado. Nesse aspecto, o teste de trilhas permite acompanhar a aquisição de uma habilidade motora. Objective: Este estudo avaliou o efeito da música em crianças submetidas a aprendizagem motora em dispositivo móvel. Methods: Estudo Controlado Randomizado cego e com seguimento Follow-up; com uma amostra de 52 crianças com idade entre 8 e 10 anos, ambos os sexos, destros, sem comprometimento neuropsicomotor, sem experiência com a tarefa. Foi utilizado o teste de trilhas adaptado para a versão digital, com 08 ambientes, na avaliação; na intervenção, associado à composição de Mozart intitulada Sonata para dois pianos (8 minutos e 42 segundos), duas repetições do teste e intervalo de um minuto entre elas no Grupo experimental com música e grupo controle sem música; E na reavaliação após uma semana de intervalo. Results: O teste de Mann-Whitney mostrou redução significativa no tempo de execução e número de erros em ambos os grupos (pré x pós). Houve uma tendência à redução de erros em todas as trilhas executadas com música em comparação ao sem música. Houve redução significativa na trilha 8, em que o ambiente é invertido e espelhado. Conclusion: O trabalho evidenciou que a música pode influenciar de forma direta na aprendizagem motora em crianças e o instrumento permite auxiliar em futuras pesquisas na área de aprendizagem motora, reabilitação e educação. Support: UNIFAL-MG Protocol: 21861319.7.0000.5142</p>



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Title	PRECLINICAL EFFICACY OF CANNABIGEROL FOR THE TREATMENT OF EARLY-LIFE SEIZURES
Authors	LILLIAN SOARES PINTO, GIOVANNA BRUNO BORGES, MATHEUS SILVA DE OLIVEIRA, ANNA CAROLINA TAVARES DE OLIVEIRA, RAFAELLA TERÊNCIO FERREIRA, RÚBIA APARECIDA FERNANDES, JOSÉ ALEXANDRE DE SOUZA CRIPPA, FABRÍCIO ARAÚJO MOREIRA, VICTOR RODRIGUES SANTOS
Affiliations	Morfologia, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy stands as a chronic neurological disorder marked by epileptic seizures, which can be categorized as either focal or generalized. Although medications like phenobarbital and valproic acid exist to manage seizures, they prove insufficient in fully suppressing all epileptic seizures and might even lead to neuronal death in immature brains. A promising remedy emerges in the form of Cannabigerol (CBG), a minor constituent of Cannabis sativa, recognized for its anti-inflammatory and neuroprotective effects. Among its known mechanisms of action, CBG regulates the endocannabinoid system, thereby implying a significant role in controlling neuronal excitation. Objective: To evaluate CBG's anticonvulsant efficacy using neonate rodent model of seizures induced by Pentylentetrazole (PTZ). Methods: The experimental protocols were approved by the Ethics Committee in Animal Research at UFMG (CEUA-261/2022). Neonate Wistar rats aged 10 days (P10, n=12 per group), females and males, weighing around 19 grams, were employed. CBG was prepared with a vehicle solution containing 2% Tween 20 and 0.9% saline, administered intraperitoneally (IP) 60 minutes prior to 100 mg/kg subcutaneous (SC) PTZ injection. CBG concentrations of 10 mg/kg, 30 mg/kg, and 100 mg/kg were tested. Following PTZ administration, the animals were observed for approximately 15 minutes in transparent acrylic boxes. Statistical analysis utilized Graphpad Prism 8, and the Kruskal-Wallis test was employed to ascertain seizure latency, types, severity, and duration. Results: Animals administered 30 mg/kg and 100 mg/kg of CBG exhibited significantly extended latency for both the first seizure onset (P=0.0001) and the most severe seizure (P=0.0002), compared to the control group. In terms of the loss of straightening reflex duration, indicative of seizures, the 10 mg/kg, 30 mg/kg and 100 mg/kg CBG-treated animals displayed notably shorter durations (P<0.0001) than the control group. The number of tonic-clonic seizures, which represent the most severe seizure behavior, showed no significant variance between CBG-treated and vehicle groups (P=0.3034). Likewise, no noteworthy distinctions emerged in the occurrence of spasm behaviors (Jerks) across groups (P=0.3395). Conclusion: These findings suggest that CBG exhibits a dose-dependent anticonvulsant effect in neonatal seizures, modeled by P10 treatment in the PTZ-induced seizure animal model. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES, Finance code 001), through the Graduate Program in Cell Biology at UFMG. FAPEMIG, CNPq. Protocol: CEUA-261/2022</p>



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14 a 17 de Setembro de 2024
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Title	MORPHOMETRIC STUDY OF THE VENTRAL DORSOLATERAL TELENCEPHALIC REGION OF <i>Leporinus macrocephalus</i> EXPOSED TO MECHANICAL-VISUAL STIMULI IN AN INHIBITORY AVOIDANCE TASK.
Authors	RAFAEL TOSHIO FUJIOKA, AMANDA SOARES COURA, YARAH LORENA DA SILVEIRA SANTOS, CAMILA GARCIA SERPA, LILIAM MIDORI IDE
Affiliations	* Departamento de Ciências Naturais, UFSJ, ** Escola Estadual João dos Santos, EEJS
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The memory mechanisms observed in teleosts have similarities with those of tetrapods. Studies indicate that the dorsolateral (DL) telencephalic region is probably homologous to the mammalian hippocampus and that its functions are related to spatial and temporal memory. DL can be subdivided into dorsal DL (DLd) and ventral DL (DLv). DLv is characterized by having smaller and lighter cells, compared to DLd. The experimental model of inhibitory avoidance is widely used in memory studies as it enables rapid learning and relatively long-lasting memory and the study of neuronal plasticity is possible through the morphometric analysis of brain sections processed histochemically with the silver (Ag) impregnation technique in the regions argyrophilic organizing nucleolar cells (AgNORs). Objective: The study was developed with the objective of evaluating learning and neuroplasticity in the ventral dorsolateral telencephalic region of <i>Leporinus macrocephalus</i> exposed to mechanical-visual stimuli in an inhibitory avoidance task. Methods: Sixteen <i>L. macrocephalus</i> were subjected to the inhibitory avoidance task without distinction of sex, aged 5 to 10 months and measuring between 10 cm and 15 cm in length. They presented standard scototaxis behavior, divided into a control (n=8) and experimental (n=8) group for the tests. The 16 animals tested behaviorally were euthanized and telencephalon slides were prepared for AgNOR neurohistochemical method and morphometry (n=80-85) through scanning and image capture in the photonic microscope. The behavioral and the histomorphometric data were analyzed using the Mann-Whitney test and the Welch t-test, respectively, with a significance level of 0.05 in all tests performed. The research project was examined and approved by CEUA/UFSJ (Protocol 023/2013). Results: The results obtained from the 15 <i>L. macrocephalus</i> demonstrated that there was a statistical difference between the absolute area of AgNORs of DLv (1.20 ± 0.29; 0.73 ± 0.28; $t=3.81$; $df=12.66$) in control (n=7) and experimental (n=8) groups, but no significant difference in the average number of AgNORs (1.45 ± 0.05; 1.41 ± 0.07; $t=1.44$, $df = 11.97$), in the relative area of AgNORs per nucleus ($3.97 \pm 0.65\%$; $3.22 \pm 0.78\%$; $t=2.03$, $df=12.98$) and in the area of the analyzed nuclei (31.43 ± 7.83; 22.79 ± 5.01; $t=1.22$, $df=10.97$). Conclusion: It is concluded that there were changes in the morphometric patterns of absolute area of AgNORs of DLv of the species <i>L. macrocephalus</i> exposed to mechanical-visual stimuli in an inhibitory avoidance task. Support: ** PIBIC-Jr/FAPEMIG Scholarship; UFSJ. Protocol: CEUA/UFSJ (Protocol 023/2013)</p>



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Title	MARKING ANALYSIS OF ARGENTOPHILIC PROTEINS IN THE NUCLEOLUS ORGANIZING REGION IN THE DORSAL DORSOLATERAL TELENCEPHALON OF <i>Leporinus macrocephalus</i> (ACTINOPTERYGII; ANASTOMIDAE) SUBJECTED TO THE INHIBITORY AVOIDANCE TASK
Authors	AMANDA SOARES COURA, RAFAEL TOSHIO FUJIOKA, LAURA KAORI MENEGUSSI, LILIAM MIDORI IDE
Affiliations	* Departamento de Ciências Naturais, UFSJ, ** Programa de Pós graduação em Ciências Morfofuncionais, UFSJ
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The dorsal or pallial region represents the largest portion of the teleost telencephalon and, based on its cytoarchitectural differentiation, the dorsolateral area (DI) occupies the most lateral portion of the dorsal everted area and presents cells organized in parallel layers. DI is subdivided into dorsal DI (DId) and ventral DI (DIv). DId is a moderate concentration of large, dark-colored cells, which gradually increase in size as they reach the more ventral portions of the area. The memory formation mechanisms observed in teleosts are similar to those of tetrapods, with DI possibly being homologous to the mammalian hippocampus. The inhibitory avoidance task, a method for observing learning according to scototaxis preference and aversive stimulus, makes it possible to assess the neuroplasticity of area DId of the telencephalon, which can be quantified by morphometric analysis of brain sections processed histochemically using the argyrophilic nucleolar organizing regions (AgNORs) staining method. Objective: The study aims to evaluate learning and neuroplasticity in the dorsal dorsolateral region of the telencephalon of <i>Leporinus macrocephalus</i> submitted to an inhibitory avoidance task with mechanical-visual stimulation.</p> <p>Methods: Sixteen <i>L. macrocephalus</i> were submitted to an inhibitory avoidance task, without distinction of sex, 5 to 10 months old, between 10 and 15 cm long, and with scototaxis behavior, divided into a control group (n=8) and an experimental group (n=8). After euthanasia, the brain was removed and fixed in 10% formalin, and the telencephalon sections were silver stained according to the AgNOR neurohistochemical method. Morphometry of 80 to 85 nuclei was performed by scanning and capturing magnified one thousand times images using a photon microscope. The behavioral and the histomorphometric data were analyzed using the Mann-Whitney test and the Welch t-test, respectively, with a significance level of 0.05 in all tests performed. The research project was approved by CEUA/UFSJ (Protocol 023/2013). Results: The results obtained from the 14 <i>L. macrocephalus</i> showed that there was a statistical difference between the size of the absolute area of AgNORs (1.35 ± 0.18; 1.16 ± 0.10; $t=2.46$, $df=9.61$) and between the area of the nuclei (40.27 ± 5.51; 32.99 ± 2.84; $t=3.11$; $df=8.99$) in the control (n=7) and experimental (n=7) groups, but there was no significant difference in the mean number of AgNORs (1.28 ± 0.09; 1.31 ± 0.13; $t=0.49$, $df= 11.13$) and the relative area of AgNORs per nucleus ($3.43 \pm 0.55\%$; $3.59 \pm 0.58\%$; $t=0.53$, $df=11.97$). Conclusion: There are changes in the histomorphometric patterns of neuronal nuclei and nucleoli in the telencephalic dorsal dorsolateral region of <i>Leporinus macrocephalus</i> submitted to an inhibitory avoidance task using mechanical-visual stimulation. Support: UFSJ Protocol: CEUA/UFSJ (Protocol 023/2013)</p>



Title	Alzheimer's Disease animal model double-transgenic mice (APP ^{swe} /PS1 ^{dE9}) show differences in metabolic and locomotor activity at 3 months of age
Authors	MARCOS YUJI SHIROMA GRAZIANO, JOÃO VICTOR SILVA NANI, ANA BEATRIZ HENRIQUE-SANTOS, ANDRÉ DE SOUZA MECAWI
Affiliations	Biofísica, UNIFESP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Alzheimer's Disease (AD) is one of the leading causes of dementia and death in the elderly population. Clinically, AD is characterized by progressive cognitive deficits, mainly in the memory. Physiopathologically, AD is characterized by the deposition of amyloid plaques in the extracellular space of the central nervous system (CNS), mainly in the cortex and hippocampus, and by the formation of hyperphosphorylated Tau proteins tangles in the axon of neurons. With advances in gene editing, new animal models for AD have been developed and validated. A well-established animal model is the double-transgenic mice strain APP^{swe}/PS1^{dE9} (APP/PS1), which shows exacerbated production of amyloid beta proteins and, consequently, accelerated deposition of amyloid plaques in the CNS, detectable as early as 6 months. Cognitive impairment can already be seen at 9 months. However, there are no description in the literature of secondary alterations, such as in the metabolism or locomotor activity of these animals compared to controls before the onset of AD. Objective: To analyze metabolic and locomotor differences between APP/PS1 mice and their controls before the deposition of amyloid plaques and cognitive impairment. Methods: APP/PS1 mice and their littermates without the transgene (WT), males (n=16; 8 APP/PS1, 8 WT), and females (n=16; 5 APP/PS1, 11 WT), at around 3 months of age, were used (CEUA 3253150224). After adaptation in the bioterium, the animals were transferred to metabolic cages (Oxymax CLAMS calorimeter) for four days for metabolic and locomotor analyses, two of which were for adaptation and two for measurements. Body mass and food and water intake, O₂ consumption, CO₂ production, indirect calorimetry and horizontal and vertical locomotor activity were analyzed. The data was evaluated by two-way ANOVA, followed by Tukey's post-test. Results were considered significant when p<0.05. Results: There were no significant differences in water or food intake between APP/PS1 and WT animals, male or female. APP/PS1 mice had higher O₂ consumption, CO₂ production and, consequently, a higher heat release rate. In addition, they showed greater horizontal and vertical locomotor activity during the dark period. Taking sex into account, it was observed that males had higher O₂ consumption and CO₂ production in the dark period, with consequent higher heat release. There was an interaction between the sex and genotype factors in terms of horizontal locomotor activity and, interestingly, it was the APP/PS1 females that showed significantly greater activity than the WT females. Conclusion: APP/PS1 animals exhibited greater metabolic and locomotor activity regardless of the time of day, with APP/PS1 males being more active during the dark period. APP/PS1 females showed greater horizontal locomotor activity compared to WT females. These findings share a glimpse of the baseline metabolism of APP/PS1 before the onset of AD and have shown us that they already show differences in relation to WT. This improved understanding of their physiological differences offers great potential to better understand the disease, further exploring their metabolic and activity rate before and after the onset of the disease and with WT, and propose new solutions to mitigate its development. Support: CAPES #001; FAPESP 2019/27581-0; Bolsa de Produtividade em Pesquisa CNPq Nível 1D Protocol: 3253150224</p>

Title	Evaluation of the effect of multimodal early life stress on PTZ-induced seizures in mice
Authors	GIOVANNA BRUNO BORGES, RAFAELLA TERCENIO FERREIRA, JÚLIA HELENA RIBEIRO E SOUZA, LILLIAN SOARES PINTO, VICTOR RODRIGUES SANTOS
Affiliations	Morfologia, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy is a chronic disease that affects thousands of individuals worldwide. Although the pathogenesis of epilepsy is multifaceted, research has presented compelling evidence that stress can act as a trigger through complex neurobiological mechanisms, modifying stress response systems. In this study, we analyzed the behavior of mice during seizures, observing the latency, duration and phases of the epileptic seizure. We used a multimodal stress protocol (ELS) that involved repeating and alternating daily stressors, gradually inducing maladaptive plasticity. Previous studies have shown that exposure to diverse and repeated stressors can have detrimental effects on the body, particularly on the central nervous system. In particular, animals that experienced stress early in life had worsened epileptic seizures and decreased latency.</p> <p>Objective: The work aims to evaluate the influence of early stress on the latency, duration and severity of PTZ-induced epileptic seizures. Methods: The experimental protocols described in this study were approved by the Ethics Committee in Animal Research of UFMG (CEUA-42/2024). Pups of C57BL/6 mice were submitted to stress from the 1st to the 9th postnatal day (P) (n=9 stressed group (SG); n=7 negative control (NC)). The ELS included alternating periods of separation of mother and pair in an acrylic box with internal separations for 60 minutes, containment with agitation at 30 rpm for 60 minutes on an agitator, and exposure to cold for 10 minutes. On P10 (SG: 4.89g±0.06; NC: 4.78g±0.29), subcutaneous doses of 80 mg/kg and 100 mg/kg of the seizure-inducing drug diluted in saline solution, pentylentetrazole (PTZ), were administered to animals in the SG and to animals that did not suffer stress, as a negative control. Subsequently, they were placed in acrylic boxes and observed for about 20 minutes, with a camera placed above the boxes. The videos were analyzed and the initial data collected stored in a spreadsheet with the parameters to be analyzed. The data will be transformed into statistical data using GraphPad Prism 8 to evaluate various crisis parameters, including seizure types, duration, severity, and latency. Results: After preliminary analyses, it was observed that in the group of control animals the latency time was approximately five minutes longer compared to the group of stressed animals. In addition, the stressed animals had longer seizures of about 15 minutes and continuous, while the control animals lasted about 10 minutes and were able to return from the seizure at least once. The stressed group also showed loss of straightening reflex more significantly. When the stressed group showed decreased latency and worsening of seizures, this indicates a potential association between stress in early life and increased susceptibility to epileptic seizures.</p> <p>Conclusion: The presented results suggest a potential association between early-life stress and increased susceptibility to epileptic seizures. These findings underscore the importance of understanding how early-life stress impacts epilepsy development and progression. Therefore, the study highlights the critical need to explore the relationship between early-life stress and epilepsy. By analyzing seizure latency, duration, and types in stressed and unstressed mice, this research aims to inform targeted therapies and therapeutic strategies to mitigate or reverse the effects of chronic early-life stress. Support: CNPq and FAPEMIG Protocol: CEUA: 42/2024</p>

Title	Neuroprotective effects of gold nanoparticles biofunctionalized with glutathione in an in vitro oxygen and glucose deprivation model
Authors	BEATRIZ LOPES TECEDOR BASSI, ALINE DOS SANTOS VIEIRA, LUCAS ALENCAR SOARES, ARIADNE PEREIRA LIMA AMORIM, CAMILLA STEPHANE OLIVEIRA SILVA, LUIZ ORLANDO LADEIRA, GISELE EVA BRUCH, ANDRÉ RICARDO MASSENSINI
Affiliations	Fisiologia e Biofísica, UFMG, UNIVERSIDADE FEDERAL DE MINAS GERAIS
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Gold nanoparticles (AuNP) have garnered attention as potential neuroprotective agents in animal models of brain diseases, including ischemic stroke, which is characterized by the occlusion or blockage of a blood vessel. Studies have already shown a decrease in infarct volume, functional recovery, and attenuation of oxidative stress and inflammation in animals treated with AuNPs and submitted to ischemia. In addition to acting as a treatment, these nanomaterials also act as nanocarriers, increasing the biodistribution and effectiveness of substances that are rapidly degraded by the body, such as glutathione (GSH). GSH is the peptide in the greatest amount in the body and is a key element in redox balance.</p> <p>Objective: Thus, this study aimed to evaluate the effectiveness of the treatment of gold nanoparticles functionalized with glutathione on the effects of cerebral ischemia. Methods: Gold nanoparticles were synthesized and then biofunctionalized with GSH (AuNP-GSH). For characterization, an analysis of the shape and mass of gold was performed by Surface Plasmonic Resonance (SRP), measured by UV-VIS spectrophotometry; its size (DLS, Dynamic Light Scattering) and charge (zeta potential, PZ) were measured using the ZetaSizer Nanoseries equipment. For the cerebral ischemia model, hippocampal slices from 36 male CD1 mice 9-11 weeks old (CEUA/UFMG: 270/2020) were used. The slices were divided into a control plate with aCSF (Artificial Cerebrospinal Fluid) with glucose and bubbled with O₂ and CO₂ and an ischemia plate with ACSF without glucose and bubbled with N₂ and CO₂. The experimental groups were added: control, GSH (100ug/mL), AuNP (800, 8 ug/mL) and concentration x response curve AuNP-GSH (0.08, 800ug/mL). The period of ischemia lasted 60 minutes and reperfusion 120 minutes. Cell damage was analyzed by lactate dehydrogenase (LDH) release and neurotoxicity by glutamate release. Brain, kidney, and liver were dissected 24h after intravenous injection of 1mg/kg Au for biodistribution analysis. Results were analyzed using Anova Two-Way (p<0.05). Results: The AuNP showed a λ_{max} of 530nm and a charge of -31.4mV, while the AuNP-GSH had a 517nm and -27mV, its spherical shape being inferred and showing the shift of the maximum peak and the charge caused by the modification of the surface by the binding of GSH. The mass of gold in the AuNP solution was 82mg/L, while that of AuNP-GSH was 44mg/L caused by centrifugation of the latter. Among control groups, it was observed that there was greater cellular damage and glutamate release in the slices submitted to ischemia. It was observed neuroprotection in the treatment group with AuNP-GSH compared to the control group in LDH analysis (3.629 vs 15.933 U/mg protein, p<0.001) and a significant decrease in glutamate release (14.912 vs 28.280 nmol/mg protein, p=0.028) during the ischemic process. It could be found both treatment groups on the liver and only GSH-AuNP in the kidney. Conclusion: The successful synthesis and modification of AuNP with GSH, as demonstrated by the characterization results, as well as decrease of LDH and glutamate release, highlight the potential of AuNP-GSH as a protective agent against cellular toxicity. Further investigations are warranted to gain a deeper understanding of the interaction between gold nanoparticles and other detrimental pathways associated with cerebral ischemia. Support: CNPq; CAPES Protocol: CEUA/UFMG: 270/2020</p>



Title	Roles of PKR in analgesia, tolerance, opioid dependence, and hyperalgesia following an inflammatory pain mice model
Authors	ANDREA MAIA CARVALHO, TERRENCE TEIXEIRA, SONIA ZANON, GUILHERME LUCAS
Affiliations	Neurociências e comportamento, USP, Fisiologia, USP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Opioids, including morphine, are extensively used to manage acute postoperative and moderate to severe pain. However, their prolonged use is associated with opioid-induced conditions such as analgesic tolerance and addiction. Paradoxically, opioids have been implicated in exacerbating pain. Double-stranded RNA-dependent protein kinase (PKR) has been involved in interferon induction, innate antiviral immunity, tumour suppression, and stress signals. Thus, PKR emerges as a significant player in chronic pain pathways and represents a new putative target for the treatment of neuroinflammatory diseases, including opioid abuse disorders. Objective: Investigate the effect of PKR inhibition on morphine-induced analgesia, hyperalgesia, opioid tolerance, and dependence in mice. Methods: This study utilized a plantar incisional pain model in adult PKR+/+, PKR-/-, and C57Bl/6 mice of both sexes. Mice received morphine (1, 2, or 4 mg/kg; s.c.) one hour and 72 hours after incisional plantar lesion. Thermal hyperalgesia was evaluated by immersing the lesioned paw in water at 49°C. Morphine tolerance development was assessed by administering morphine (4.0 mg/kg) three times daily for 5 days starting 72 hours post-incision, with one group receiving PKR inhibitor (250 µg/kg) before each morphine injection. Opioid dependence was evaluated in naïve mice by treating them with morphine (10 mg/kg, s.c.) twice daily for 5 days, followed by naloxone (10 mg/kg, i.p.) on day 6. Morphine-induced hyperalgesia was investigated by treating naïve mice with low doses of morphine (1.0, 2.0, and 4.0 mg/Kg). PKR inhibitor (250 µg/Kg) was also administered before the lowest dose of morphine (1.0 mg/Kg). Results: In the incisional model using PKR knockout mice, it was found that PKR deficiency did not affect thermal and mechanical hypersensitivity in the acute stage. In the chronic stage, however, PKR knockout completely reversed thermal hyperalgesia three days after the injury but did not affect mechanical allodynia. All doses of morphine caused significant analgesia, as observed by reduced thermal hyperalgesia measured by paw withdrawal latency after thermal stimulation. Yet, when PKR was pharmacologically inhibited, morphine analgesia was markedly reduced at all doses. Additionally, the development of drug tolerance was observed at doses of 2 and 4 mg/Kg but not at 1 mg/kg in the acute phase (1h post-injury) and persistent phase (72h post-injury) of the inflammatory process. PKR inhibition before morphine injection significantly influenced the development of morphine analgesic tolerance. In C57Bl/6 mice, opioid dependence was observed in males treated with PKR inhibitor before morphine administration or naloxone injection. These animals showed a significant reduction in the number of jumps. No difference was observed in female mice. In hyperalgesia, the results showed that saline injection did not change the latency to respond to thermal noxious stimulation in naïve mice. Conversely, morphine caused hyperalgesia in a dose-dependent manner, whereas the higher dose induced analgesia. However, PKR inhibition before a low dose of morphine administration significantly reversed the hyperalgesic effect in the first 60 minutes after opioid administration. Conclusion: PKR plays a paradoxical role in pathological pain and opioid analgesia following peripheral inflammatory lesions. Moreover, PKR inhibition seems to reduce or revert opioid-mediated effects such as tolerance, dependence, and hyperalgesia. Support: CNPq Protocol: 1056/2022</p>



Title	Influência da separação materna no estresse oxidativo e nas respostas defensivas comportamentais de ratos e ratas Wistar.
Authors	MARIANA LIMA FARIAS, LETÍCIA H. O. CASSIMIRO, PEDRO ALVES MACHADO JÚNIOR, AMANDA NUNES COSTA, LUCAS GABRIEL VIEIRA, FRANK SILVA BEZERRA, DEOCLÉCIO ALVES CHIANCA JR, FERNANDA C. DO SANTOS SILVA, RODRIGO CUNHA A. DE MENEZES, SYLVANA I. S. R. DE NORONHA
Affiliations	Departamento de Ciências Exatas e Biológicas, ICEB, Laboratório de Fisiologia Cardiovascular, LFC, Departamento de Ciências Exatas e Biológicas, ICEB, Laboratório de Fisiopatologia Experimental, LAFEX
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A exposição a eventos adversos ou traumáticos de maneira precoce na vida pode aumentar a vulnerabilidade para o desenvolvimento de psicopatologias na vida adulta, dentre elas o comportamento de ansiedade. A separação materna é um modelo amplamente utilizado para mimetizar os efeitos de uma experiência traumática no início da vida e está associado ao desenvolvimento de comportamento relacionado a ansiedade em roedores. Além disso, está associada a estresse/dano oxidativo de regiões encefálicas e periféricas relevantes na regulação do comportamento animal. Entretanto, os mecanismos responsáveis pelo comportamento de ansiedade resultante da separação materna ainda não estão completamente elucidados. Objective: Avaliar os efeitos da separação materna sobre: 1) parâmetros biométricos (peso e índice de adiposidade); 2) Sobre os danos oxidativos em núcleos centrais (hipocampo e hipotálamo) e das glândulas adrenais e; 3) sobre o comportamento do tipo ansiedade em machos e fêmeas. Methods: Foram utilizados 19 ratos e 22 ratas Wistar (CEUA: Nº 2065030823), previamente submetidos ao protocolo de separação materna, ou mantidos sem submissão ao protocolo (controle). Entre 100 e 107 dias após o nascimento, foram realizados os testes comportamentais. O protocolo de separação materna (SM) ocorreu durante o período de amamentação, onde os filhotes foram separados de suas progenitoras por um período de 3 horas durante 13 dias. A avaliação dos parâmetros comportamentais foi obtida através da exposição aos testes comportamentais do labirinto em Cruz-elevado (LCE), caixa claro/escuro (CE) e campo aberto (CA). Foram isolados o hipocampo, hipotálamo e glândulas adrenais, para a avaliação do estresse/dano oxidativo a partir da contagem de proteínas totais, e antioxidantes enzimáticos superóxido dismutase (SOD) e catalase (CAT), e dano lipídico a partir da peroxidação lipídica (TBARS). Results: Houve uma diferença do acúmulo de tecido adiposo entre machos e fêmeas. O ganho de peso semanal foi similar entre os sexos. Porém houve hiperplasia do tecido inguinal de machos ($p = 0.0283$), e hipoplasia dos tecidos adiposos parametrial ($p = 0.0018$), inguinal ($p = 0.0022$) e retroperitoneal ($p = 0.0290$) em fêmeas. Ocorreu um aumento no índice de adiposidade em machos ($p = 0.0397$) e uma diminuição desse índice em fêmeas (0.0033) sob SM. O peso da adrenal aumentou de peso em ratas sob SM ($p = 0.0285$). Em relação ao estresse oxidativo, no hipocampo, observamos que houve redução da SOD ($p = 0.0198$) e CAT ($p = 0.0165$), e no aumento de TBARS ($p = 0.05$) em machos, mas não em fêmeas. No hipotálamo, observamos SOD próxima da significância em fêmeas ($p = 0.0593$) e TBARS aumentada ($p = 0.0424$), e CAT aumentada em machos ($p = 0.0445$). Na adrenal, SOD ($p = 0.0331$) e TBARS ($p = 0.0671$) estão aumentadas ou próximas da significância em machos e CAT ($p = 0.0026$) aumentada em fêmeas. Em relação à ansiedade, não houve diferença no teste do LCE. No CE, as fêmeas mostram valores próximos da significância em relação a maior permanência no escuro ($p = 0.0666$) e menor tempo no claro ($p = 0.0629$). No CA, os machos percorrem maior número de quadrantes na periferia do aparato ($p = 0.0203$). Conclusion: A partir dos nossos resultados podemos concluir que a SM impacta no acúmulo abdominal de gordura, peso da adrenal, estresse/dano oxidativo e comportamento de ansiedade/exploração de maneira sexo-dependente. Support: CAPES, Fapemig, CNPq e UFOP Protocol: Os protocolos experimentais fo</p>

Title	EXPOSURE TO UNPREDICTABLE CHRONIC MILD STRESS CAUSES ANXIETY-TYPE BEHAVIOR IN MALE RATS
Authors	AMANDA NUNES COSTA, MARIANA MARTINS VIEIRA, LUCAS GABRIEL VIEIRA, DEOCLÉCIO ALVES CHIANCA JUNIOR, RODRIGO CUNHA ALVIM DE MENEZES
Affiliations	Departamento de Ciências Biológicas, UFOP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chronic stress is a well-established public health concern. Characterized by psychophysiological responses to challenging situations, it is linked to the development of various illnesses including mental disorders. The World Health Organization even considers stress the 'health epidemic of the 21st century' due to its widespread prevalence. Objective: Evaluate the anxiety-type behavior of rats submitted to two or four weeks of unpredictable chronic mild stress protocol (UCMS). Methods: Male Wistar rats with approximately 300-350g (CEUA UFOP nº 8013230522) were submitted to two or four weeks of UCMS. The protocol includes the following stressors: 1) forced swimming in group (20 minutes); 2) food restriction (12 hours); 3) interruption of light/dark cycle (12 hours); 4) high humidity (4 hours); 5) dump and dirty bedding (4 hours); 6) social isolation (4 hours); 7) intermittent shaking (4 hours); 8) uncovered floor (4 hours); 9) physical restraint (1 hour); 10) wet cage (4 hours); 11) cold exposure (90 minutes). The protocol was performed at different times of the day, in a random order. After two or four weeks of stress, the rats were submitted to the following behavioral tests: elevated plus maze (EPM), dark/light box and open field or sucrose preference test. After the behavioral tests, the animals were submitted to euthanasia with overdose of ketamine (300 mg/kg), xylazine (21 mg/kg) and fentanyl (0.3 mg/kg). The brain and blood were collected for posterior analyses. The statistical analyses were made by GraphPad Prism. The quantitative data was submitted to Shapiro Wilk Test to analyze the normal distribution. Then, the data was submitted to Unpaired Test T. Results: The rats submitted to 2 weeks of UCMS showed in the EPM: 1) less time spent in open arms (CON 97.81 ± 14.34 (n=11) vs UCMS 45.38 ± 12.22; p= 0.0115); 2) reduction in the number of entries in open arms (CON 4.909 ± 0.5633 (n=11); UCMS 2.182 ± 0.4635 (n=11); p=0.0013); 3) less time spent in the center (CON 45.99 ± 3.724 (n=10); UCMS 25.81 ± 4.286 (n=10); p=0.0023); 4) reduction in the number of entries in the center (CON 10.64 ± 0.7894; UCMS 7.727 ± 0.8851; p=0.0235); 5) enhance in time spent in closed arms (CON 150.9 ± 12.92; UCMS 222.8 ± 15.84; p=0.0022). There were no differences between the groups in any of the parameters evaluated in the open field test, dark/light box nor in the sucrose preference test. After four weeks of UCMS, the animals submitted to stress spent less time in the open arm of the EPM (CON 155 ± 19.62 (n=6); UCMS 68.54 ± 26.44 (n=6); p=0.0254). In the dark/light box there were no difference between groups. In the open field test, animals submitted to stress spent less time grooming (mean CON 19.77 ± 2.088 (n=6); UCMS 11.19 ± 2.478 (n=6); p=0.0244). There were no difference between the groups in the sucrose preference test. Conclusion: UCMS (2 or 4 weeks of exposition) induced anxiety related behavior in male rats but did not induce depression-like behavior. Support: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior, Brasil (CAPES), Finance Code 001, CNPQ, FAPEMIG, UFOP Protocol: 8013230522</p>



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Title	Inulin supplementation partially reverses recognition memory deficits and mitigates brain redox imbalance induced by high-fat diet-induced obesity in female rats
Authors	LUCAS GABRIEL VIEIRA, SYLVANA IZAURA RENDEIRO NORONHA, AMANDA NUNES COSTA, FERNANDA CALCILDA SILVA, DEOCLÉCIO ALVES CHIANCA JÚNIOR, RODRIGO CUNHA ALVIM DE MENEZES-
Affiliations	Departamento de Ciências Biológicas, UFOP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introduction: Obesity is a worldwide public health problem associated with cognitive and mental health problems, both humans and rats. Studies assessing fiber supplementation in behavioral and cognitive deficits caused by a high-fat diet (HFD) in female rats are still scarce. Here, we analyzed the impact of a HFD induced-obesity associated with fiber supplementation on anxiety-related defensive behavior, cognitive responses and social interaction in female Wistar rats. We have also evaluated oxidative stress in these animals' hippocampus. Objective: To evaluate the impact of HD-induced obesity associated with prebiotic supplementation on anxiety-related defensive behavior, cognitive responses and social interaction in female Wistar rats as well as determine oxidative damage in the hippocampus of these animals. Methods: Methods: Female Wistar rats (n=56; CEUA#8744280818) were randomly divided into four groups: control diet [(CD; 11% fat/n = 14), high-fat diet (HFD;45% fat/n = 14)], control diet inulin (CDi; 860 mg/kg/ml) and high-fat diet inulin (HFDi; 860 mg/kg/ml). Rats were subjected to a 9-week nutritional protocol. They administered inulin supplementation via orogastric gavage (860 mg/kg/ml). All rats were tested in the elevated plus-maze (EPM), open-field (OF), object recognition test (ORT), on short- and long-term duration (60 min and 24hs), and the social interaction test. Results: Results: HFD-induce obesity (CD: 238.71 ±3.52 vs. HFD: 261.60 ±6.61; p= 0.0015) did not change the anxiety-like responses (p>0.05). Treatment with inulin increased the locomotor activity in OF and numbers of entries in the open arm in the EPM (CDi: 7.64 ± 1.230 vs. HFi: 10:14 ± 0.6782; p=0.0073). However, we observed the animals fed the HFD had a longer time of exploration in the new object paradigm when compared to control animals in the short term, with a significant increase in the recognition index in the HFD group when compared to the CD animals (CD: 0.5761 ± 0.20 vs. HFD: 0.6889 ± 0.21; p=0.0010). In the social interaction test, the animals fed the HFD had a shorter interaction time and a lower number of interactions (CD: 97.2 ± 9.397 vs. HFD: 32.9 ± 2.508; p= 0.0001). HFD promoted a cerebral redox imbalance with protein and lipid damage in the hippocampus (CD: 9.15 ± 0.76 vs. HFD: 11.39 ± 0.98 and CD: 8.92 ± 1.05 vs. HFD: 11.03 ± 0.79; p=0.004). The inulin treatment reversed the protein and lipid damages protein in the hippocampus (CDi: 3.46 ± 0.04 and HFDi: 2.89 ± 0.82), F (1, 43) = 56.51; p= 0.0001). Conclusion: Conclusion: HFD impaired social interaction, possibly because of an imbalance in oxidative stress redox and Inulin supplementation partially reverses brain redox imbalance. However, we found increased object recognition in the short-term analysis an recognition memory and the and supplementation with inulin reversed this result. Our results increase the understanding of how a HFD and effects the prebiotics in be affects social behavioral and cognitive process in female rats. Support: Support: This work was carried out with the support of CAPES, UFOP and CNPQ. Protocol: CEUA UFOP, 8744280818</p>



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Title	EFFECT OF INTRA-HIPPOCAMPAL ELECTRICAL STIMULATION, ORGANIZED IN TIME, ON FEAR MEMORY ACQUISITION
Authors	PAULA GONÇALVES VIEIRA TEIXEIRA, FLÁVIO AFONSO GONÇALVES MOURÃO, LEONARDO DE OLIVEIRA GUARNIERI, GRACE SCHENATTO PEREIRA MORAES, MÁRCIO FLÁVIO DUTRA MORAES
Affiliations	Fisiologia e Farmacologia, UFMG
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cognitive neuronal processing depends not only on the location of neural activity but also on the precise temporal patterns that emerge from neural assemblies. Research has shown that stimulation patterns composed of binary-coded words, consisting of six discharges distributed across 10 bins (i.e. purposely dividing the period within the range of a theta oscillation), can differentially modulate polymodal associative regions such as the amygdaloid complex and the hippocampus. We hypothesize that stimuli applied to the hippocampus during classical fear conditioning (a hippocampus-independent memory task) will enhance long-range connectivity, contingent on the `word regularity` of the stimuli. Thus, the `word regularity` of the stimuli is expected to recruit hippocampal circuitry in a manner similar to contextual fear conditioning. Objective: This study aims to investigate if binary-coded stimuli (BCS, i.e. six stimuli distributed across 10 bins of a 140 ms period oscillation) applied to CA3 of the ventral hippocampus, during auditory fear conditioning (AFC), facilitates the formation of an aversive memory depending on the word-regularity. Methods: Classical conditioning was carried out using a homemade device using an electric shock to the feet lasting 2s and intensity of 0.4mA, as an unconditioned stimulus (US). Adult male C57BL/6 mice were subjected to AFC and divided into 3 groups: Control, BCS-reg (regular BCS composed of the same sequence of stimulation during the 140ms periods, i.e. same words) and BCS-rand (random BCS composed of the multiple sequences of stimulation during periods, i.e. randomized words). Conditioned stimuli (CS) were combined with a sound (1KHz for 30s) and during conditioning. The BCS were applied to the ventral hippocampus CA3 (BCS-reg or BCS-rand). Memory was tested 24 hours after conditioning. After the last test session, brains were harvested and processed for c-Fos, Dapi and NeuN. CEUA/UFMG: 339/2023 . Two-way ANOVA compared the different groups. Results: The results reveal a significant difference ($p=0.04$) between the BCS-reg(69.47%±STD) and Control (Freezing 41.25%±STD) groups at the time of the sound, on the day of the test. Showing that BCS-reg facilitated the acquisition of fear memory at the time of conditioning. However, there is no significant difference between BCS-rand(45.63%±STD) and Control (Freezing 41.25%±STD; $p=0.99$), and BCS-rand(Freezing 45.63%±STD) and BCS-reg(Freezing 69.47%±STD; $p=0.69$) during the sound. In the pre-sound and post-sound phase, there was no statistical difference between the groups. The results for c-Fos and NeuN immunolabeling are still being quantified. Conclusion: According to the results, the application of BCS-reg to the hippocampus during conditioning suggests that `word regularity` on temporally coded stimulation is paramount to establish long-range connectivity to conditioned response circuitry generating freezing behavior. The use of the cued US auditory conditioning task applying BCS-reg to the hippocampus facilitates its recruitment, potentiating fear memory. The hippocampal c-Fos-labeled immunoreactive profile should be fully quantified by the poster presentation session. Support: This study was partially funded by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: PROTOCOL CEUA UFMG: 339/2023</p>

Title	Comorbidity have lower onset threshold than spontaneous seizures, but share common triggering mechanisms
Authors	LEONARDO DE OLIVEIRA GUARNIERI, JOÃO PEDRO DE CARVALHO MOREIRA, FLÁVIO AFONSO GONÇALVES MOURÃO, MATHEUS COSTA PASSOS, MARCIO FLÁVIO DUTRA MORAES,--
Affiliations	Departamento de Fisiologia, Universidade Federal de Minas Gerais
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Various animal models of epilepsy, especially those linked to genetics, often show susceptibility to proconvulsant agents. The `double-hit hypothesis` suggests an initial insult can lead to heightened susceptibility and network imbalance. This implies shared mechanisms may drive network predisposition to abnormal activity. Abnormal connectivity and information transfer between neural substrates may play a central role in seizure predisposition. Lesser degrees of these disarrangements might lead to functional compromises associated with epilepsy comorbidities instead of full-blown seizures. For example, depression and epilepsy show a bidirectional interaction where each condition increases the risk of the other. This concept might extend to other comorbidities sharing neurobiological pathways with seizure susceptibility. This work designed a protocol to examine if different degrees of a double-hit insult (one causing status epilepticus leading to spontaneous seizures, and another subthreshold to seizure induction) could generate behavioral traits associated with comorbidities. Objective: The study aimed to determine if signs of comorbid diseases are present in a pilocarpine-induced temporal lobe epilepsy model, even without seizures, exploring the possible relationship between the neural pathways shared by comorbidities and epilepsy. Methods: Male C57/Bl6 mice, 6 weeks old, were used, 10 animals per group. To address this issue, the experiment was designed to explore subthreshold insults for seizures in the established pilocarpine (PILO) temporal lobe epilepsy model (PiloTLE). The goal is to determine whether traces of signs related to comorbid diseases are present even in the absence of seizures. Half the dose of PILO used for seizure induction (150 mg/kg) was compared against the vehicle group and the PiloTLE epilepsy model (300 mg/kg). Intellicages were used to quantify the circadian cycle, cognitive flexibility, and sucrose preference. In order to evaluate depression and anxiety traits, groups were subjected to forced swimming, elevated plus maze (EPM), and open field (OF) behavioral tests. Memory tests evaluating social recognition were also conducted. Results: Animals receiving 150mg/kg (Pilo150) and 300mg/kg (Pilo300) of pilocarpine showed no difference in total distance traveled in the OF test but spent less time in the central area (Control – 41.10±2.98; Pilo150 – 21.04±2.04; Pilo300 – 12.27±1.89), with Pilo300 showing a greater reduction ($p < 0.05$). In the EPM test, pilocarpine groups had fewer open arm crossings (Control – 13.40±1.19; Pilo150 – 4.90±0.92; Pilo300 – 4.55±0.76) and less open arm time (Control – 29.37±2.21; Pilo150 – 15.01±1.07; Pilo300 – 9.57±1.37). For social memory, Pilo150 and Pilo300 groups could not remember the previously presented animal after 24 hours. In sucrose consumption, Pilo150 (24.84±2.68) and Pilo300 (21.91±2.51) differed from control (45.32±2.40) up to the 12th hour. Pilo150 showed a preference for sucrose between 12-48h (36.23±2.70), while Pilo300 showed no preference throughout. In cognitive flexibility, the control group showed success above 25% from the second day (36.37±2.84), Pilo150 after the third day (36.59±3.12), and Pilo300 remained near 25%, indicating no learning (25.94±1.81). Conclusion: Our results clearly demonstrate a spectrum between signs associated with comorbidities at one end and the emergence of seizures at another for this particular PiloTLE animal model of epilepsy Support: Fapemig; CNPq; CAPES Protocol: CEUA: 339/2023</p>

Title	EVALUATION OF THE EFFECTS OF NEUROPEPTIDE Y ON BEHAVIOR OF ADOLESCENT RATS SUBMITTED TO SINGLE PROLONGED STRESS
Authors	MARIANA MARTINS VIEIRA, AMANDA NUNES COSTA, LETÍCIA HELENA DE OLIVEIRA CASSIMIRO, FERNANDA CACILDA DOS SANTOS SILVA, DEOCLÉCIO ALVES CHIANCA JÚNIOR, RODRIGO CUNHA ALVIM DE MENEZES
Affiliations	Departamento de Ciências Biológicas, UFOP
Session	7-Neurofisiologia
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introduction: Neuropeptide Y (NPY), a 36-amino acid endogenous molecule, plays a crucial role in modulating orexigenic and behavioral functions. It is primarily found in the central and peripheral nervous systems. The primary NPY receptors mediating these actions are Y1 and Y2, expressed in various brain regions, including the hypothalamus, prefrontal cortex, hippocampus, and amygdala. These regions are associated with stress responses in mammals and the development of post-traumatic stress disorder (PTSD). In rats, a single prolonged stress session has been shown to induce symptoms related to PTSD. The prevalence of PTSD in adults is 5.6%, while in adolescents, the prevalence of this disorder is even higher, affecting 7.8% of trauma-exposed youth. Despite this, the neurobiology of PTSD in adolescents remains poorly understood. Aim: This study aimed to investigate the effects of NPY on the behavior of adolescent rats subjected to an experimental single prolonged stress protocol. Objective: Aim: This study aimed to investigate the effects of NPY on the behavior of adolescent rats subjected to an experimental single prolonged stress protocol. Methods: Material and methods: Male Wistar rats aged 28-30 days (CEUA UFOP nº 5253121122) were subjected to the single prolonged stress (SPS) protocol, consisting of three stressors: physical restraint in an acrylic tube for 2 hours, forced swimming in a group for 20 minutes, and immediate exposure to ether until loss of consciousness. Upon completion of the session, the rats were returned to their home cages and undisturbed for 7 days. After this period, animals received an intraperitoneal injection of NPY (60 ug/kg), Diazepam (0.75mg/kg), or saline. After 30 minutes, the rats were subjected to the following behavioral tests in sequence: elevated plus maze, light-dark box, and open field. At the end of the experiments, the rats were euthanized with an anesthetic overdose of ketamine (300 mg/kg), xylazine (21 mg/kg), and fentanyl (0.3 mg/kg) i.p. Blood, adrenal glands, and brain were collected and stored for subsequent molecular and morphological analyses. Behavioral data were analyzed and quantified. Statistical analysis was performed using GraphPad Prism version 8.0.2. 2019 statistical software. Quantitative data were first subjected to a Shapiro Wilk test for normal distribution analysis. After confirming the normal distribution of the data, the Two-Way ANOVA test was used. Results: Results: The analyzed parameters did not show any differences in the results of the elevated plus-maze test. Similarly, in the light-dark box test, no differences were found between the groups. However, in the open field test, the time spent in the periphery of the stressed group increased (274.7 ± 11.08 CON vs 288.1 ± 1.329 SPS; $F(1, 13) = 6.259$; $p=0.0204$); and consequently decreased in the center of the apparatus compared to the non stressed animals [26.92 ± 9.416 CON vs. 11.94 ± 1.315 F ($1, 13) = 7.260$; $P=0.0184$)] The NPY treatment had no effect on any of the behavioral parameters. Conclusion: Conclusion: Animals subjected to stress developed an anxiety-like behavioral phenotype. However, NPY treatment failed to alter behavior in SPS-subjected animals. Support: SUPPORT: CAPES, CNPQ, FAPEMIG, UFOP Protocol: 5253121122</p>

Title	Hydralazine attenuates renal fibrosis through an antioxidant mechanism dependent on NADPH oxidase inhibition
Authors	JENNYFER MARTINS DE CARVALHO, VALÉRIA BIANCA DE SOUZA SANTOS, MARRY ANEYTS DE SANTANA CIRILO, LARYSSA BEATRIZ SILVA NASCIMENTO, WEDJA STEPHANY DE ASSIS LIMA, JOSÉ ANDERSON DA SILVA GOMES, FERNANDA DAS CHAGAS ANGELO MENDES TENÓRIO, NATÁLIA TABOSA MACHADO CALZERRA, LEUCIO DUARTE VIEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, UFPE, Departamento de Histologia e Embriologia, UFPE
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chronic kidney disease (CKD) is a pressing public health problem primarily characterized by renal fibrosis. Despite its recognized impact, therapeutic approaches for CKD remain limited. Hydralazine (HZ) is a peripheral vasodilator that has protective effects on kidney injury independent of its hemodynamic action; however, its mechanism of renoprotection is not fully elucidated. Objective: Our study aims to investigate the effects of low-dose HZ treatment in rats, specifically in preventing renal fibrosis induced by unilateral ureteral obstruction (UUO). It was also investigated whether these effects are related to the modulation of enzymes involved in renal redox status. Methods: The protocol described was approved by the ethics committee for animal experimentation (nº109/19). Male Wistar rats (120 days, 300-350g, n=16) were subjected to renal injury by UUO and divided into two groups: i) untreated group (UUO, n=8); and ii) hydralazine-treated group (5 mg/kg, on alternate days; UUO+HZ, n=8). Additionally, a group of rats underwent sham UUO surgery (Sham, n=8). Ten days after surgery, the animals were euthanized, and urine, blood, and kidneys were collected. The differences between groups' means were compared using a one-way analysis of variance followed by Tukey's test and considered significant at $p < 0.05$. Results: Twenty-four hours after Sham/UUO surgery, it was observed that the UUO group had higher serum creatinine levels (51%, $p < 0.05$) than the Sham group. Ten days after surgery, serum creatinine levels were still higher (45%, $p < 0.05$) in the UUO group than in the Sham group. Additionally, the UUO group had higher renal collagen deposition (174%, $p < 0.05$) and proteinuria (82%, $p < 0.05$), as well as higher lipid peroxidation (49%, $p < 0.05$), higher NADPH oxidase activity (100%, $p < 0.001$), and lower catalase activity (49%, $p < 0.05$) than the Sham group. On the other hand, the UUO group that received HZ showed a reduction in serum creatinine levels (25%, $p < 0.05$) and an increase in creatinine clearance (180%, $p < 0.05$) compared to the UUO group. Furthermore, HZ prevented the increase in proteinuria (32%, $p < 0.05$) and renal collagen deposition (20%, $p < 0.05$) induced by UUO. It was also observed that the UUO+HZ group presented lower renal lipid peroxidation than the untreated UUO group (30%, $p < 0.05$), as well as lower NADPH oxidase activity (53%, $p < 0.01$), and higher activity of superoxide dismutase (30%, $p < 0.05$) and catalase (60%, $p < 0.001$). Conclusion: Our results indicate that hydralazine presents protective effects on renal fibrosis that may be linked to the modulation of enzymes involved in renal redox balance. These findings underscore the promising role of HZ in the treatment of CKD Support: CNPQ and CAPES Protocol: 109/19</p>

Title	Reactive oxygen species disrupt renal hemodynamics and cardiac ATPase activity in a model of paraquat-induced renocardiac syndrome
Authors	VALÉRIA BIANCA DE SOUZA SANTOS, MARRY ANEYTS DE SANTANA CIRILO, JENNYFER MARTINS DE CARVALHO, HUMBERTO MUZI-FILHO, ADALBERTO VIEYRA, NATÁLIA TABOSA MACHADO CALZERRA, LEUCIO DUARTE VIEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, UFPE, Centro Nacional de Biologia Estrutural e Bioimagem, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cardiorenal syndrome can be triggered by paraquat (PQT, 1,1'-dimethyl-4,4'-bipyridinium dichloride), a herbicide banned in many countries due to its high toxicity. This compound may induce cardiac dysfunction secondary to acute renal injury. In recent studies, we observed that PQT induces changes in renal tubular ATPases mediated by reactive oxygen species production. Therefore, it is also reasonable that PQT contributes to cardiac injury by directly affecting cardiac ATPases due to ROS production, establishing a cycle of mutual dysfunction between the kidney and the heart. Objective: We investigated in rats the acute effects of paraquat exposure on renal hemodynamics, cardiac ATPases, and the redox balance of the kidney and heart. We also investigated whether the effects are blunted by treatment with the antioxidant tempol.</p> <p>Methods: The protocol described was approved by the ethics committee for animal experimentation (107/2023). Male Wistar rats (120 days; 300–350 g) were subjected to administration of PQT (20 mg/kg, ip; n=10) or 0.9% NaCl (Control group; n=5). Part of PQT-treated rats (n=5) received previous treatment with tempol (10 mg/kg in drinking water). After 24 hours, the animals were submitted for surgical procedures to evaluate renal hemodynamics, and, in the end, the kidney and left ventricle samples were collected. The differences between the group's means were assessed by one-way ANOVA followed by Tukey's test at $p < 0.05$.</p> <p>Results: PQT increased serum markers of renal and cardiac injury/function: urea (40%; $p < 0.01$); creatinine (28%, $p < 0.05$), total creatine kinase ($> 200\%$, $p < 0.01$) and creatine kinase MB isoform ($> 200\%$, $p < 0.01$). The PQT administration also led to reduction in renal blood flow (25%, $p < 0.05$), glomerular filtration rate (52%, $p < 0.001$), and filtration fraction (43%, $p < 0.05$), as well as promoted a decrease in mean arterial pressure (24%, $p < 0.001$) and an increase in heart rate (7%, $p < 0.05$), in comparison to Control rats. In the left ventricle, paraquat administration led to reduced ($\text{Na}^{++}\text{K}^{+}$) ATPase and Na^{+}-ATPase activity ($\sim 30\%$, $p < 0.05$), along with increased SERCA and PMCA activities ($\sim 50\%$, $p < 0.05$). In the kidney and left ventricle of the PQT group, it was observed higher lipid peroxidation (20-70%, $p < 0.05$), along with increased NADPH oxidase activity (70-100%, $p < 0.05$) and decreased catalase activity (50-80%, $p < 0.05$). Treatment with tempol prevented changes in serum markers of renal and cardiac injury/function and renal hemodynamic and left ventricular ATPase changes, alongside restoration of redox balance in both tissues.</p> <p>Conclusion: The results highlight that paraquat-induced oxidative stress promotes alterations in the intricate relationship between the kidneys and heart, underscoring the therapeutic potential of antioxidants in the prevention and treatment of this syndrome. Support: CAPES, CNPq Protocol: 107/2023</p>

Title	Maternal pre-conception acute kidney injury increases maternal and fetal oxidative stress during gestation in rats
Authors	LETICIA LEITE FERREIRA, JENNYFER MARTINS DE CARVALHO, VALÉRIA BIANCA DE SOUZA SANTOS, JÉSSICA SANTOS SCHIRATO ALBUQUERQUE, NATÁLIA TABOSA MACHADO CALZERRA, LEUCIO DUARTE VIEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, UFPE
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Previous episodes of maternal acute kidney injury (AKI) increase the risk of complications during pregnancy, which, in turn, can impair fetal development and increase the risk of chronic diseases in adulthood. It is known that the redox balance at the maternal-fetal interface is essential for normal intrauterine development and that AKI is correlated with elevated oxidative stress during the acute phase of the disease and after recovery. Objective: To evaluate, in rats, whether pre-conception AKI induces changes in the redox balance in the maternal-fetal environment. Methods: Wistar female rats (120 days; 200-250 g) were subjected to AKI induction by bilateral ischemia-reperfusion through clamping the renal arteries for 30 minutes (IR group, n=7). A group of females underwent sham surgery (Sham group, n=5). The AKI induction was confirmed by increased serum urea (420%, p<0.001) and creatinine (120%, p<0.01) levels in the IR group compared to the Sham group. After 30 days, recovery of renal function was confirmed by the absence of statistical differences in serum urea and creatinine values between the groups. Once renal function recovery was confirmed, the females were mated, and on the 20th day of gestation, they were euthanized for the collection of the liver and a pool of placentas and fetal livers of each mother. Tissue redox balance was investigated by evaluating lipid peroxidation, basal production of superoxide anions (Basal Superox), NADPH oxidase activity, superoxide dismutase (SOD) activity, and catalase activity. The Ethics Committee for Animal Experimentation of UFPE approved the project (No. 110/2023). Differences between groups were compared using the unpaired t-test and considered significant when p<0.05. Results: The IR group showed no significant difference in body mass gain during the gestation compared to Sham rats (116 vs. 106 g; p=0.59), nor was there a significant difference in the number of pups per litter (9.4 vs. 9.6; p=0.95) or fetal body mass (3.9 vs. 4.0 g, p<0.59). Serum urea and creatinine levels remained unchanged between the groups on the 20th day of gestation. Although no late impact of IR was observed on these parameters, the IR group showed higher lipid peroxidation in the maternal liver (108%, p<0.05) and fetal liver (24%, p<0.05) than the Sham group. In the IR mothers' livers, there was an increase (84%, p<0.05) in Basal Superox and a reduction (40%, p<0.01) in catalase activity compared to the Sham group, while in the fetuses' livers of the IR group, there was also an increase in NADPH oxidase activity (66%, p<0.01) in addition to an increase (80%, p<0.05) in Basal Superox and a decrease (55%, p<0.01) in catalase activity. No differences were observed in placental lipid peroxidation between the groups; however, the placentas of the IR group had higher Basal Superox (140%, p<0.01) and higher catalase activity (63%, p<0.05) than placentas of the Sham group. The tissue SOD activity was not significantly different between the groups. Conclusion: Although the mothers showed recovery of renal functional markers, alterations in maternal/fetal redox balance indicate that AKI increases the risk of late complications in intrauterine development, which may promote the emergence of diseases in the offspring's adulthood. Support: CAPES, CNPq Protocol: 110/2023</p>



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Title	Estudo da vulnerabilidade do rim remanescente em decorrência de nefrectomia unilateral, quando submetido à nefropatia cristalina
Authors	NEYDIANA BELIZE DE PINA LOPES, JULIANA MARTINS DA COSTA PESSOA, MARIA OLIVEIRA DE SOUZA
Affiliations	Fisiologia e Biofísica, Universidade de São Paulo
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A incidência de doença renal progressiva é um problema sério de saúde pública e o transplante renal é a melhor alternativa para pacientes em fase terminal. Entretanto, no doador, a nefrectomia unilateral (NU) pode resultar na sobrecarga do rim remanescente, podendo se tornar um fator relevante no desenvolvimento de injúria renal aguda (IRA) e aumentar a vulnerabilidade do rim remanescente à doença renal crônica (DRC). Objective: O presente estudo tem como objetivo investigar a função do rim remanescente após a nefrectomia unilateral, sua resposta à nefrolitíase e os possíveis fatores e mecanismos envolvidos no seu estado de vulnerabilidade. Methods: Camundongos C57BL/6J com oito semanas (n=23) foram divididos em quatro grupos: sham, submetidos a NU, oxalato de sódio (injeção intraperitoneal de 9 mg/100 g de NaOx para induzir nefrolitíase, 24 horas antes da eutanásia) e NU tratado com oxalato de sódio (NU/NaOx). Seis dias após a cirurgia sham ou NU e 24 horas antes da eutanásia, os camundongos foram tratados de acordo com o respectivo grupo e colocados em gaiolas metabólicas para o monitoramento de parâmetros metabólicos e da função renal. Ao final das vinte e quatro horas, os animais foram submetidos à anestesia com isoflurano (0,8 L/min/taxas de 5%), coleta de sangue e urina, remoção do rim esquerdo e eutanásia por exsanguinação, conforme protocolo aprovado pelo comitê de ética (CEUA-ICB/USP, nº 4550140422). Results: Uma semana após a cirurgia, os animais NU apresentaram um aumento significativo no fluxo urinário ($p<0,04$), na relação peso do rim/peso corporal ($p<0,003$) e na creatinina plasmática ($p<0,004$) quando comparados aos animais sham. Também apresentaram um aumento significativo na expressão de RNAm para Mki-67 ($p<0,02$), um biomarcador da regeneração tubular e reparo renal após a IRA. Ainda nesse grupo, observamos um aumento na expressão de RNAm para Col1A1 ($p<0,05$) e Col4A1 ($p<0,05$) e na expressão proteica de um marcador específico de macrófagos, F4/80 ($p<0,004$). Diante do insulto com NaOx, os animais NU/NaOx apresentaram hipertrofia renal mais pronunciada ($p<0,02$), maior acúmulo de creatinina no plasma ($p<0,003$) e maior expressão de RNAm para fatores de injúria tubular, como Havcr1 (Kim-1) ($p<0,006$) e LCN2 (NGAL) ($p<0,0006$) e expressão proteica de Kim-1 ($p<0,003$), quando comparados aos animais NaOx. Conclusion: Nossos achados indicam que o rim remanescente apresenta vulnerabilidade, o que afetou sua resposta ao insulto e pode potencialmente dificultar a melhora e contribuir para o desenvolvimento da DRC. Support: Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP) e Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Protocol: 4550140422</p>



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Title	Nephroprotective effects of cannabidiol on ischemia-reperfusion-induced renal injury occurs through modulation of redox balance in Wistar rats
Authors	ROSANA PEREIRA NOBRE DE LIMA, JENNYFER MARTINS DE CARVALHO, NATÁLIA TABOSA MACHADO CALZERRA, LEUCIO DUARTE VIEIRA FILHO
Affiliations	Fisiologia e Farmacologia, UFPE
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The endocannabinoid system has recently emerged as a key player in physiological homeostasis across various biological systems, playing diverse roles in hormonal, metabolic, and immune balance. Cannabidiol (CBD), a phytocannabinoid primarily derived from <i>Cannabis sativa</i>, may modulate oxidative stress resulting from tissue injuries. Therefore, CBD may be able to present nephroprotective effects; however, the protective mechanisms of CBD on kidney injury remain poorly understood. Objective: This study aimed to investigate the impact of CBD treatment on redox balance alterations associated with acute kidney injury (AKI) induced by ischemia-reperfusion (IR) in adult Wistar rats. Methods: Wistar male rats (120 days; 300-350 g) were submitted to AKI induction by renal IR bilateral (IR; n=10) or Sham surgery (Sham; n=10). The renal IR was performed by clamping the renal arteries for 30 minutes. Part of the groups were treated daily with CBD (10 mg/kg, i.p.; Sham+CBD, n=5; IR+CBD, n=5), starting one day before surgery. After three days, the rats were anesthetized (ketamine/xylazine; 80/10 mg/kg, i.p.) to collect the renal cortex and blood samples. The blood samples were used to evaluate serum levels of creatinine and urea. In the renal cortex, it was evaluated lipid peroxidation, reactive oxygen species (ROS), NADPH oxidase activity, superoxide dismutase (SOD) activity, and catalase activity. The Ethics Committee for Animal Experimentation of UFPE approved the project (No. 094/2022). Multiple comparisons between groups were performed by two-way ANOVA followed by Tukey's test and considered significant at $p < 0.05$. Results: After 24h, it was observed that serum creatinine (86%, $p < 0.001$) and urea (~600%, $p < 0.01$) were higher in the IR group than Sham group. The effects of IR increasing serum creatinine (~100%, $p < 0.01$) and urea (~400%, $p < 0.01$) were also observed after 72h of the surgery. The CBD treatment attenuated the renal IR-induced changes by decreasing serum creatinine (~50%, $p < 0.001$) and urea (~70%, $p < 0.001$). Regarding renal oxidative stress, the IR group presented higher lipid peroxidation (110%, $p < 0.001$) and ROS levels (53%, $p < 0.01$) than the Sham group, in parallel to an increment of NADPH oxidase activity (50%, $p < 0.01$) and a decrease of the activity of SOD (70%, $p < 0.01$) and catalase (63%, $p < 0.01$). The IR group treated with CBD presented lower (~50%, $p < 0.001$) renal lipid peroxidation and ROS production compared to the non-treated IR group. Moreover, it was also observed reduction of NADPH oxidase activity (27%, $p < 0.05$) and elevation of SOD (~500%, $p < 0.001$) and catalase (~250%, $p < 0.001$) activities in the kidney of the IR+CBD group in comparison to IR rats. The effects of CBD in Sham condition were characterized only by an elevation of SOD activity (77%, $p < 0.01$; Sham+CBD vs. Sham). Conclusion: CBD reduced oxidative stress and improved kidney function by preserving serum creatinine and urea levels. The results indicate that CBD may effectively prevent and treat IR-induced AKI, suggesting its role as an antioxidant protector of kidney function. Support: FACEPE, PIBIC, CNPq. Protocol: approval nº 0094/2022 CEUA-UFPE</p>



Title	Dapagliflozina e seu impacto na função renal de ratos wistar não diabéticos: um estudo experimental
Authors	ISABELA BORGES DA MOTA SILVEIRA, DÉBORA CONTE KIMURA LICHTENECKER, ROGÉRIO ARGERI, GUIOMAR NASCIMENTO GOMES
Affiliations	Medicina Translacional, UNIFESP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Os inibidores do cotransportador de sódio/glicose (SGLT2) incluindo a dapagliflozina, fazem parte de uma classe de fármacos usados no tratamento do diabetes mellitus; agem no túbulo proximal renal, levando à glicosúria e redução da hiperglicemia. Esses medicamentos também têm sido indicados pelos seus efeitos cardioprotetor e renoprotetor. No entanto, há poucos estudos experimentais em murinos induzidos ou não à doença, ressaltando a necessidade de mais estudos para o esclarecimento dos diversos efeitos deste fármaco. Objective: Avaliação dos efeitos do tratamento com dapagliflozina na morfologia e na função renal de ratos Wistar (machos) não diabéticos. Methods: Ratos Wistar com 3 meses foram divididos em dois grupos: Controle (C) e Dapagliflozina (D). O grupo D recebeu dapagliflozina por gavagem, na dose de 3mg/kg, durante 4 semanas. Os animais foram colocados em gaiolas metabólicas para coleta de urina de 24 horas seguida da coleta de sangue. Foram analisadas concentrações plasmáticas de sódio, potássio, ureia, ácido úrico e creatinina. E excreção urinária de glicose, proteínas, sódio, potássio, amônia e ácidos tituláveis. Foram avaliados 8 animais em cada grupo. Results: Com apenas 15 dias de tratamento observamos aumento significativo do fluxo urinário (C:0,026±0,002;D: 0,059±0,003 mL/min/kg), consumo hídrico (C: 27,12±2,42; D: 51,87±2,89 mL), e glicosúria (C:0,0007±0,0001;D:1,971±0,2629g/24h) confirmando a ação do medicamento. Os animais do grupo D apresentaram proteinúria (C:0,9830±0,1780;D:8,8670±0,4760mg/24h) entretanto não apresentaram alteração significativa no clearance de creatinina (C: 0,72± 0,05 ; D:0,61±0,05ml/min/g PR). Porém, houve aumento significativo na concentração plasmática de uréia (C: 36,50± 0,982; D: 52,25±2,389 mg/dL) e de ácido úrico (C:0,773±0,076; D:1,730±0,219mg/dL), e da excreção urinária de amônia (C:1,082±0,070;D:8,021±0,952uEq/mL) e ácidos tituláveis (C:0,503±0,238;D:2,072±0,835uEq/mL). Em relação a excreção urinária de eletrólitos observamos aumento da excreção de sódio (C:1,4270±0,0660;D:2,1170±0,2700mEq/24h) e de potássio (C:3699,0±226,0;D:5627,4±432,0mEq/24h) em comparação com os animais controle, certamente em consequência do efeito do medicamento. Conclusion: Os dados obtidos neste estudo confirmam os efeitos diuréticos, natriuréticos e glicosuricos do medicamento. Porém a proteinúria e a elevação da concentração plasmática de uréia sugerem certo grau de disfunção renal. As alterações significativas da excreção renal de ácidos podem ser decorrentes de efeitos metabólicos. Estas alterações devem ser melhor investigadas visto que em longo prazo podem repercutir de forma acentuada na função renal. Support: Capes Protocol: CEUA-UNIFESP 5985180423</p>

Title	Tamm-Horsfall protein mediates renoprotective effects in crystalline nephropathy
Authors	LARISSA DE ARAÚJO, MARIA OLIVEIRA DE SOUZA
Affiliations	Fisiologia e Biofísica, USP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Tamm Horsfall protein (THP) is the most common mucoprotein excreted in urine. It is produced especially in the kidney by renal tubular cells in the thick ascending limb of the loop of Henle (TAL). THP has an important immunomodulatory role and its biosynthesis seems to be dynamic and undergoes variations in pathological conditions, including crystalline nephropathy. Crystalline nephropathy (formation of crystals in the kidney) is related to acute kidney injury (AKI) affecting 5 to 10% of the world's population, and its prevalence has increased in recent years. We hypothesize that the immunomodulatory function of THP is impaired in acute kidney injury induced by crystalline nephropathy, and the exogenous administration of THP can play a renoprotective role in the disease. Objective: The current study aims to understand the role of exogenous THP administration in an experimental model of crystalline-induced AKI. Methods: Eight-week-old C57BL/6J mice were randomly allocated into four groups: 1. Control (saline 0.9%, i.p); 2. THP (exogenous THP–5µg/animal, single injection i.p); 3. NaOx (sodium oxalate–9mg/100g of body weight, single injection i.p); 4. NaOx administration and THP treatment. The animals were placed in metabolic cages for 24 hours before euthanasia and organ harvest. The results presented as mean ± S.D. were analyzed by two-way ANOVA and a Bonferroni post hoc test using GraphPad Prism software. p<0.05 was considered statistically significant. Results: Treatment with exogenous THP alone did not change any parameter analyzed. Urinary THP excretion was decreased in the NaOx group [(arbitrary units) NaOx:100.1±20.2 vs. Control:195.2±7.9, p=<0.0001] and the co-treatment with exogenous THP prevented that change [(arbitrary units) NaOx+THP:169.3±31.8 vs. NaOx:100.1±20.2, p=0.0002. Interaction: p=0.0012]. Using immunofluorescence imaging, we observed that the treatment with NaOx induced THP cluster formation in the tubular lumen, which was prevented by concomitant with exogenous THP. Treatment with NaOx significantly increased mRNA expression for KIM-1, Ki67, MCP-1, TNFα, IL-1β, and IL-6, consistent with kidney injury. Co-treatment with exogenous THP prevented these changes (Fold change from control for NaOx+THP vs. NaOX, respectively): KIM-1 [95.2±121.7 vs. 730.0±182.5, p=<0.0001. Interaction p=0.0001], Ki67 [2.0±1.0 vs. 5.7±1.7, p=0.0001. Interaction p=0.0006], MCP-1 [1.9±1.8 vs. 8.2±3.8, p=0.0008. Interaction p=0.0030], TNFα [1.3±0.7 vs. 4.0±2.2, p=0.0087. Interaction p=0.0216], and IL-6 [5.4±7.5 vs. 84.4±46.2, p=0.0002. Interaction p=0.0010]. Conclusion: Our results indicate that exogenous THP may have a renoprotective effect in nephropathy crystalline-induced AKI. Support: FAPESP Protocol: 3894050221</p>

Title	Contribution of the p38MAPK signaling pathway and the Egr-1 transcription factor in glomerulosclerosis.
Authors	HEITOR MACEDO BRAZ, MARIA OLIVEIRA DE SOUZA
Affiliations	Departamento de Fisiologia e Biofísica, USP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chronic kidney disease (CKD), characterized by the progressive loss of kidney function, is one of the most serious public health problems. Its progression is followed by focal and segmental glomerulosclerosis (FSGS) Objective: This study aims to look at how ERK/p38MAPK and Egr-1 pathways interact in the signaling of Adriamycin (ADR)-induced FSGS. Methods: 8-week-old BALB/c mice received a single dose of ADR via the tail vein (10 mg/kg) and the control (CTL) group received 0.9% NaCl solution. Both groups were monitored for 28 days and then euthanized. Kidney function, morphology and protein expression were evaluated. Immortalized mouse podocytes were treated by ADR [10⁻⁶ M] for 15 min, 30min, 1h, 6h and 24 h followed by protein expression. Statistical analyses were done using t test with Welch correction. Results: The ADR treatment did not change the creatinine and urea plasmatic levels when compared with the CTL group. [Creatinine, mg/dL: (CTL: 0.23±0.05 vs. ADR:0.25±0.12, p= 0.7427), Urea, mg/dL: (CTL: 59.60±4.97 vs. ADR: 70.76±60.39, p=0.6181). ADR showed a higher urinary flow rate than the CTL animals [μL/min (CTL: 0.11±0.06 vs. ADR: 0.91±0.38, p=0.0005). The ADR treatment induced a body weight loss when compared to the CTL group. [g (CTL: 2.00±1.05 vs.-2.75±2.71, p=0.0013). Food and water intake were not different between the groups. [Food intake, g/24h (CTL: 5.60±1.50 vs. ADR: 6.25±1.66, p=0.4054), (Water intake, ml/24h (CTL: 2.40±0.84 vs. ADR: 3.62±1.50, p=0.0655). About podocyte protein expression, the p38MAPK was increased after ADR treatment for 15 min, 6h and 24h [arbitrary units, 15 min: (CTL: 0.57±0.15 vs. ADR: 2,52±1,43, p= 0.0206, n=6), (arbitrary units, 6h: (CTL: 0.43±0.20 vs. ADR: 0.85±0.18, p=0.0040, n=6), (arbitrary units, 24h: (CTL: 0.45±0.35 vs. ADR: 1.46±0.57, p=0.0142). In addition, the Egr-1 was significantly increased after 24h, 6h and 1h of treatment with ADR [10⁻⁶M] [AU, 24h: (CTL: 0.13±0.06 vs. ADR: 0.93±0.16, p= 0,0009, n=6), AU, 6h: (CTL: 0.26±0.15 vs. ADR: 0.99±0.19, p=0.0002, n=6), AU, 1h: (CTL: 0.14±0.07 vs. ADR: 1.01±0.15, p=<0,0001, n=6) . About the glomerulosclerosis index (GSI), there were significant differences between the groups. (GSI: (CTL: 0,04+-0,05 vs. 2,39+-0,81, p=0,0101). Conclusion: Our results indicate that the activation of p38MAPK by an insult corroborates the activation of the nuclear transcription factor Egr-1 and thus the development of FSGS as shown in the treated animals with ADR. Support: Government support – non-US Protocol: 9397130723</p>

Title	EFEITOS DA TERAPIA HORMONAL CRUZADA E DO EXERCÍCIO FÍSICO DE RESISTÊNCIA SOBRE A FUNÇÃO RENAL DE RATAS WISTAR
Authors	ISADORA GONÇALVES ALMEIDA, EMILY ROCHA CORDEIRO, NATHÁLIA BESERRA DA SILVA, ISABELA BORGES DA MOTA SILVEIRA, LETICIA MARIA MONTEIRO, ROGERIO ARGERI, DÉBORA CONTE KIMURA LICHTENECKER, GUIOMAR NASCIMENTO GOMES
Affiliations	Departamento de Fisiologia, UNIFESP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A terapia hormonal cruzada (THC) consiste no uso de hormônios esteroides para modificações de características sexuais secundárias. Estudos experimentais em modelos de THC sugerem a ocorrência de alterações no sistema renal com esse procedimento; por outro lado, a atividade física tem sido considerada benéfica para o sistema renal. Assim, avaliamos a influência do exercício físico associado à THC sobre a função renal. Objective: Avaliar a pressão arterial e alterações morfológicas e funcionais dos rins de ratas submetidas à THC, submetidas ou não a um programa de exercício de resistência. Methods: Ratas Wistar com dois meses de idade foram distribuídas em quatro grupos experimentais: SV, sedentárias tratadas com veículo (óleo vegetal); SH, sedentárias tratadas com hormônio; EV, exercício tratadas com veículo; EH, exercício tratadas com hormônio. Para a THC, administramos cipionato de testosterona 3mg/kg (i.m) a cada 10 dias por 8 semanas. O treinamento resistido progressivo foi feito em escada de escalada vertical, 5 x por semana em dias consecutivos com dois dias de descanso, durante as últimas 6 semanas do protocolo experimental. Após este período, foram feitas coletas de amostras de urina em gaiolas metabólicas e de sangue por punção da artéria caudal. Avaliamos: Carga máxima (CM), pressão arterial (PA), peso corporal (PC), gonadal (PG) e valores sanguíneos de pH, pCO₂, HCO₃, fluxo urinário (V), concentração plasmática de ureia (Ur-pl) e creatinina (Cr-pl), clearance de creatinina (CLcr). CEUA/UNIFESP: 9009241022. Resultados apresentados como média±desvio-padrão; ANOVA e Teste T, p>0,05. Results: A THC resultou em aumento do PC sem, no entanto, alterar os valores de PA, [PC(g): SV: 244,7±18,6; SH 281,2±28,7; EV: 251,4±24,7; EH: 273,5±14,0; P=0,002]; [PA(mmHg): SV: 119,1±4; SH: 117,0±12; EV: 119,5±10; EH: 128,2±10; P = 0,1781]]. Houve diminuição do PG nos grupos SH e EH [PG (g): SV: 1,11±0,2; SH: 0,67±0,3; EV: 0,96±0,2; EH: 0,86±0,1; P=0,0007]]. A Cr-pl foi modulada tanto pela THC como pelo exercício [Cr-pl (mg/dL): SV: 0,34±0,03; SH: 0,29±0,03; EV: 0,47±0,07; EH: 0,38±0,03; P<0,0001]]. O mesmo ocorreu com o CLcr [CLcr (mL/min/kg): SV: 5,9±0,7; SH: 7,3±1,2; EV: 5,6±0,9; EH: 6,2±0,5; P=0,0064]]. Não houve diferenças entre os grupos em V e Ur-pl. O pH apresentou-se mais baixo apenas no grupo EV [pH: (SV: 7,36±0,04; SH: 7,38±0,04; EV: 7,09±0,15; EH: 7,35±0,04; P<0,0001)]. Não foram observadas alterações significativas nos valores sanguíneos de pCO₂ e HCO₃. Não houve diferenças significativas de CM [CM (g): EV: 661,0±52; EH: 689,7±63; P = 0,3722]]. Conclusion: As alterações corporais resultantes da THC não foram modificadas pelo exercício resistido. O exercício físico exerceu efeito significativo sobre a concentração plasmática de creatinina. A THC não resultou em maior força (aumento da carga máxima) na situação de exercício. Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) e Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) Protocol: CEUA/UNIFESP: 9009241022</p>

Title	The <i>Syagrus coronata</i> seed oil prevents renal injury induced by ischemia-reperfusion in rats by antioxidant mechanism
Authors	FERNANDO SILVEIRA ROCHA, VALÉRIA BIANCA SOUZA SANTOS, JENNYFER MARTINS CARVALHO, LETICIA LEITE FERREIRA, NATÁLIA TABOSA MACHADO, MARCIA VANUSA SILVA, MARIA TEREZA SANTOS CORREIA, LEUCIO DUARTE VIEIRA
Affiliations	Departamento de Fisiologia e Farmacologia, UFPE, Departamento de Bioquímica, UFPE
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Acute kidney injury (AKI) is a common clinical condition associated with significant morbidity and mortality, and oxidative stress plays a crucial role in its pathophysiology. Traditional therapies are limited in efficacy and associated with various side effects, highlighting the need for novel therapeutic strategies. The <i>Syagrus coronata</i>, commonly known as licuri palm, is native to Brazil, and the fixed oil extracted from the seeds contains bioactive compounds with potential antioxidant and anti-inflammatory properties.</p> <p>Objective: To investigate the nephroprotective capacity of the fixed oil from <i>S. coronata</i> seeds (Scor-Oil) in rats submitted to AKI by renal ischemia-reperfusion (IR), investigating whether it is effective in modulating renal oxidative stress and redox balance. Methods: Adult male rats (300-350g, 90–120 days) were subjected to renal injury by ischemia-reperfusion (IR, n=16) through clamping of the renal artery for 30 minutes or underwent Sham surgery (SHAM, n=4). Part of the IR rats was treated daily with Scor-Oil (75, 150, 300 mg/kg, ip; n=4 per dose) or vehicle (100 µL/kg, ip) starting 24 hours before IR surgery. After three days, the rats were anesthetized (ketamine/xylazine; 80/10 mg/kg, i.p.) to collect the renal cortex, blood, and urine samples. The blood samples were used to evaluate serum levels of creatinine and urea. In urine, protein excretion was estimated through the protein-to-creatinine (Ptn-Creat) ratio. In the renal cortex, lipid peroxidation, reduced/oxidized glutathione (GSH) content, basal superoxide production, and NADPH oxidase activity were evaluated. The Ethics Committee for Animal Experimentation of UFPE approved the project (No. 109/2023). Multiple group comparisons were performed by one-way ANOVA followed by Tukey's test and considered significant at $p < 0.05$. Results: After 24 hours of renal IR, increased serum levels of creatinine (330%, $p < 0.001$) and urea (186%, $p < 0.001$) were observed compared to the Sham group. Serum levels of creatinine (360%, $p < 0.001$) and urea (94%, $p < 0.01$) remained elevated in the IR group compared to the Sham group in blood samples collected after 72 hours. The IR group also presented a higher (220%, $p < 0.05$) Ptn-Creat ratio than the Sham group. The IR groups treated with Scor-Oil at doses of 75 or 150 mg/kg did not present different serum levels of urea, creatinine, or Ptn-Creat ratio compared to the untreated IR group. On the other hand, the IR group treated with the highest dose of Scor-Oil (300 mg/kg) presented lower serum levels of urea (36%, $p < 0.05$) and creatinine (80%, $p < 0.01$) than the untreated IR group, as well as lower Ptn/Cr (67%, $p < 0.05$). The IR group presented alterations in the redox balance of the renal cortex, characterized by: i) increased lipid peroxidation (134%, $p < 0.05$); ii) decreased GSH content (39%, $p < 0.05$); iii) increased basal superoxide production (290%, $p < 0.001$); and iv) increased NADPH oxidase activity (35%, $p < 0.05$). The IR group treated with Scor-Oil (300 mg/kg) presented decreased lipid peroxidation (52%, $p < 0.05$) and basal superoxide production (70%, $p < 0.001$) and elevated GSH levels (180%, $p < 0.05$) in comparison to non-treated; however, the NADPH oxidase activity was not different between groups. Conclusion: These preliminary results suggest that the fixed oil from <i>S. coronata</i> seeds attenuates renal injury induced by ischemia-reperfusion through the modulation of superoxide anion production independent of NADPH oxidase. Support: CAPES and CNPq Protocol: 109/23</p>



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Title	Alterações renais e metabólicas no modelo de sobrenutrição perinatal e o efeito do óleo de peixe
Authors	SOFÍA TOMASELLI ARIONI, DENNIS LEGIZAMAN, GABRIEL PEREIRA, RICARDO FERNANDEZ
Affiliations	FISIOLOGIA, UNIVERSIDADE FEDERAL DO PARANÁ, UFPR
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A obesidade é uma pandemia que já afeta cerca de 2 bilhões de pessoas. A obesidade infantil persiste na vida adulta junto com as comorbidades a ela relacionadas, incluindo alterações na função renal. Ratos provenientes de ninhadas reduzidas sofrem alterações metabólicas tornando-se indivíduos adultos obesos. O óleo de peixe, rico em ácidos graxos n-3, é considerado um modulador do sistema imune, do metabolismo lipídico e energético. Objective: O objetivo do presente trabalho foi avaliar longitudinalmente a função renal num modelo animal de obesidade por sobrenutrição perinatal e observar o efeito do óleo de peixe sobre as funções renal e metabólica. Methods: Neonatos de ratos da linhagem Wistar machos foram randomizadas em ninhadas de 10 animais, formando o grupo controle (CTL) e ninhadas reduzidas para 3 animais ao terceiro dia pós-natal, formando o grupo obeso (OBS). Dos 60 aos 150 dias foi realizado o experimentos longitudinal. Dos 150 aos 180 dias os animais foram separados em grupo controle (CTL), grupo obeso (OBS), grupo controle suplementado (CTL-S) e grupo obeso suplementado (OBS-S), tendo estes dois últimos recebido óleo de peixe via oral a uma dose de 1g/kg por 30 dias. Results: Ao longo do experimento longitudinal, o grupo OBS teve maior ganho de peso bruto que o grupo CTL. Apesar disso, a ingestão de comida não foi diferente entre os grupos, mas a ingestão de água e a diurese foram reduzidas no grupo OBS. O clearance de creatinina caiu significativamente no grupo OBS aos 150 dias, demarcando o início das alterações renais causadas pelo modelo de obesidade. Além disso, uma maior excreção de albumina na urina ocorreu aos 90 e 120 dias no grupo OBS. Aos 180 dias, o grupo OBS teve maior peso que o grupo CTL, a ingestão de comida permaneceu igual entre os grupos, mas a ingestão de água e a diurese foram reduzidas nos grupos OBS e OBS-S. O grupo OBS teve maior peso da gordura mesentérica em relação ao grupo CTL e o grupo OBS-S teve redução neste parâmetro em relação ao grupo OBS. Os animais do grupo OBS e CTL não apresentaram diferenças na glicemia basal, na tolerância a glucose e ou perfil lipídico. No entanto, a suplementação reduziu o colesterol total nos grupos CTL-S e OBS-S. O LDL foi reduzido no grupo CTL-S e o HDL foi reduzido no grupo OBS-S. O clearance de creatinina foi reduzido nos grupos OBS e OBS-S e estes grupos tiveram maior albuminúria. O manejo de Na⁺ não foi modulado pela obesidade, mas foi aumentado no grupo CTL-S. Apesar disso, os grupos OBS e OBS-S tiveram maior excreção bruta de Na⁺. O clearance osmolar também não diferiu entre os grupos, mas os grupos obesos tiveram maior osmolaridade urinária e menor clearance de água livre. A concentração de adiponectina plasmática não diferiu entre os grupos, mas a suplementação tendeu a aumentar este parâmetro no grupo CTL-S. A concentração de TNFα no tecido renal foi aumentada nos grupo obesos. A concentração urinária de TXB2 foi reduzida nos grupos obesos, e a suplementação reduziu a concentração urinária de metabólitos da PGE2 na urina. Conclusion: Portanto, o modelo gerou obesidade e provocou inflamação e redução da função renal. O óleo de peixe melhorou parâmetros metabólicos e modulou a PGE2 renal mas não levou a uma melhora significativa na função renal dos animais obesos. Support: CNPq Protocol: CEUA/BIO – UFPR, no. 1438</p>



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Title	INGESTION OF EUPHORBIA TIRUCALLI (AVELOZ) LATEX INCREASES OXIDATIVE STRESS AND RENAL VASCULAR RESISTANCE IN RATS
Authors	LETICIA VERONÉS MARSAGLIA, EDGAR HELL KAMPKE, HELLEN SILER VASCONCELLOS, LEONARDO DA SILVA ESCOUTO, LUCIANA POLACO COVRE, AGATA LAGES GAVA, ELISARDO CORRAL VASQUEZ, RICARDO MACHADO KUSTER, MARIA EDUARDA DE SOUSA BARROSO, SILVANA DOS SANTOS MEYRELLES-
Affiliations	Integrative Physiology Laboratory, UFES, Experimental Hypertension Laboratory, UFES, Infectious Diseases Unit of UFES, UFES, Translational Physiology and Pharmacology Laboratory, UVV, Department of Chemistry, UFES
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Euphorbia tirucalli (Aveloz) is a plant commonly used by the population for cancer treatment; however, studies on the actions of this plant have been predominantly conducted in vitro. Objective: To characterize the effects of Aveloz ingestion on renal function and oxidative stress production in healthy animals. Methods: Wistar rats were divided into: Control (CT, n=5-8) treated with water (1 mL) and Aveloz (AV, n=5-8) treated with Euphorbia tirucalli latex (13.47 mg/kg/1mLH₂O) administered by gavage for 15 days. Renal function was evaluated through glomerular filtration rate (GFR), renal plasma flow (RPF), renal blood flow (RBF), and renal vascular resistance (RVR). Renal tissues were analyzed for levels of advanced oxidative protein products (AOPP), myeloperoxidase (MPO) enzyme activity, levels of reactive oxygen species (ROS) using the fluorescent marker hydroxyphenyl fluorescein (HPF) for peroxynitrite quantification, and nitric oxide levels using 4,5-diaminofluorescein (DAF). Results: Ingestion of Aveloz for 15 days significantly decreased (p<0.05) GFR (CT: 8.42±1.36 vs. AV: 3.91±1.08 mL/min/Kg), RPF (CT: 23.84±2.2 vs. AV: 17.5±2.2 a.u.), and RBF (CT: 39.1±3.2 vs. AV: 27.7±3.6 a.u.) and significantly increased (p<0.05) RVR (CT: 4.17±0.36 vs. AV: 6.35±0.59 a.u.). Aveloz also significantly increased (p<0.05) renal levels of HPF (CT: 1176±90.4 vs. AV: 1442±74.7 a.u.) and DAF (CT: 2020±174 vs. AV: 2737±249 a.u.) and plasma levels of AOPP (CT: 1785±366.3 vs. AV: 2774±231.2 µMol/L) and MPO (CT: 0.002±0.0002 a.u. vs. AV: 0.0029±0.0002 a.u.). Conclusion: Our results demonstrated that ingestion of Aveloz for 15 days significantly alters kidney function, increases ROS production, and elevates oxidative stress, and inflammatory levels in the kidneys. These findings emphasize the importance of conducting further studies to assess the physiological effects of chronic Aveloz ingestion on the renal function. Support: Nacional Council for Scientific and Technological Development (CNPq), Coordination for the Improvement of Higher Education Personnel (CAPES) and Espírito Santo Research Support Foundation (FAPES). Protocol: CEUA-UFES nº 01/2022.</p>

Title	Determinants of estimated Glomerular Filtration Rate in Young Medicine students/Luanda-Angola
Authors	LUÍSA ESPERANÇA SOARES NSILOULOU DA SILVA, NATÁLIA D DOS SANTOS FERNANDES, ISABEL MUÍNGA, DANIEL PIRES CAPINGANA, ISAURA CONCEIÇÃO ALMEIDA LOPES, PEDRO MAGALHÃES, AMÍLCAR BERNARDO TOMÉ DA SILVA
Affiliations	Departamento Fisiologia e Farmacologia, UAN, Universidade Agostinho Neto
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chronic kidney disease (CKD) in the early stages does not present clinical manifestations and, therefore, people only seek health facilities when they present symptoms and signs, which coincides with the terminal phase of the disease. The use of serum creatinine has been encouraged as a form of screening for CKD and has been shown to increase the number of suspected cases. Currently, it is not uncommon to record changes in kidney function in young people. Objective: identify the factors associated with the estimated glomerular filtration rate (eGFR) in a young population. Methods: Cross-sectional, observational study with a convenience sample of 135 (female 54%) young medical students at the Agostinho Neto University in Luanda/Angola. Carried out in the functional testing laboratory of the Department of Physiology and Pharmacology. Participants were instructed to fast for 10-14 hours, a blood sample was taken by venipuncture to perform biochemical tests with measurement of creatinine, urea, uric acid, lipid profile on the Spectrophotometer, model BTS 350, BioSystems SA and electrolytes in the Medica® brand device, model EasyLyte Na/K/Cl/Li. Participants were instructed to collect urine for 24 hours. Anthropometric and hemodynamic measurements were performed. The project was approved by the Independent Ethics Committee of the Faculty of Medicine of the Agostinho Neto University and the significance level for all tests was set at $\alpha < 5\%$. Results: Of the total number of participants, 73 (54%) were female, the average age of the sample was 23.4 ± 5.5 years, with an eGFR of 128.2 ± 20.2 ml/min/1.73m², with 60% of participants having a value above 125 ml/min/1.73m². High blood pressure was recorded in 7.4%, with SBP of 114.8 ± 12.4 mmHg; DBP 68.7 ± 8.3 mmHg, while 15.6% were overweight/obese with a mean BMI 22.4 ± 4.5 kg/m²; WC 73.6 ± 11.5 cm; WHR 0.80 ± 0.12 and Uric acid 4.89 ± 1.2 mg/dL. Significant association of eGFR with WC: $\beta = -0.681$ $p < 0.0001$; PP: $\beta = 0.411$ $p < 0.0001$; WHR: $\beta = 0.313$ $p < 0.0001$; Uric acid: $\beta = 0.119$ $p < 0.0001$; BMI: $\beta = 0.242$ $p < 0.0001$; Multivariate linear regression analysis (Stepwise-forward) identified WC as the main determinant of eGFR in the first model, PP in the second model, while WHR, \acute{A}c. Uric and BMI appeared in the third, fourth and fifth model respectively. Conclusion: We can conclude that anthropometric (WC, WHR and BMI), hemodynamic (PP) and biochemical (uric acid) parameters were identified as the main determinants of eGFR in young people. Support: FUNDO PETRÓLEO E DIRECÇÃO DA FACULDADE DE MEDICINA Protocol: COMITÉ DE ÉTICA INDEPENDENTE D</p>

Title	Terapia hormonal cruzada em ratos de ambos os sexos: repercussões renais
Authors	ISADORA GONÇALVES ALMEIDA, NATHALIA BESERRA DA SILVA, DEBORA CONTE KIMURA LICHTENECKER, ROGÉRIO ARGERI, LETÍCIA MARIA MONTEIRO, EMILY ROCHA CORDEIRO, GUIOMAR NASCIMENTO GOMES
Affiliations	Fisiologia Renal, UNIFESP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Existem diferenças fisiológicas entre homens e mulheres que podem influenciar na evolução das doenças. Complicações renais tendem a ser mais frequentes em homens e são relacionadas à testosterona, por outro lado o estradiol nas mulheres em idade fértil está associado a efeitos renoprotetores. A utilização de hormônios esteroides para modificações dos caracteres sexuais secundários vem aumentando, mas ainda existem poucas informações sobre sua influência sobre a função renal, assim, a utilização de modelo experimental mimetizando seu uso como terapia hormonal cruzada contribui para aprofundar o conhecimento neste assunto. Objective: Investigar os efeitos renais da terapia hormonal cruzada (THC) em ratos de ambos os sexos. Methods: Ratos Wistar de ambos os sexos foram distribuídos aleatoriamente em quatro grupos experimentais: FC (fêmeas controle), MC (machos controle), FH (fêmeas hormonizadas), MH (machos hormonizados). Os animais controle receberam injeção intramuscular de veículo (óleo de gergelim), as fêmeas hormonizadas receberam cipionato de testosterona, e os machos hormonizados receberam algestona acetofina + enantato de estradiol, durante 8 semanas. Foram avaliadas: medidas corporais, pressão arterial caudal, parâmetros bioquímicos sanguíneos e urinários, clearance de Inulina e PAH. Estudo aprovado pelo CEUA/UNIFESP, nº 9009241022. Dados apresentados como média \pm erro padrão, teste estatístico utilizado: teste T de student, $p \leq 0,05$. Results: Observamos que a THC alterou o peso corporal tanto nos machos como nas fêmeas (FC: 241.2\pm4.3; FH: 272.6\pm7.5; MC: 396.4\pm12.2; MH: 288.2\pm8.5g). Os valores de pressão arterial obtidos nos grupos FC e FH foram semelhantes (FC: 119.1\pm1.3; FH: 121.0\pm5.0mmHg). Nos machos a hormonização resultou em redução significativa da PA em comparação com o MC (MC: 134.8\pm3.1; MH: 123.2\pm1.7mmHg). A análise da excreção urinária de proteínas apresentou valores semelhantes nos grupos FC e FH (FC: 0.26\pm0.02; FH: 0.30\pm0.03mg/24h). Nos machos com hormonização resultou em redução significativa da proteinúria em comparação com o MC (MC: 0.47\pm0.05; MH: 0.29\pm0.03mg/24h). Também no clearance de inulina não foram observadas alterações causadas pela hormonização nas fêmeas (FC: 7.16\pm0.42; FH: 7.79\pm1.01 mL/min/Kg), entretanto, observamos redução significativa deste parâmetro nos machos hormonizados (MC: 7.34\pm0.41; MH: 4.41\pm1.08 mL/min/Kg). Não foram observadas alterações no clearance de PAH. Em relação à excreção de ácidos, novamente foram observadas alterações apenas nos machos que receberam a terapia de hormonização cruzada (MC: 5.90 \pm 0.63; MH: 3.09 \pm 0.39 μEq/min.kg). Não houve diferenças significativas nos grupos de fêmeas. Quanto à fração de excreção de sódio, observou-se uma redução nos animais FH (FC: 0.46\pm0.03; FH: 0.26\pm0.03 %) e aumento nos animais MH em comparação aos seus respectivos grupos controle; (MC: 0.27 \pm 0.01; MH: 0.38\pm0.03 %). Conclusion: Os resultados obtidos sugerem que a terapia hormonal cruzada em ratos foi capaz de fazer modificações corporais alterando também a função renal principalmente no grupo MH, possivelmente em função da redução da produção de testosterona endógena. No entanto, são necessárias novas investigações e análises para melhor compreender as consequências e os mecanismos subjacentes deste procedimento. Support: FAPESP; CAPES Protocol: 9009241022</p>

Title	Paricalcitol prevents renal fibrosis induced by unilateral ureteral obstruction by inhibition of TGF-β1/MMP-2 signaling pathway: role of redox balance
Authors	MARRY ANEYTS SANTANA CIRILO, NATALIA KRYZIA SANTOS LIMA, FERNANDA PRISCILA BARBOSA RIBEIRO, JENNYFER MARTINS CARVALHO, JEADĂ KAROLLYNE SILVA, GUILHERME CAVALCANTE FREITAS, LEUCIO DUARTE VIEIRA
Affiliations	DEPARTAMENTO DE FISIOLOGIA E FARMACOLOGIA, UFPE
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Paricalcitol (PCT), a synthetic analog of calcitriol, could be a valuable approach to decrease renal fibrosis; however, the protective mechanisms associated with vitamin D receptor activation need further clarification. Objective: This study evaluated whether PCT protective effects on renal fibrosis involve modulating renal redox balance and the activity of matrix metalloproteinases 2 and 9 (MMP-2 and 9) in rats subjected to renal injury by unilateral ureteral obstruction (UUO). Methods: Adult male rats (120 days, 300-350g), (N=32), were divided into four groups: i) Sham (n=8), which rats were submitted to sham surgery (i.e., with no ureteral obstruction) and treated with the vehicle of PCT (propylene glycol; 100 μL/kg, i.p.); ii) Sham+PCT (n=8), which rats were submitted to a sham surgery and treated with PCT (0.8 μg/kg of body weight, i.p.); iii) UUO (n=8), which rats were subjected to UUO and vehicle administration; and, iv) UUO+PCT (n=8), which rats were submitted to UUO and received PCT treatment. The treatment with PCT/vehicle occurred in 4 doses (the first one administered 24 hours after surgery and following on alternate days). After seven days of surgery, the animals were allocated in metabolic cages for 24 h and then anesthetized with thiopental (80 mg/kg, i.p.) to the collection of the obstructed kidney to collagen deposition, redox balance, MMP-2 and MMP-9 activities and TGF-β1 content. The Ethics Committee for Animal Experimentation of UFPE approved the project (No. 074/2019). Multiple comparisons between groups were performed using the two-way ANOVA followed by Tukey's test and considered significant at $p < 0.05$. Results: The UUO group presented higher serum levels of creatinine (44%, $p < 0.05$) and urea (57%, $p < 0.001$), lower creatinine clearance (60%, $p < 0.05$) and higher proteinuria (35%, $p < 0.05$) than Sham group. These changes were blunted by PCT treatment, i.e., there was no difference between UUO+PCT and Sham rats. The UUO increased the collagen deposition in the glomerulus (53%, $p < 0.001$) and cortical tubulointerstitial area (150%, $p < 0.001$) in the obstructed kidney in comparison to the Sham group. The UUO rats also presented higher (35%, $p < 0.01$) TGF-β1 content, higher MMP-2 activity (~300%, $p < 0.001$), and lower MMP-9 activity (35%, $p < 0.001$) in the renal cortex in comparison to Sham rats. On the other way, PCT treatment decreased the collagen deposition in both the glomerulus and cortical tubulointerstitial area (~25%, $p < 0.001$; UUO+PCT vs. UUO), in parallel to a reduction of TGF-β1 content and MMP-2 activity (~45%, $p < 0.01$). Furthermore, in the obstructed kidney of UUO group in comparison with the Sham group, it was observed higher lipid peroxidation (43%, $p < 0.01$), together with increase in the NADPH oxidase activity (49%, $p < 0.05$) and decrease of the activity of SOD (27%, $p < 0.01$) and catalase (55%, $p < 0.001$), while UUO+PCT group presented lower renal lipid peroxidation (31%, $p < 0.01$), lower NADPH oxidase activity (31%, $p < 0.01$) and higher SOD (31%, $p < 0.01$) and catalase (52%, $p < 0.05$) activities in comparison to UUO group. Conclusion: PCT attenuated UUO-induced renal fibrosis by inhibiting the signaling pathway involving reactive oxygen species \rightarrow TGF-β1 \rightarrow MMP-2. Therefore, PCT may be a useful adjuvant drug to mitigate the progression of renal failure. Support: CAPES and CNPq Protocol: 74/2019</p>

Title	Dapagliflozin improves tubule-interstitial injury in subclinical acute kidney injury by modulating O-linked Glc-NAcylation
Authors	RODRIGO ALVES DA SILVA PERES, ANA CAROLINA FIGUEIREDO PINTO, DOUGLAS ESTEVES TEIXEIRA, RODRIGO PACHECO SILVA AGUIAR, CARLOS PEREZ GOMES, WAGNER BARBOSA DIAS, ANA ACACIA SÁ PINHEIRO, CELSO CARUSO NEVES
Affiliations	Clementino Fraga Filho University Hospital, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, UFRJ, Carlos Chagas Filho Institute of Biophysics, Federal University of Rio de Janeiro, Rio de Janeiro, Brazil, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Subclinical acute kidney injury (subAKI) is characterized by markers of tubular injury without changes in glomerular function. SubAKI is a risk factor for AKI and chronic kidney disease (CKD) development. Currently, the treatment of subAKI is still limited. Recently, the use of SGLT2 inhibitors has shown improved kidney function parameters in different models of kidney diseases. However, the effects of dapagliflozin, a SGLT2 inhibitor, on the development of subAKI and its associated mechanisms are under investigation.</p> <p>Objective: The present work aimed to investigate the effects of dapagliflozin on parameters of renal function and tubule-interstitial injury in a mouse model of subAKI and its associated mechanisms. Methods: The subAKI model was induced in male BALB/c mice (n=10), 6-8 weeks old (CEUA-UFRJ 083/23). Four experimental groups were generated: 1) control (CTL), mice received vehicle; 2) subAKI, mice received BSA (10 g/kg/day i.p.) for 7 days; 3) subAKI+DAPA, mice received BSA (10 g/kg/day i.p.) and dapagliflozin (1 mg/kg/day by oral gavage) for 7 days; 4) DAPA, mice received dapagliflozin (1 mg/kg/day by oral gavage) for 7 days. Forty-eight hours prior to the end of treatment, all mice were kept in metabolic cages for urine collection. Then, all mice were euthanized for blood and kidney collection. Blood and urine were used for renal function analysis. The results are expressed as mean \pm SD. Results: Glomerular function parameters, including plasma creatinine, creatinine clearance, and blood urea nitrogen (BUN) were not different of CTL group. However, 24h proteinuria, UPCr, and albuminuria were increased in subAKI (21.18 ± 5.16 mg/24h; 30.52 ± 9.8 and 50.42 ± 4.92 fold of control) and attenuated in subAKI+DAPA (14.09 ± 4.57 mg/24h; 19.36 ± 6.86 and 17.56 ± 3.37 fold of control) compared to CTL (5.48 ± 2.29 mg/24; 8.31 ± 1.56 and 1.00 ± 0.45, respectively). Cortical albumin-FITC uptake decreased in subAKI (0.32 ± 0.18 fold of control) and reversed in subAKI+DAPA (0.87 ± 0.59 fold of control) in comparison to CTL (1.00 ± 0.46). Urinary β2-microglobulin and γ-GT as well as tissue expression of KIM-1 increased in subAKI (18873 ± 5157 intensity density, 297 ± 133 U/g creatinine, and 0.52 ± 0.12 AU) when compared to CTL (0.100 ± 0.00, 196.40 ± 75.48 U/gCr, and 0.06 ± 0.04 AU). This effect was attenuated in subAKI+DAPA group (5628 ± 3676; 202.40 ± 95.70; and 0.31 ± 0.07, respectively). Besides, subAKI group showed increased cortical interstitial space (20.72 ± 2.00 % of total area) and collagen deposition (7.88 ± 2.09 % of total area) compared to CTL (7.75 ± 0.44 and 2.38 ± 0.26). Dapagliflozin treatment partially reversed these effects in subAKI+DAPA group (9.98 ± 2.95 and 3.01 ± 0.85, respectively). The increased total protein O-GlcNAcylation in the kidney cortex observed in subAKI (4.25 ± 2.22 fold of control) was attenuated in subAKI+DAPA (1.39 ± 0.34 fold of control) compared to CTL (1.00 ± 0.18). Dapagliflozin alone showed no difference of the parameters analyzed when compared to CTL.</p> <p>Conclusion: These results suggest that dapagliflozin treatment prevents the development of tubular injury observed in subAKI. This effect is possibly associated with the attenuation of increased protein O-GlcNAcylation in the kidney cortex in subAKI. Further analysis will contribute to better characterize the mechanisms of dapagliflozin to improve kidney function. Support: FAPERJ, CNPq, CAPES Protocol: CEUA-UFRJ 083/23</p>

Title	EMPAGLIFLOZIN BLUNTS RENAL MAGNESIUM WASTING THROUGH EFFECTS ON THE TAL AND DCT IN RATS WITH CISPLATIN-INDUCED HYPOMAGNESEMIA.
Authors	ERIKA FERNANDES DE JESUS, WEVERTON MACHADO LUCHI, PAULO COELHO CASTRO, FLAVIA LETICIA MARTINS, MARCOS VINICIUS CAETANO, ANTONIO CARLOS SEGURO, ADRIANA CASTELLO COSTA GIRARDI
Affiliations	Hospital Universitário Cassiano Antônio de Moraes., UFES, Laboratório de Genética e Cardiologia Molecular, FMUSP, Hospital das Clínicas da Faculdade de Medicina, USP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The chemotherapeutic agent cisplatin is known to cause hypomagnesemia and renal magnesium (Mg) wasting, potentially due to damage to the thick ascending limb (TAL) and distal convoluted tubule (DCT), which are key sites for regulated Mg reabsorption. Recent clinical studies have demonstrated that SGLT2 inhibitors increase serum Mg concentrations in diabetic patients. However, the potential therapeutic use of SGLT2 inhibitors for cisplatin-induced hypomagnesemia has not yet been investigated.</p> <p>Objective: This study tested the hypothesis that SGLT2 inhibitors restore serum magnesium levels in cisplatin-induced hypomagnesemia and, if so, aimed to elucidate the potential mechanisms. Methods: Clinical Study: A 38-year-old female patient with persistent hypomagnesemia (1.1 mg/dL) and fractional excretion of Mg (FEMg)>10% due to past cisplatin nephrotoxicity was treated with oral dapagliflozin for one month. Experimental Study: Male Wistar rats (8 weeks old) were treated weekly with cisplatin (Cis, 2.5 mg/kg, or vehicle, ip) for five weeks. After three weeks of treatment, Cis or vehicle-treated (Ctrl) rats were randomized and orally treated or not with EMPA (10 mg/kg/day) for two weeks. Serum and urinary Mg and creatinine were measured using end-point reaction colorimetry. The expression of the Na/K/Cl cotransporter (NKCC2), claudin-16, claudin-19, Na/Cl cotransporter (NCC), the transient receptor potential cation channel member 6 (TRPM6) and member 7 (TRPM7) was evaluated by immunoblotting and qPCR. NKCC2 and NCC activities were determined by furosemide (50 mg/kg) and hydrochlorothiazide (HCTZ, 50 mg/kg) challenge tests. Results: After one month of dapagliflozin treatment, the serum Mg level increased to 1.7 mg/dL, and FEMg decreased from 12% to 7.9% in the hypomagnesemic patient. Cis-treated rats developed hypomagnesemia (1.42±0.05 vs. 2.19±0.03 mg/dL, P<0.0001) and increased FEMg (14.3±1.3 vs. 0.48±0.10%, P<0.0001). Consistent with the clinical data, EMPA restored serum Mg levels (2.21±0.05 mg/dL, P<0.0001) and reduced FEMg (2.2±0.2%, P<0.0001) in cis-treated rats. Notably, Cis rats showed decreased NKCC2 mRNA levels, increased protein abundance, and decreased phosphorylation levels. Cis-EMPA rats had higher NKCC2 mRNA and protein levels than Cis rats. Additionally, Cis rats exhibited a lower natriuretic response to furosemide, which was restored by EMPA. The protein abundance of claudin-16 was reduced in Cis rats in both the cortical and medullary renal regions and was restored by EMPA. In the medullary region, claudin-19 protein levels were higher in Cis rats compared to controls, and EMPA reduced claudin-19 protein expression in the medullary region compared to Cis rats but not in the cortical region. TRPM7 protein levels increased in Cis rats and were reduced by EMPA. The mRNA and protein abundance of NCC and TRPM6 and NCC phosphorylation, were reduced in Cis rats and rescued by EMPA. Ctrl-EMPA rats displayed higher NCC and TRPM6 mRNA and protein expression and NCC phosphorylation levels than untreated controls. Additionally, the natriuretic response to HCTZ in Cis rats was lower, and higher in Ctrl+EMPA rats than in other groups, with no differences observed between controls and Cis-EMPA rats. Conclusion: Empagliflozin mitigates renal magnesium wasting and restores serum magnesium levels in cisplatin-induced hypomagnesemia. The beneficial effects of the SGLT2 inhibitor are linked to the restoration of the levels of phosphorylated NKCC2, TRPM6, NCC, and phosphorylated NCC, and the normalization of NKCC2 and NCC activities. Support: FAPESP Protocol: 1739/2022</p>



Title	Elevated systemic levels of angiotensin-(1-7) modulate renal dysfunction observed in the early phase of Diabetic Kidney Disease
Authors	LAURA BARROSO FERREIRA DE OLIVEIRA, MARIANA RODRIGUES CAMPOS, VITORIA LUIZA LACERDA, ARTHUR FORNAZARI IOST, KAMYLLÉ SILVA FERRAZ, LETÍCIA CRISTINE CARDOSO DOS SANTOS, PAULA PEIXOTO CAMPOS LOPES, MARIA APARECIDA RIBEIRO VIEIRA, MARIA JOSÉ CAMPAGNOLE-SANTOS, CELSO CARUSO-NEVES, ROBSON AUGUSTO DOS SANTOS, DIOGO DE BARROS PERUCHETTI
Affiliations	Fisiologia e Biofísica, UFMG, Patologia, UFMG, Fisiologia e Biologia Celular, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The deleterious effects of hyperglycemia on glomerular and tubular cells are crucial in the development of Diabetic Kidney Disease (DKD). However, the mechanisms involved in this process are still elusive. Objective: In this present work, we aimed to study the potential modulatory effect of angiotensin-(1-7) [Ang-(1-7)], a component of the Renin-Angiotensin System, in DKD. Methods: We used 16-week-old male L3292 transgenic rats, which present high systemic levels of Ang-(1-7), and Sprague Dawley (SD) rats as the respective controls. Type 1 diabetes mellitus was induced by a single injection of streptozotocin (STZ, 55 mg/kg). Four groups were generated: 1) SD-ND, normoglycemic SD rats (control, n=8); 2) SD-D, diabetic SD rats (n=8); 3) L3292-ND, normoglycemic L3292 rats (n=9); 4) L3292-D, diabetic L3292 rats (n=9) (CEUA-UFMG #29/2023). All analyses were performed after 3 weeks of diabetes. Results: Diabetic groups presented similar levels of hyperglycemia (4.0-fold) as well as similar levels of increased glycosuria and urinary volumes (4.0-fold). Creatinine clearance (a marker of glomerular function) only increased (2.5-fold) in the L3292-D group. Regarding renal protein handling, despite a similar increase in proteinuria and renal clearance of proteins (3.0-fold and 2.81-fold, respectively) in both SD-D and L3292-D groups, the protein filtration was only increased (1.5-fold) in the L3292-D group. In addition, we observed a 1.35-fold increase in FEproteins associated with a 40% reduction in cortical albumin-FITC uptake in the SD-D group. Interestingly, these deleterious effects were not observed in the L3292-D group. Furthermore, a significant increase (8.4-fold) in urinary γ-glutamyl transferase, a proximal tubule injury marker, was observed only in the SD-D group. Conclusion: Altogether, our preliminary data suggest that higher systemic levels of Ang-(1-7) promote dual effects on diabetic kidneys; it contributes to glomerular hyperfiltration while attenuating tubular dysfunction at early stages of DKD. Support: PRPQ-UFMG; inct NANOBIOFAR; CNPq Protocol: CEUA-UFMG #29/2023</p>



Title	SARS-CoV-2 Spike protein inhibits proximal tubule (Na⁺/K⁺)ATPase activity through activation of Toll-Like Receptor 4/NF-κB and inhibition of Protein Kinase B
Authors	ANA CAROLINA DE FIGUEIREDO PINTO, ISABELLY FERREIRA VIEIRA, DIOGO DE BARROS PERUCHETTI, DOUGLAS ESTEVES TEIXEIRA, RODRIGO PACHECO DA SILVA DE AGUIAR, ANA ACÁCIA DE SÁ PINHEIRO, CELSO CARUSO NEVES
Affiliations	Biofísica, Universidade Federal do Rio de Janeiro, Departamento de Fisiologia e Biofísica, Universidade Federal de Minas Gerais
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: COVID-19 is a multi-organ syndrome caused by SARS-CoV-2 infection. COVID-19-related kidney damage is associated with worse outcome, being proximal tubule epithelial cells (PTECs) a major target site for viral infection. Importantly, SARS-CoV-2 Spike protein (S protein) has a well-known role in cellular dysfunction, thus contributing to COVID-19 pathogenesis. COVID-19 patients commonly present an impairment in sodium (Na⁺) balance, frequently presenting increased Na⁺ excretion and hyponatremia. (Na⁺/K⁺)ATPase is a central transporter involved in Na⁺ handling along the nephron and specially in PTECs. Based on these observations we hypothesized that the PTECs sodium pump could be a target to SARS-CoV-2 infection. Objective: To evaluate the modulation of (Na⁺/K⁺)ATPase activity by S protein and the possible mechanisms involved. Methods: LLC-PK cells, a porcine PTEC cell line, was used. Cells were incubated with 5 µg/µL S protein. Pharmacological treatments were performed as indicated. (Na⁺/K⁺)ATPase activity was measured by ouabain-sensitive ATPase activity, and it was expressed as nmol Pi x mg⁻¹ x min⁻¹ (Mean ± SD). (Na⁺/K⁺)ATPase α1 catalytic subunit expression was detected by immunoblotting or by flow cytometry. To compare differences between groups, one-way analysis of variance (ANOVA) was used followed by Tukey's post-test. When indicated, the t test was used. P < 0.05 was considered statistically significant. Results: LLC-PK1 cells incubated with S protein for 16 hours showed a reduced (Na⁺/K⁺)ATPase activity (1.6 ± 0.3, control, and 1.0 ± 0.2, S protein). This effect was not observed when the cells were incubated for 2 hours (2.1 ± 1.4). Accordingly, (Na⁺/K⁺)ATPase α1 subunit expression was reduced by S protein incubation for 16 hours by 47%. To investigate the role of TLR4 in S protein effect, 5 µg/mL LPS-RS, a TLR4 antagonist, was used. Incubation with LPS-RS blocked the inhibitory effect of S protein on (Na⁺/K⁺)ATPase activity. Furthermore, incubation of LLC-PK1 cells with 0.5 µg/mL LPS, a TLR4 agonist, mimicked the effect of S protein. LPS-RS also blocked the inhibition of (Na⁺/K⁺)ATPase activity induced by LPS. Downstream to TLR4, we observed that inhibition of NF-κB with peptide inhibitor SN50 (1 µg/mL) blocked the inhibition of (Na⁺/K⁺)ATPase activity induced by S protein. We further explored the possible role of protein kinase B (AKT) inhibition on this process. Incubation with AKT inhibitors wortmannin (100 nM) and MK-2206 (1 µM) mimicked the inhibition of (Na⁺/K⁺)ATPase activity induced by S protein. Additionally, the coincubation with 10 mM LiCO₃, an AKT activator, blocked the inhibition promoted by S protein. Conclusion: These results suggest that S protein inhibits (Na⁺/K⁺)ATPase activity in PTECs. This process is dependent on the activation of TLR4/NF-κB signaling and inhibition of AKT activity. This mechanism may help to clarify the impairment of Na⁺ handling observed in COVID-19 patients. Support: FAPERJ, CNPQ and CAPES Protocol: N.A.</p>

Title	Activation of Ang II/AT1R axis mediates the tubular injury associated with proteinuria observed in the early stage of diabetic kidney disease
Authors	MARIANA RODRIGUES CAMPOS, PEDRO HENRIQUE DE SENA REIS SEABRA, LAURA BARROSO FERREIRA DE OLIVEIRA, VITÓRIA LUIZA LACERDA, MARIANA COELHO MORAES, LETÍCIA CRISTINE CARDOSO DOS SANTOS, PAULA PEIXOTO CAMPOS LOPES, MARIA APARECIDA RIBEIRO VIEIRA, CELSO CARUSO-NEVES, DIOGO DE BARROS PERUCHETTI
Affiliations	Fisiologia e Biofísica, UFMG, Programa Temático de Fisiologia e Biofísica Celular, UFRJ, Farmacologia, UFMG
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Diabetic kidney disease (DKD) pathogenesis involves tubular dysfunction associated with tubular proteinuria. The mechanism involved in this process is still poorly understood. Clues come from reports showing the renoprotective effects of losartan, a specific antagonist of the angiotensin type 1 receptor (AT1R), on different renal diseases. Objective: Herein, we investigated the potential role of AT1R activation in tubular proteinuria and injury at the early stage of DKD. Methods: Ten-week-old male Wistar rats were used to develop DKD using streptozotocin (STZ, 55 mg/kg i.v.). When indicated, the animals were daily treated with 30 mg/kg/day of losartan via gavage. Four groups were generated: 1) CONT, normoglycemic rats (n=9); 2) STZ, diabetic rats (n=9); 3) STZ+LOS, diabetic rats treated with losartan (n=9); 4) LOS, normoglycemic rats treated with losartan (n=9). All analyses were performed after 8 weeks (CEUA-UFMG #100/2023). Results: There were no changes in plasma creatinine, plasma urea, creatinine clearance, or glomerular structure parameters. Compared with the CONT group, the STZ group presented: 1) increased blood glucose (3-fold) and urinary flow (6-fold); 2) an increase in proteinuria (mg/48h) and renal protein clearance (2.5-fold and 12.4-fold, respectively) associated with an increased fractional excretion of proteins (4.3-fold, FEproteins, a marker of renal protein reabsorption); 3) a 3.4-fold increase in urinary γ-glutamyl transferase (a marker of tubular injury); 4) an increased kidney injury score (8.0 ± 0.89 arbitrary units) associated with a 2.45-fold increase in interstitial cell infiltration. Interestingly, except for blood glucose and urinary flow, the treatment with losartan attenuated all tubular proteinuria and injury parameters in the STZ+LOS group. No difference was observed between the CONT and LOS groups. Conclusion: Altogether, our preliminary data indicate that the activation of AT1R mediates hyperglycemia-induced tubular injury and proteinuria observed at the early stages of DKD. Support: FAPEMIG, PRPQ Protocol: CEUA-UFMG #29/2023</p>

Title	Aqueous extract of Lobeira fruits on renal function in spontaneously hypertensive rats (SHR)
Authors	CARLA CAROLINA RODRIGUES DA SILVEIRA, AMANDA DE SÁ MARTINS DE BESSA, ALINE PRISCILA PANSANI, CARLOS HENRIQUE DE CASTRO, DIEGO BASILE COLUGNATI, FERNANDA CRISTINA ALCÂNTARA DOS SANTOS, ELIZABETH PEREIRA MENDES-
Affiliations	Ciencias Fisiológicas, UFG, Morfologia, UFG
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Lobeira fruits has been used by folk medicine as hypoglycemic in diabetes disease, hypocholesterolemic and anti-inflammatory. The aqueous extract of lobeira contains bioactive components identified as antioxidant agents responsible for its pharmacological actions. Objective: We investigated whether the crude aqueous extract of Lobeira fruits (EL) would improve renal function in hypertensive rats. Methods: SHR were treated EL (SHRL1g/Kg/mL, n=10) or water (n=10) by gavage (SHRW). Approved by protocol 095/15 CEUA/UFG. Systolic blood pressure (SBP) and heart rate (HR) were monitored weekly by tail-cuff plethysmography. After 7 days of treatment the rats were placed in metabolic cages by 18 hours. Renal function was assessed by biochemical analysis of plasma and urine. Creatinine and osmolarity were evaluated in plasma and urine. Kidney, was collected, fixed in Methacarn, dehydrated, embedded in paraffin wax, sectioned and stained, to evaluate the histomorphological changes. Results: There was not changed in SBP and HR. The rats treated with LE decreased the weight (SHRW 295±6,7 vs SHRL 242±7,1 g, p=0,001) without reduces food intake. There was not changed in glomerular flow and urine flow but the lobeira treatment increased urine osmolarity (SHRW 804±99 vs. SHRL1188±140 mosm/L, p=0,035) and increased the osmolar clearance (SHRW 0,018±0,002 vs SHRL 0,027±0,003 L/min, p=0,029). In kidney histomorphological parameters increased glomerular area in rats treated with EL. Conclusion: In conclusion, these results showed that EL was able to reduce “free water clearance”, but the mechanisms must be better studied. Support: CNPq, FAPEG Protocol: 95/15</p>

Title	SARS-CoV-2 Spike protein inhibits albumin transport in proximal tubule cells through a secreted factor induced by Toll-like Receptor 4 signaling
Authors	MYLENA OLIVEIRA DE FARIA SUISSO, GIULIANNE BASTOS SERPA, DOUGLAS ESTEVES TEIXEIRA, RODRIGO PACHECO DA SILVA DE AGUIAR, ANA ACACIA PINHEIRO CARUSO NEVES, CELSO CARUSO-NEVES
Affiliations	IBCCF, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The Covid-19 pandemic, declared by World Health Organization (WHO) in March 2020, affected people worldwide becoming a global public health concern. It reached countless people, and it was responsible to the death of more than 7 million. Nowadays, it is well known that SARS-CoV-2 infection causes multiple organ damage. COVID-19 severity is strictly associated with kidney damage, particularly with the development of tubule interstitial injury (TII) even in the absence of changes in glomerular flow rate. Interestingly, it has been shown that TII development could be linked to modifications in protein reabsorption in proximal tubule epithelial cells (PTECs). In this context, our group showed that SARS-CoV-2 spike protein (S protein) inhibits albumin endocytosis in PTECs what could be interconnected with TII genesis. It was shown that ACE2 and renin-angiotensin system were not involved indicating the involvement of other receptor in this process. In this regarding it has been shown that molecular pattern recognition receptors, such as Toll like receptor 4 (TLR4), mediates the effect of S protein in different organs. Objective: The aim of the present study was to investigate the involvement of TLR4 in the inhibitory effect of S protein on the albumin endocytosis in PTECs. Methods: LLC-PK1, a porcine PTECs line, was used as model. Cells were incubated with 5 µg/mL S protein or 0.5 µg/mL LPS, a TLR4 agonist, as indicated for 16h. Additionally, conditioned medium (CM) were generated by pre-incubation LLC-PK1 cells for 16h with different compounds. Then, supernatant was transferred to unstimulated LLC-PK1 cells for 2 hours. Albumin endocytosis was measured by BSA-FITC uptake. One-Way ANOVA with multiple comparisons (Tukey's post-test) was performed to test statistical significance (p<0.05) when comparing 3 or more experimental groups. Results: Initially, we investigated the participation of secreted factors in the effect of S protein on the PTECs albumin uptake. Incubation of LLC-PK1 cells with S protein inhibited BSA-FITC uptake by 30%. Co-incubation with Brefeldin A, an inhibitor of the secretory pathway, blocked S protein effect in a dose dependent way (0.01-1.0 µg/mL). Incubation of LLC-PK1 cells with CM, obtained by pre-incubation of the cells with S protein, also inhibited BSA-FITC uptake at a similar degree. Importantly, the incubation of the cells with LPS promoted an inhibitory effect similar to that observed with S protein. The inhibitory effect of S protein or LPS on the albumin endocytosis was completely blocked by LPS-RS, an TLR4 antagonist. Addition of 5 µg/mL LPS-RS blocked the effect of CM, obtained by pre-incubation of the cells with S protein. SN50 at 1 µg/mL, a NF-κB inhibitor, partially blocked the inhibitory effect of S protein on the BSA-FITC uptake. Conclusion: These results suggest that S protein inhibits albumin uptake in PTECs by TLR4-mediated secretion of intracellular factor. This effect involves, at least in part, NF-κB activation. These results clarify possible mechanisms involved in COVID-19-induced kidney injury. Support: FAPERJ, CNPq and CAPES Protocol: N.A.</p>

Title	HP β CD-Ang-(1-7) treatment ameliorates tubular proteinuria and kidney injury in Subclinical Acute Kidney Injury animal model
Authors	VITÓRIA LUIZA LACERDA, MARIANA CAMPOS RODRIGUES, LAURA BARROSO FERREIRA DE OLIVEIRA, MARIA APARECIDA RIBEIRO VIEIRA, ROBSON AUGUSTO SOUZA SANTOS, CELSO CARUSO-NEVES, DIOGO DE BARROS PERUCHETTI, DIOGO DE BARROS PERUCHETTI
Affiliations	Fisiologia e Biofísica, UFMG, Programa Temático de Fisiologia e Biofísica Celular, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Subclinical Acute Kidney Injury (SubAKI) is a clinically silent syndrome associated with tubular injury and proteinuria without changes in glomerular function. Previous works point out the overactivation of the intrarenal classical arm of the Renin-Angiotensin System (RAS) in this process. It is known that the balance between the classical arm and the alternative arm of RAS, which involves angiotensin-(1-7) [Ang-(1-7)], determines the outcome of different diseases. However, the potential role of Ang-(1-7) in subAKI still needs to be elucidated. Objective: We aimed to study the potential effects of oral treatment with Ang-(1-7) on proteinuria in a subAKI animal model. Methods: Eight-week-old female C57Bl6 mice were used to generate the following groups: 1) CONT (n=5), control; 2) subAKI (n=5), mice treated with i.p. injection of 10g/kg/day bovine serum albumin (BSA) and oral doses of hydroxypropyl β-cyclodextrin (HPβCD) for 7 consecutive days; 3) subAKI+Ang-(1-7) (n=5), mice treated with BSA and 30μg/kg/day Ang-(1-7) included in HPβCD [HPβCD-Ang-(1-7)] via gavage; and 4) Ang-(1-7) (n=5), mice treated with HPβCD-Ang-(1-7) alone (CEUA-UFMG #164/2023). Then, the animals were housed in metabolic cages to collect 24h urine for biochemical analysis. Results: No changes were observed in urinary volume, urinary flow, or the glomerular function parameters assessed. Compared to the CONT group, the subAKI group presented an increase in: 1) proteinuria and urinary protein mass (mg/24h) by 10-fold and 8-fold, respectively; and 2) urinary g-GT activity (U/L), a specific tubular injury marker, by 8-fold. Co-treatment with HPβCD-Ang-(1-7) attenuated these alterations observed in subAKI (subAKI+Ang-(1-7) group). Conclusion: Our preliminary data suggest that the oral formulation of Ang-(1-7) ameliorated the development of proteinuria and tubular injury observed in subAKI. Support: CnPQ Protocol: protocolo do CEUA: 164/2023</p>

Title	The role of the renal nerves on mechanisms of proteinuria in renovascular hypertension
Authors	AMANDA COSTA VEIGA, RODRIGO PACHECO SILVA-AGUIAR, RUY RIBEIRO CAMPOS JÚNIOR, ANA ACÁCIA PINHEIRO, CÁSSIA MARTA DE TOLEDO BERGAMASCHI, CELSO CARUSO-NEVES, ERIKA EMY NISHI
Affiliations	Fisiologia, UNIFESP, Biofísica, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Elevated levels of proteinuria, especially albuminuria, are considered a risk predictor for cardiovascular disease, mortality, and possibly renal changes in arterial hypertension (AH) individuals. Our previous studies showed a role for the renal nerves in maintaining AH and renal changes in an experimental model of renovascular hypertension (2K-1C). Objective: In this study, we evaluated whether the renal nerves are involved in the mechanisms of protein endocytosis by the proximal tubule (PT) in 2K-1C rats. Methods: We used the Goldblatt model of 2K-1C (n=6-7/group) and a control group (n=6-7/group) of male Wistar rats. After 4-5 weeks of renal artery clipping, total renal denervation (DNx) was performed in the ischemic kidney (visible nerve bundles were cut + 10% phenol application), or the animals were treated with hydralazine (25mg/kg/day for 1 week). PT endocytosis of albumin was evaluated after intra-arterially infusion of fluorescein-conjugated bovine serum albumin (FITC-BSA) after 2 or 1 week of each protocol, respectively. Results: Both DNx (136 ± 40 mmHg) and hydralazine (127 ± 11 mmHg) partially decreased blood pressure in 2K-1C rats (182 ± 24 mmHg) while baseline heart rate was unchanged. There was a decrease in albumin reabsorption by the PT in both clipped (70 ± 14 % of control) and contralateral (80 ± 14 % of control, p<0,05) kidneys in 2K-1C rats. Both treatments improved albumin reabsorption and tubular function. However, only DNx normalized glomerular function in hypertensive rats which was evaluated by plasma creatinine and WT-1 positive podocyte nuclei and albuminuria. Megalin receptor was more internalized in the PT of 2K-1C rats though its abundance was unchanged. Conclusion: Taken altogether, our results suggest that elevated blood pressure contributes to decreased albumin reabsorption by the PT, while the renal nerves play an important role in glomerular damage in 2K-1C rats. Further experiments are required to determine the underlying mechanisms of glomerular and tubular damage leading to proteinuria in this model of AH. Support: FAPESP, Capes and CNPq. Protocol: 6414190520</p>



Title	INTERMITTENT FASTING MODULATES KIDNEY FUNCTION IN FEMALE RATS
Authors	ARTHUR FORNAZARI IOST, LEONARDO OLIVEIRA GUARNIERI, LAURA BARROSO FERREIRA DE OLIVEIRA, MARIANA RODRIGUES CAMPOS, OLÍVIA RAMOS COSTA VAL PEDROSA, MARIA APARECIDA RIBEIRO VIEIRA, DIOGO DE BARROS PERUCHETTI
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Dietary restrictions have been gaining interest among large populations worldwide. In particular, some reports have shown the beneficial effects of intermittent fasting (IF) protocols on different neurological and cardiovascular diseases. However, the effects on the kidneys are still poorly understood.</p> <p>Objective: We aimed to verify the potential impact of IF on renal function. Methods: Female Wistar rats (8-10 weeks old) were randomly divided into two experimental groups: 1) CONT (control group, n=4) – with free access to chow; and 2) IF (intermittent fasting group, n=5), rats subjected to the IF protocol [fasting: 18h (from “zeitgeber time” (ZT)=8 up to ZT=24)/ feeding: 6h (from ZT=1 up to ZT=7)] for 4 weeks. During the feeding period, the rats had free access to chow (CEUA-UFMG#13-2023). Once a week, the rats were housed in metabolic cages (during the feeding period) to measure chow and water intakes, as well as to collect urine for biochemical analysis. Results: Compared to the CONT group, the IF group showed a reduction in body weight (BW, 15%), which was observed despite an increase in water intake (3.0-fold) and food intake (6.0-fold). The IF group also presented a reduction in urinary volume (64%, mL/6h/kg BW) after 2 weeks of diet restriction. No significant alterations were observed in urinary creatinine concentrations. Interestingly, urinary glucose mass was reduced (44%) in the IF group. However, proteinuria and UPCr (the ratio between urinary proteins and creatinine) were increased (1.8-fold and 1.6-fold, respectively). A positive Pearson correlation was found between BW and glycosuria ($r=0.4906/R^2=0.2407/P=0.001$), while an inverse Pearson correlation was found between BW and proteinuria ($r=-0.7169/R^2=0.5140/P<0.0001$). Conclusion: Our preliminary findings suggest that the 4-week IF protocol modulates renal function, especially the mechanisms involved in renal proteins and glucose handling. Support: CNPq Protocol: CEUA-UFMG #13/2023</p>

Title	Investigating the possible role of gold nanoparticles on protein handling by renal proximal tubule epithelial cells
Authors	LIVIA RIBEIRO GOMES, LAVINIA REIF CORREA DE OLIVEIRA, SARAH APARECIDA DOS SANTOS ALVES, PATRICIA MACHADO RODRIGUES E SILVA MARTINS, MARCO AURÉLIO MARTINS, PEDRO LEME SILVA, PATRÍCIA RIEKEN MACEDO ROCCO, ANA ACACIA DE SÁ PINHEIRO, CELSO CARUSO NEVES
Affiliations	Carlos Chagas Filho Institute of Biophysics, UFRJ, Laboratory of Inflammation, FIOCRUZ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Proximal tubule epithelial cells (PTECs) play a crucial role in kidney albumin reabsorption, which can occur through receptor-mediated endocytosis or by a receptor-independent mechanism. In several kidney diseases, protein reabsorption by PTECs can be impaired, leading to proteinuria, a classical marker of pathogenesis and progression in both acute and chronic kidney diseases. One of the main challenges today is identifying new treatments to prevent the progression of kidney disease. Nanotechnology, through the development of nanometer-scale materials and components, has emerged in recent years as a potential therapy for various pathologies. In this context, our group has recently demonstrated that 10 nm gold nanoparticles (AuNPs) can reverse damage induced by high protein concentrations on PTECs using both in vivo and in vitro models. AuNPs reduce tubule-interstitial injury during subclinical acute kidney injury induced in mice by albumin overload. Furthermore, treating PTECs with AuNPs prevents the decrease in albumin endocytosis caused by high albumin concentrations. The literature suggests that nanoparticles up to 10 nm can be freely filtered in glomerular regions and reabsorbed by PTECs. However, the potential interaction between PTECs' albumin endocytosis and AuNPs has not been fully clarified. Objective: The aim of the present study was to investigate the potential role of AuNPs in protein endocytosis in PTECs. Methods: We used LLC-PK1 cells, a porcine PTEC line, as our model. Protein endocytosis was determined using BSA-FITC as a tracer, while DQ-BSA was employed to measure protein lysosomal degradation. To analyze fluid-phase endocytosis, we used Dextran-FITC. Differences between groups were compared using one-way analysis of variance (ANOVA) followed by Tukey's post-test. When appropriate, the t-test was used. A p-value of < 0.05 was considered statistically significant. Results: To verify the possible effect of AuNPs on protein handling by PTECs, LLC-PK1 cells were treated with 1 µg/ml AuNPs (10 nm) for either 30 minutes (acute) or 16 hours (chronic). Acute treatment with AuNPs did not alter fluid-phase endocytosis or lysosomal degradation compared to the control. However, chronic treatment induced a 1.45-fold increase in fluid-phase endocytosis (n=5) and a 1.14-fold increase in albumin lysosomal degradation (n=5). Interestingly, chronic incubation of LLC-PK1 cells with AuNPs increased albumin uptake in the presence of 10 mg/mL albumin by 1.6-fold (n=2). However, AuNP treatment did not change albumin uptake in the presence of 100 µg/mL albumin (Control: 127750.2 ± 40959.8; AuNP: 119077.4 ± 28006.1). Conclusion: Here, we demonstrated that AuNPs modulate albumin endocytosis in LLC-PK1 cells, opening new possibilities for understanding the effects on PTECs protein reabsorption. Support: FAPERJ, CAPES, CNPq Protocol: N.A.</p>

Title	Aldosterone receptor is involved in the development of subclinical acute kidney injury
Authors	JOÃO PAULO ZUMACK, ANA CAROLINA FIGUEIREDO PINTO, RODRIGO ALVES DA SILVA PERES, RODRIGO PACHECO DA SILVA DE AGUIAR, ISABELLY FERREIRA VIEIRA, ANA ACACIA PINHEIRO CARUSO NEVES, CARLOS PEREZ GOMES, CELSO CARUSO NEVES
Affiliations	General Medicine, UNIRIO, Fisiologia e Biofísica celular, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Excessive aldosterone activity causes renal damage, what is associated with fibrosis and pro-inflammatory response, leading to the development and/or progression of renal diseases. Finerenone, a non-steroidal mineralocorticoid receptor antagonist, became a hope in the treatment of renal disease due to its nephroprotective effects. However, its mechanism of action is not completely understood. Nowadays, the challenge is to identify the early stage of kidney damage to initiate precocious treatment and improve patient outcome. In this regard, it has been identified a syndrome called subclinical acute kidney injury (subAKI), whose biomarkers of tubular damage are observed in urine without change in glomerular function, assessed by KIDGO classification. It has been proposed that the mechanism underlying the development of tubule-interstitial injury (TII) in subAKI involves changes in albumin endocytosis machinery in PTECs. Indeed, megalin knockout in OK cells, a model of PTECs, induces a pro-inflammatory response. However, the role of aldosterone in this process is still to be determined. Objective: Evaluate the effect of finerenone on the genesis TII in subAKI. Methods: A subAKI model was developed by administration of BSA (10 g/kg/day) in male BALB/c mice (6-8 weeks-old) (CEUA 083/23). The treated animals received 10 mg/kg/day finerenone. At day 7, the animals were placed into metabolic cages for 24-hour urine collection and euthanized for blood and kidney tissue collection. The Shapiro-Wilk test was used to evaluate normal data distribution. To compare differences between groups, one-way analysis of variance (ANOVA) was used followed by Tukey's post-test. Results: Finerenone treatment did not modify arterial blood pressure and urinary potassium excretion (control values: systolic arterial pressure 90 ± 14 mmHg; diastolic arterial pressure 67 ± 20 mmHg; mean arterial blood pressure 75 ± 17 mmHg; urinary potassium $313,8 \pm 87,3$ mmol/L; potassium clearance $0,053 \pm 0,025$ mL/min; 24 hour potassium $0,30 \pm 0,13$ mEq/24h; fractional excretion of potassium $35,84 \pm 15,34$ %). Glomerular function, measured by plasma creatinine, urea, and creatinine clearance (eGFR), was not changed in all groups tested (control values: plasma creatinine $0,49 \pm 0,11$ mg/dL; plasma urea 62 ± 10 mg/dL; eGFR $0,144 \pm 0,089$ mL/min). Finerenone ameliorated proteinuria, including urinary protein concentration, 24-hour proteinuria, proteinuria-to-creatinine ratio (UPCr). Immunodetection analysis confirmed the reduction of albuminuria in the finerenone-treated animals. SDS PAGE of urine showed that finerenone avoided the development of medium and lower molecular weight proteinuria observed in subAKI group. TII development, measured by urinary γ-GT activity, was avoided by finerenone treatment. Additionally, finerenone also avoided the reduction of tubular sodium reabsorption, measured by renal sodium excretion fraction (FENa+), and cortical (Na+/K+)ATPase activity observed in subAKI. Conclusion: According to our data, finerenone was able to reduce TII in animals with subAKI, demonstrating its significant potential in reversing the progression of nephropathies. Support: FAPERJ, CNPq, CAPES Protocol: 083/23</p>



Title	CHARACTERIZATION OF RENAL FUNCTION OF THE WILD RODENT <i>Cerradomys goytaca</i> REVEALS A HIGH URINARY CONCENTRATION CAPACITY.
Authors	PEDRO CORRÊA NASCIMENTO, LUZIA AUGUSTA VALERIANO-MONICI, CAROLINA AUGUSTA DE BARROS SILVA, GUSTAVO DE CASTRO NASCIMENTO, LANA SOARES SALES, CARLOS ALBERTO DE SOUZA FILHO, EDGAR M. S. WAN DER MAAS, JONES B. GRACELI, PABLO RODRIGUES GONÇALVES, JACKSON DE SOUZA-MENEZES
Affiliations	NUPEM, UFRJ
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: <i>Cerradomys goytaca</i> is an endemic rodent of the Jurubatiba National Park Sandbank. To date, no studies have described the renal system of <i>C. goytaca</i> and its adaptation to this ecosystem. Objective: This study evaluates the renal function and morphology of adult female <i>C. goytaca</i>. Methods: Experimental procedures were approved by the CEUA (01200.001568/2013-87) at the Federal University of Rio de Janeiro. The study used 10 adult females <i>C. goytaca</i> (15 to 50 weeks) and 20 females <i>Rattus norvegicus</i> (control species) of the same age, bred and kept in a bioterium. Blood and urine samples were collected through metabolic cages. Renal function was assessed through clearance, fractional excretion, and urinary excretion of creatinine, Na⁺, K⁺, glucose, urea, and osmolality. Renal mass index was determined by the relation between kidney and body weights. Histological analysis of the kidney was performed using HE staining. Results were expressed as mean ± SEM, and significance was determined using the Student's t-test. Results: The right and left renal mass index (g/kg), urine osmolality (mmol/kg), tubular water reabsorption (ml/min/kg), food intake (g/day/kg), clearance (ml/min/kg), fractional excretion (%), and urinary excretion (mg/day/kg) of sodium, potassium and glucose were higher in <i>C. goytaca</i> (6.68±0.66, 6.69±0.68, 1205±173, 0.051±0.013, 79.72±20.83, 0.02±0.005, 1.12±0.20, 7.55±1.46, 0.09±0.01, 3.81±0.37, 0.87±0.14, 0.02±0.009, 0.75±0.22, 29.94±9.09, respectively, p < 0.05) compared to <i>R. norvegicus</i> (3.42±0.19, 3.20±0.17, 448±46, 0.01±0.006, 4.85±1.22, 0.01±0.002, 0.44±0.09, 3.56±0.54, 0.06±0.005, 2.14±0.47, 0.48±0.05, 0.001±0.0001, 0.05±0.01, 1.84±0.22, respectively). The count of: glomeruli, cortical tubules, and medullary tubules; relative area of: the renal corpuscle, glomeruli, and urinary space; GFR (ml/min/kg), creatinine urinary excretion (mg/day/kg), urinary flow (ml/day/kg), clearance(ml/min/kg), fractional excretion (%) and urinary excretion (mg/day/kg) of urea were lower in <i>C. goytaca</i> (0.71±0.039, 0.77±0.012, 0.60±0.0094, 0.46±0.063, 0.54±0.075, 0.64±0.050, 2.41±0.42, 19.54±3.56, 47.68±6.95, 8.85±4.18, 114.10±28.69, and 376.40±218.70, respectively, p < 0.05) compared to <i>R. norvegicus</i> (1.00±0.097, 1.00±0.062, 1.00±0.097, 1.0±0.10, 1.0±0.052, 1.0±0.015, 5.36±1.10, 40.89±7.14, 95.21±13.92, 22.76±4.12, 829.70±228.50, and 3516±570.10, respectively). Conclusion: Our results suggest a higher urinary concentration capacity in adult females of <i>C. goytaca</i>, mediated by adaptations in glomerular filtration rate (GFR), medullary water reabsorption, and kidney morphology. Support: FAPERJ e CAPES Protocol: 01200.001568/2013-87</p>



Title	Development of tubular proteinuria in adulthood after postnatal stress induced by maternal separation
Authors	PEDRO HENRIQUE DE SENA REIS SEABRA, MARIANA RODRIGUES CAMPOS, MARIA APARECIDA RIBEIRO VIEIRA, BRUNA LOPES RESENDE, BRUNO REZENDE DE SOUZA, DIOGO DE BARROS PERUCHETTI
Affiliations	Fisiologia e Biofísica, UFMG
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Postnatal stress (PNS), better known as childhood stress, induces systemic dysfunctions in adulthood, such as behavioral, metabolic, and cardiovascular dysfunctions like hypertension. These observations have been made in experimental models of PNS such as maternal separation (MatSep). Interestingly, alterations in renal vascular architecture have been observed in adulthood associated with changes in the components of the renin-angiotensin system (RAS) induced by MatSep. In this context, there is an association between hypertension, RAS modulation, tubular proteinuria, and kidney disease. Objective: To investigate the possible involvement of proteinuria development and impairment of renal function in adulthood after PNS. Methods: The experimental model of postnatal stress induced by maternal separation was used. Male C57BL6 mice were either separated from the mother daily for 6 hours from the 2nd postnatal day until the 14th day or left undisturbed. Thus, 02 experimental groups were generated: 1) Control group (n=4); 2) MatSep group (n=8), animals subjected to the maternal separation protocol (CEUA-UFMG#157/2023). At the 8th week of life, the animals were placed in metabolic cages for 24-hour urine collection, as well as for the analysis of behavioral parameters of water and food intake. Urine samples were used to determine the concentrations of total protein and creatinine using commercial colorimetric kits (Labtest). Kidney tissues were collected for histological analysis to analyze the glomerular and tubular architecture. Results: A reduction in body weight (20%), with no significant alteration in food intake, was observed in the MatSep group compared to the control group. Furthermore, a 75% increase in water intake (mL/24h) was observed, as well as a 47% reduction in urinary volume (mL/24h) in the MatSep group compared to the control group, indicating a reduction in renal function in animals subjected to the protocol. To investigate a possible development of renal injury, the next step was to determine the level of proteinuria (a known marker of kidney disease). We observed a significant increase of 20x in the concentration of total proteins in urine (mg/dL), 25x in proteinuria levels (mg/24h), and 27x in the ratio between urinary proteins and creatinine (UPCr) in the MatSep group compared to the control group. Conclusion: Our preliminary data found a functional renal loss associated with the development of proteinuria in adulthood after PNS. These findings are important for understanding the impact of systemic effects in adulthood triggered by chronic stress in childhood, as well as for developing strategies to predict the occurrence of kidney disease in the adult population in general. Support: PRPQ, Pró Reitoria de Pesquisa Protocol: CEUA UFMG 157/2023</p>

Title	PHYSICAL EXERCISE AND CURCUMIN SUPPLEMENTATION MITIGATE KIDNEY DAMAGE AND EXTRACELLULAR MATRIX PROTEIN ACCUMULATION IN FEMALE RATS WITH TYPE I DIABETES DEPRIVED OF OVARIAN HORMONES
Authors	SUZETE CARVALHO LANDULFO LUZ, MARINA MORENA BRITO FARIAS, GABRIELA FREITAS SILVA BITENCOURT, BEATRIZ DOS ANJOS OLIVEIRA, LUANA PEREIRA OLIVEIRA, FLÁVIO SILVA DE JESUS, GABRIELA SANTOS LIBARINO, AMÉLIA CRISTINA MENDES DE MAGALHÃES GUSMÃO, LILIANY SILVA BRITO DO AMARAL, TELMA DE JESUS SOARES
Affiliations	Departamento de Biointegração, UFBA
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Damage to the architecture of renal tissue and excessive deposition of extracellular matrix (ECM) proteins are among the main characteristics of diabetic kidney disease (DKD), with postmenopausal women being more likely to develop this pathology with high morbidity and mortality. Furthermore, hormone replacement therapy presents controversial results and studies are scarce in women with type I diabetes. Therefore, it is necessary to search for new low-cost therapeutic approaches that delay the onset and/or progression of renal dysfunction, Objective: To evaluate the impact of aerobic physical exercise and/or curcumin (CUR) supplementation on structural changes and expression of TGF-β and ECM proteins in DRD in ovariectomized (OVX) rats. Methods: 24 female Wistar rats, aged 10 weeks, weighing 180-220g, underwent OVX and diabetes induction, with a single dose of streptozotocin (40 mg/kg bw,IV). The rats were distributed into 4 groups (n=6): Sedentary diabetic OVX- SDO, sedentary diabetic OVX+curcumin- SDO+CUR, trained diabetic OVX- TDO and trained diabetic OVX+curcumin- TDO+CUR. For 8 weeks, the rats trained on a treadmill and the treated groups received curcumin (100 mg/kg bw, gavage). The rats were weighed weekly and, 48 hours after the end of the protocol, they were euthanized to remove the kidneys. Histological and immunostaining analyzes for TGF-β, fibronectin and collagen IV were performed. Data were analyzed using GraphPad Prisma 5.0, Anova Two-way or Kruskal-wallis software and Bonferroni and Dunn post-tests, respectively. The results were expressed as mean+SD, considering statistical differences when $p < 0.05$. Results: Exercise and curcumin, singly, reduced tubulointerstitial injury scores (0.88 ± 0.16; 1.08 ± 0.08), hydropic degeneration (2.68 ± 0.28; 2.23 ± 0.79), tubular dilation (1.51 ± 0.33; 2.44 ± 0.84), cellular infiltrate (0.00 ± 0.00; 0.01 ± 0.02), TGF-β immunostaining (4.64 ± 0.70; 6.62 ± 1.02), fibronectin (2.70 ± 0.69; 2.14 ± 0.75) and collagen IV (3.57 ± 0.48; 2.58 ± 0.49) when compared to the group SDO (1.66 ± 0.10; 5.25 ± 2.19; 4.31 ± 1.34; 2.05 ± 2.00; 9.69 ± 1.89; 6.03 ± 1.89; 7.60 ± 2.63), $p < 0.001$, respectively. However, only exercise was able to reduce edge loss in brush (0.02 ± 0.03) versus the SDO group (0.26 ± 0.20), as well as, only the combined treatment attenuated the loss of body weight (17.33 ± 26.71) versus SDO+CUR (-13.89 ± 25.41), $p < 0.05$. Conclusion: Exercise and curcumin, singly, attenuated tubulointerstitial injury, hydropic degeneration, tubular dilation, inflammatory cell infiltrate, expression of TGF-β, fibronectin and collagen. Only the combined treatment mitigated body weight loss. However, we did not observe significant synergistic effects in the combined treatment group in this experimental model of DRD in ovariectomized rats. Support: CNPq and Fapesb. Protocol: CEUA/UFBA, protocol 096/21.</p>

Title	Differential effects of three training protocols on renal interleukin-11 levels and reduced apoptosis in rats with cisplatin nephrotoxicity
Authors	CAROLINE ASSUNÇÃO OLIVEIRA, ÉRIKA AZENATHE BARROS MERCÊS, FERNANDA SANTOS PORTELA, JÚLIA MAFRA DE BENEDICTIS, LAÍS MAFRA DE BENEDICTIS, ANTÔNIO VICTOR BRITO DA SILVA, JOÃO DE ASSIS GONÇALVES CAMPANATI, FABRÍCIO FREIRE DE MELO, MÁRCIO VASCONCELOS OLIVEIRA, AMÉLIA CRISTINA MENDES DE MAGALHÃES, TELMA DE JESUS SOARES, LILIANY SOUZA DE BRITO AMARAL
Affiliations	Fisiologia, UFBA
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Cisplatin (CP) is an antineoplastic widely used to treat different types of solid tumors. However, its use is mainly limited by high nephrotoxicity, which is manifested by acute kidney injury (AKI). The pathophysiology of AKI is complex and involves the activation of several apoptotic signal pathways. Reactive oxygen species and mechanical stress are known to increase IL-11 production, a pleiotropic cytokine with anti-apoptotic and anti-necrotic effects, which confers renoprotection. Objective: Thus, the objective of this study was to compare the impact of high-intensity interval training (HIIT) with low (LIT) and moderate (MIT) intensity continuous training on renal IL-11 levels and expressions of apoptotic markers in rats with CP nephrotoxicity. Methods: To this end, female Wistar rats were divided into five groups (n=7 in each group): control and sedentary (C+S); treated with CP and sedentary (CP+S); treated with CP and subjected to LIT (CP+LIT); treated with CP and subjected to MIT (CP+MIT), and treated with CP and subjected to HIIT (CP+HIIT). This study was approved Ethics Committee in Animal Experimentation of the UFBA/IMS (protocol 056.2018). Training protocols consisted of running on a motorized treadmill, 5 days a week, for 8 weeks. At the end of the protocols, the rats received a single injection of CP (5 mg/kg), and 7 days after the injection, they were euthanized. We assessed the renal immunolocalization of Bax, Bcl-2, and cleaved caspase-3. The IL-11 and p53 renal levels were also determined. Results: Our data demonstrate a more significant increase in p53 levels in CP+S (315+93,99) compared to the C+S group (p<0.05). However, although all training protocols attenuated this effect, HIIT (76,67+10,23) was more effective than LIT (173,09+25,98) and MIT (111,9+21,22) (p<0.05). It was a significant increase in renal IL-11 levels in the LIT (35,89+3,7), MIT (56,11+6,94), and HIIT (79,08+5,40) in relation to CP+S (12,93+1,61) (p<0.05) in an intensity-dependent manner, so with effects more prominent with HIIT. We observed negative correlations between Bax and IL-11 (Pearson's brightness coefficient $r=-0.70$, $P<0.0001$), caspase-3 and IL-11 (Pearson's brightness coefficient $r=-0.69$, $P<0.0002$), and p53 and IL-11 (Pearson's brightness coefficient $r=-0.81$, $P<0.0001$), and positive correlation between Bcl-2 and IL-11 (Pearson radiance coefficient $r=0.63$, $P<0.001$). Conclusion: In conclusion, the present study suggests that HIIT provides superior renoprotection than continuous training of low and moderate intensities, beneficially modulating apoptotic signaling pathways and consequently attenuating CP-induced AKI in this experimental model. Such an effect may be related, at least in part, to the increase in renal IL-11 levels induced by training in an intensity-dependent manner. Support: This work was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), grant number: 433542/2018-7, and Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB), grant number:1144/2021. Protocol: Ethics Committee in Animal Exp</p>

Title	ACE2 MODULATES PROXIMAL TUBULE ALBUMIN ENDOCYTOSIS THROUGH ANGIOTENSIN II / AT1R AXIS
Authors	HELENA RIBEIRO PEIXOTO, RODRIGO PACHECO DA SILVA DE AGUIAR, DIOGO PERRUCHETI, ANA ACACIA DE SA PINHEIRO, CELSO CARUSO NEVES
Affiliations	Carlos Chagas Filho Institute of Biophysics, UFRJ, Department of physiology and biophysics, UFMG
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Proximal tubule epithelial cell (PTEC) albumin endocytosis is an important process to avoid urinary albumin excretion, and this importance is highlighted by the fact that albuminuria is an independent risk factor for all-cause mortality and correlated with kidney disease progression. Albumin reabsorption occurs through receptor-mediated endocytosis, being megalin, cubilin and amnionles the receptor complex involved. Recent evidence suggests that this process is highly dynamic and regulated by different peptides, including renin-angiotensin system, RAS. Our group has demonstrated that Angiotensin II (Ang II) / AT1 receptor (AT1R) signaling decreases albumin endocytosis in PTECs by reducing megalin expression. However, the effects of the angiotensin converting enzyme type 2 (ACE2) in this process are still unknown. Objective: Study the role of ACE2 in albumin endocytosis in PTECs. Methods: PT cell lines LLC-PK1, HEK-293, and HEK-293 overexpressing human ACE2 (hACE2-HEK-293) were used. FITC-albumin, DQ-albumin, and FITC-dextran uptake were measured by cell-associated fluorescence. The indirect ELISA method was used to measure the extracellular concentration of Angiotensin II when indicated. Specific inhibitors and antagonists for ACE2 (MLN-4760), AT1R (Losartan), MASR (A779) and MK-2206 (AKT) were employed. Expression of megalin and cubilin in HEK-293 and hACE2-HEK-293 was verified by immunofluorescence and confocal microscopy. Immunoblot was used to measure AKT activity. A murine model of subclinical acute kidney injury (subAKI), induced by injection of 10 g/kg of bovine serum albumin in BALB/C mice for 7 days was used. NephroSeq database was accessed for correlation studies with human patient data. Statistical analysis was performed with GraphPad Prism 7. Results: hACE2-HEK-293 cells had a selective increase in receptor-mediated endocytosis of albumin, measured by increased FITC-albumin (2,2x) and DQ-albumin (1,5x) endocytosis, with no changes in fluid-phase endocytosis, measured with FITC-dextran. hACE2-HEK-293 also showed an increased albumin binding (1,8x) to the cell's surface, which indicated increased receptor expression. Indeed, megalin mRNA and protein expression in hACE2-HEK-293 cells were increased, without changes in cubilin protein expression. Extracellular Ang II levels were reduced in hACE2-HEK-293. Overnight treatment with ACE2 inhibitor MLN-4760 reduced FITC-albumin endocytosis in HEK-293 and ACE2-HEK-293 and the addition of losartan, an AT1R antagonist, blocked the inhibitory effect of MLN-4760. Losartan and A779 alone showed no effect on FITC-albumin endocytosis. hACE2-HEK-293 showed higher AKT activity, and incubation with AKT inhibitor MK-2206 decreased FITC-albumin uptake in both HEK-293 and hACE2-HEK-293 cells. LLC-PK1 cells treated with MLN-4760 showed lower FITC-albumin and DQ-albumin endocytosis associated with higher supernatant Ang II levels. In vivo, proteinuria was negatively correlated with ACE2 expression in cortical renal tissue of mice with subAKI. Database analysis showed reduced expression of Ace2, Agtr2, and Mas1, and increased Ace in proximal tubule cells from patients with acute kidney injury compared to healthy patients. Conclusion: ACE2 promotes receptor-mediated endocytosis by downregulating Ang II/AT1R signaling. ACE2 increases AKT activity and the expression of Megalin, ensuring a higher uptake of albumin in PT cells. Support: FAPERJ / CAPS / CNPQ Protocol: A13/20-045-17</p>

Title	ANÁLISE HISTOLÓGICA COMPARATIVA DO TECIDO RENAL DE RATOS WISTAR MACHOS E FÊMEAS SUBMETIDOS A PROTOCOLO DE EXERCÍCIO FÍSICO DE RESISTÊNCIA
Authors	EMILY ROCHA CORDEIRO, DEBORA C. KIMURA LICHTENECKER, NATHALIA BESERRA DA SILVA, LETICIA MARIA MONTEIRO, ROGERIO ARGERI, ISADORA GONCALVES ALMEIDA, ISABELA BORGES DA MOTA SILVEIRA, GUIOMAR NASCIMENTO GOMES
Affiliations	Fisiologia Renal, Unifesp
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O exercício físico de resistência está associado a diversos benefícios à saúde, incluindo força muscular, redução da pressão arterial e melhora do perfil lipídico. Alguns estudos apontam que a atividade física pode até retardar o declínio da função glomerular na doença renal crônica. Entretanto também há evidências que o exercício de resistência pode causar aumento da atividade nervosa simpática renal causando intensa vasoconstrição, o que poderia levar a alterações morfofuncionais renais. Objective: Avaliar e comparar os efeitos do treinamento físico de resistência sobre parâmetros morfofuncionais renais em ratos Wistar de ambos os sexos. Methods: Ratos Wistar com dois meses de idade foram distribuídos em quatro grupos experimentais: MS- Machos Sedentários; ME- Machos Exercício; FS- Fêmeas Sedentárias; FE- Fêmeas Exercício. Os grupos Exercício foram submetidos a um programa de treinamento resistido progressivo em escada vertical, 5 vezes por semana em dias consecutivos com dois dias de descanso, durante 6 semanas. Ao final do período de treinamento, foi medida a pressão arterial (PA), e depois os animais foram colocados em gaiolas metabólicas para coleta de amostras de urina, seguida de coleta de sangue por punção da veia caudal para avaliação do clearance de creatinina (Clcr-método de Jaffé) seguida da coleta dos rins para análise dos parâmetros morfológicos renais: tubularização glomerular, características das artérias renais (diâmetro, espessura e razão média/lúmen), expressão de alfa-SM-actina (marcador de lesão renal) e de CD68 (macrófagos) por imunohistoquímica. CEUA/UNIFESP: 9009241022. Resultados apresentados como média±erro-padrão; Two-way-ANOVA, p>0,05. Results: O treinamento de resistência não causou alterações significativas nos valores de PA dos grupos estudados [PA (mmHg): MS: 134±3; ME: 123±3; FS: 119±1; FE: 119±3; (P sex =0,0014)], porém resultou em queda do Clcr no grupo FE [Clcr (mL/min/kg): MS: 7,4±0,44; ME: 7,0±0,37; FS: 6,4±0,36; FE: 5,4±0,27; (P sex =0,0010)]. A frequência de tubularização glomerular foi maior nos machos que nas fêmeas e o exercício não modificou este parâmetro [(%): MS: 11,6±1,8; ME: 10,9±1,8; FS: 7,9±1,0; FE: 5,4±0,5; P sex =0,0047)]. Em relação às características vasculares, observamos que a relação entre espessura e diâmetro arterial (vasos com diâmetro entre 6,8 e 626,1 µm) apresentou correlação positiva em todos os grupos (r de Spearman, MS: 0,73; ME: 0,78; FS: 0,70; FE: 0,82), sem diferença significativa entre as tangentes dos grupos. A razão média/lúmen dos vasos estudados foi maior nas fêmeas e o exercício aumentou esta razão. (M/L: MS: 5,5±0,1; ME: 8,1±0,7; FS: 8,7±0,5; FE: 10,6±1,2; P sex =0,0014, P exercício =0,0088). Não foram observadas alterações significativas na expressão de alfa-SM-actina e de CD68. Conclusion: De acordo com os dados obtidos até o momento, o programa de exercício resistido de seis semanas não apresentou impacto significativo na pressão arterial, entretanto resultou em alterações morfofuncionais principalmente nas fêmeas, grupo que apresentou diminuição no clearance de creatinina e aumento na razão M/L vascular renal. Mais estudos são necessários para confirmar estes achados. Support: FAPESP Protocol: CEUA/UNIFESP: 9009241022</p>

Title	KIDNEY DAMAGE IN PATIENTS WITH LONG COVID
Authors	CAIO VETTORAZZI BARBOZA MENÁRIO, RODRIGO PACHECO SILVA-AGUIAR, GABRIELA DA SILVA NASCIMENTO, NINA ROCHA GODINHO DOS REIS VISCONTI, LUANA DE SOUZA ANDRADE, FERNANDA CARVALHO DE QUEIROZ MELLO, JOSÉ ROBERTO LAPA E SILVA, NAZARETH DE NOVAES ROCHA, CAMILA MARINELLI MARTINS, FERNANDA FERREIRA CRUZ, ANA ACÁCIA DE SÁ PINHEIRO, PEDRO LEME SILVA, PATRICIA RIEKEN MACÊDO ROCCO, CELSO CARUSO NEVES
Affiliations	Carlos Chagas Filho Institute of Biophysics, UFRJ, Institute of Thoracic Diseases, UFRJ, Biomedical Institute, UFF, Research Consulting LTDA, AAC&T
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: COVID-19 severe cases progress clinically with multiple organ dysfunction syndrome (MODS). ACE2-expressing tissues are susceptible to SARS-CoV-2 infection, and COVID-19-induced kidney injury is associated with mortality and morbidity. Long COVID occurs when symptoms persist or appear three months after acute COVID-19 infection. In this syndrome, patients may present subclinical acute kidney injury (subAKI), a condition characterized with increased tubular injury markers and albuminuria in the absence of KDIGO criteria of renal dysfunction. How Long COVID correlates with glomerular and tubular injury is not well defined yet. Objective: Evaluate renal outcomes in patients diagnosed with Long COVID and correlate with the temporal course of the disease. Methods: This is a cross-sectional clinical study on patients diagnosed with COVID-19 between March 2020 and April 2022. Patients admitted to the ward or intensive care unit (ICU) for COVID-19, whose clinical diagnosis was determined by a positive result in RT-PCR tests or associated with a chest computed tomography image suggestive of viral pneumonia were included. Inclusion criteria included being over 18 years-old and signing the Free and Informed Consent Form. The exclusion criteria were patients with a previous diagnosis of kidney disease and pregnant or breastfeeding women. The project was approved by the Research Ethics Committee (CAAE: 53517521.6.0000.5257). Participants (n=75) were divided into three groups: 6 (n=36), 12 (n=24) and 24 (n=15) months post-COVID-19 (MPC). Clinical and laboratory data were evaluated during hospitalization and after discharge through outpatient follow-up. The estimated glomerular filtration rate (eGFR) was assessed using the CKD-EPI method and expressed in ml/min/1.73m². The tubular injury score was developed to measure the degree of tubular injury. The clinical spectrum of SARS-CoV-2 infection was defined according to criteria established by the National Institutes of Health (NIH). The chi-square and Kruskal-Wallis tests with Bonferroni adjustments were used for statistical analyses. Results: The general population had a median age of 59 years and 58.6% were women. Overall, 50.7% of patients showed a reduction in eGFR, being 34.6% of patients presenting mild reduction (between 90-60 ml/min/1.73m²) while 16% showed a marked reduction (<60 ml/min/1.73m²). The prevalence of mild reduction in eGFR (between 90-60 ml/min/1.73m²) was higher in those patients with a longer period after infection (6-MPC: 27.7%; 12-MPC: 37.5%; 24-MPC: 46.6%). For those patients with a marked reduction in eGFR (<60 ml/min/1.73m²), the prevalence was not different between the groups (6-MPC: 16.7%; 12-MPC: 16.7%; 24-MPC: 13.3%). Overall, 50.6% of patients scored on the tubular injury score, which considered changes in albuminuria, urinary excretion of β2-microglobulin and/or KIM-1. Conclusion: Data suggests that glomerular injury is progressive and more prevalent over time while tubular injury, present in all groups, tends to be less prevalent over time. Our results reinforce the importance of long-term monitoring of renal biomarkers in patients infected with COVID-19. Support: FAPERJ, CNPq, CAPES Protocol: CAAE: 53517521.6.0000.5257</p>

Title	Deletion of proximal tubule dipeptidyl peptidase 4 attenuates angiotensin II-induced blood pressure rise and enhances NHE3 phosphorylation at serine 552 in the kidneys of male and female mice
Authors	FLAVIA LETICIA MARTINS, JOÃO CARLOS RIBEIRO SILVA, RAVI NISTALA, ADRIANA CASTELLO COSTA GIRARDI
Affiliations	Laboratório de genética e cardiologia molecular, InCor, HC, FMUSP, Center of Precision Medicine, CPM, MU, Institute For Human Performance, UMU
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Dipeptidyl peptidase 4 (DPP4) associates with the Na⁺/H⁺ exchanger isoform 3 (NHE3), and DPP4 inhibitors decrease NHE3-dependent sodium reabsorption in the renal proximal tubule. Angiotensin II (Ang II) is a key mediator of renal sodium and water retention, partly through activation of proximal tubule NHE3. Recent studies suggest a potential crosstalk between Ang II/AT1R activation and DPP4 activity, but the effect on renal sodium handling and blood pressure remains unclear. Objective: This study hypothesized that specific deletion of DPP4 in the renal proximal tubule mitigates Ang II-induced blood pressure elevation in male and female mice, potentially due to NHE3 downregulation in the renal proximal tubule. Methods: Male and female mice with proximal tubule (PT)-specific or global DPP4 knockout (ACUC32701), along with wild-type controls (C57BL/6) and 11-weeks-old, were acutely administered either Ang II (1000 ng/kg/min) or saline. Blood pressure was measured before and one hour after Ang II administration using tail-cuff plethysmography. Kidneys were then collected for protein analysis. Results: Acute Ang II stimulation increased DPP4 activity in both male (PT-specific: 167±7 vs. 100±6 %wild-type, P<0.0001, and global DPP4: 153±3 vs. 100±2 %wild-type, P<0.0001) and female (PT-specific: 160±6 vs. 100±4 %wild-type, P<0.0001, and global DPP4: 131±5 vs. 100±2 %wild-type, P<0.001) wild-type mice. Blood pressure did not significantly differ between male and female wild-type and their respective PT-specific or global DPP4 knockout mice. However, both male and female PT-specific (male: 17±1 vs. 29±1 mmHg, P<0.0001 and female: 20±1 vs. 28±2 mmHg, P<0.01) or global DPP4 (male: 24±1 vs. 34±2 mmHg, P<0.0001 and female: 25±2 vs. 32±3 mmHg, P<0.05) knockout mice showed a reduced blood pressure response to acute Ang II administration compared to wild-type counterparts. Phosphorylation of NHE3 at serine 552 (pS552-NHE3), indicative of NHE3 inhibition, was higher in wild-type females than males (wild-type PT-specific: 158±12 vs. 100±5 %wild-type male, P<0.01, and wild-type global DPP4: 271±17 vs. 100±3 %wild-type male, P<0.0001). Notably, pS552-NHE3 levels were higher in both male and female PT-specific (male: 247±6 vs. 100±5 %wild-type, P<0.0001, and female: 196±6 vs. 100±3 %wild-type, P<0.0001) or global DPP4 (male: 498±25 vs. 100±3 %wild-type, P<0.0001, and female: 344±18 vs. 100±3 %wild-type, P<0.0001) knockout mice compared to wild-type controls. Additionally, the increase in pS552-NHE3 one hour after Ang II administration was greater in PT-specific (male: 331±11 vs. 242±14 %wild-type, P<0.0001, and female: 291±11 vs. 193±18 %wild-type, P<0.0001) or global DPP4 (male: 716±32 vs. 469±23 %wild-type, P<0.0001, and female: 471±23 vs. 316±22 %wild-type, P<0.0001) knockout mice of both sexes compared to wild-type animals. Ang II-induced DPP4 activity was higher in male wild-type mice than females (153±3 vs. 131±5 %wild-type saline male, P<0.01). Conclusion: In conclusion, our data suggest that DPP4 absence reduces Ang II-induced blood pressure rise, possibly via Ang II/AT1R signaling pathways affecting NHE3 phosphorylation. These effects were more pronounced in males. The similarity in responses between PT-specific and global DPP4 knockout mice underscores the role of proximal tubule DPP4 in regulating blood pressure and NHE3 in response to Ang II. Support: FAPESP, 2021/14534-3 e NIH/NIDDK-5K08DK115886 Protocol: (ACUC32701)</p>

Title	Alta dose de apelina-13 exógena não previne a lesão renal aguda induzida por isquemia e reperfusão
Authors	GUILHERME LOPES GONÇALVES, JULIANA MARTINS DA COSTA PESSOA, MARIANA CHARLEAUX DE PONTE, MARIA OLIVEIRA DE SOUZA
Affiliations	Fisiologia e Biofísica, USP
Session	5-Fisiologia Renal
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A lesão renal aguda (LRA) isquêmica representa uma condição clínica desafiadora e potencialmente grave, caracterizada pela redução abrupta do fluxo sanguíneo renal. O sistema apelinérgico desempenha papel crucial na fisiologia cardiovascular e no balanço hidroeletrólítico, sendo recentemente objeto de estudos relacionados aos rins. Embora a apelina-13 tenha demonstrado resultados positivos na atenuação de efeitos específicos como a lesão mitocondrial, a lesão endotelial e os fatores pró-fibróticos, os mecanismos tubulares envolvidos e os potenciais efeitos adversos ainda não são claros. Objective: Sendo assim, o presente estudo tem como objetivo investigar os efeitos da via de sinalização ativada por apelina-13 sobre o a LRA induzida por isquemia e reperfusão (I/R) utilizando abordagens in vivo. Methods: Todos os protocolos foram aprovados pelo comitê de ética em experimentação animal. Camundongos machos C57Bl/6 com idade de 8 semanas foram previamente tratados com veículo (PBS 1X, pH 7,2) ou alta dose de apelina-13 (200 µg/kg/dia, dividida em duas administrações intraperitoneais ao dia (12/12 h) por 5 dias e submetidos à cirurgia de I/R renal ou sham no quarto dia. A eutanásia foi realizada após 48 h. Foram avaliados parâmetros histológicos na coloração de HE, assim como a concentração de creatinina e ureia no plasma, além de expressão de KIM-1, NGAL, megalina, Ki67 e pERK 1/2 por imuno-histoquímica. A análise estatística foi realizada por ANOVA two-way seguida de pós teste Tukey. Os resultados são expressos como média ± desvio padrão. Results: O tratamento com alta dose de apelina-13 no grupo apelina-13 + I/R não atenuou a lesão tubular e sustentou o nível de creatinina [mg/dl; Veículo/Sham (0,225 ± 0,06); Apelin-13/Sham (0,215 ± 0,04); Veículo/I/R (0,423 ± 0,10); Apelin-13/I/R (0,387 ± 0,21), n = 6 a 8]) e ureia [mg/dl; Veículo/Sham (68,3 ± 12,2); Apelin-13/Sham (59,2 ± 7,38); Veículo/I/R (183,4 ± 70,3); Apelin-13/I/R (166,4 ± 100,4), n = 6 a 11)] plasmáticas. O tratamento com alta dose de apelina-13 no grupo submetido à I/R manteve o índice de marcação de imuno-histoquímica de KIM-1 [unidades arbitrárias (ua); Veículo/Sham (1542 ± 2042); Apelin-13/Sham (667 ± 1433); Veículo/I/R (20058,1 ± 18379); Apelin-13/I/R (12970 ± 10696), n = 7 a 11]) e NGAL [ua; Veículo/Sham (3593 ± 4194); Apelin-13/Sham (2231 ± 2326); Veículo/I/R (20291 ± 2671); Apelin-13/I/R (16915 ± 7546), n = 7 a 11]) em relação ao grupo veículo + I/R. O tratamento com apelina-13 no grupo submetido à I/R também não reestabeleceu a marcação de megalina quando comparado ao grupo veículo + I/R [ua; Veículo/Sham (46726 ± 13954); Apelin-13/Sham (39136 ± 14348); Veículo/I/R (17686 ± 7606); Apelin-13/I/R (25071 ± 18031), n = 7 a 11]). Além disso foi observado que o grupo apelina-13 + I/R apresentou significativamente uma menor marcação de Ki67 [células/campo; Veículo/Sham (2,1 ± 1,2); Apelin-13/Sham (0,6 ± 0,5); Veículo/I/R (91 ± 12); Apelin-13/I/R (17 ± 14), n = 7 a 11]) e pERK 1/2 [ua; Veículo/Sham (3449 ± 526); Apelin-13/Sham (3283 ± 931); Veículo/I/R (6354 ± 1881); Apelin-13/I/R (2660 ± 1083), n = 6 a 11]) quando comparado ao grupo veículo + I/R, o que sugere comprometimento no processo de reparo tubular após a isquemia. Conclusion: Em conjunto, esses dados preliminares fornecem insights importantes para a compreensão do papel do sistema apelinérgico na LRA. Esses achados podem ter implicações clínicas relevantes, destacando a complexidade dessa condição e a necessidade de prevenções eficazes para a LRA. Support: FAPESP Protocol: CEUA ICB/USP nº 2717131222</p>

Title	Blockade of oxytocinergic signaling in the brainstem did not change the hypercapnic ventilatory response in male and female mice
Authors	MICHAELA TAMEIROS CONDÉ, EMMANUEL VERÍSSIMO DE ARAÚJO, ANA CAROLINA THOMAZ TAKAKURA, BÁRBARA FALQUETTO, THIAGO DOS SANTOS MOREIRA
Affiliations	Departamento de Fisiologia e Biofísica, USP, Departamento de Farmacologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Oxytocin receptor densities have been shown to be higher in some brain regions in females compared to males, which might reflect the importance of oxytocin in maternal behaviors. Within the brainstem we have several groups of neurons involved in respiratory regulation. A significant proportion of them are glutamatergic neurons, express the transcription factor Phox2b, receive oxytocinergic projections, and play a relevant role in the process of central chemoreception and respiratory control. In addition, these neurons are also regulated by afferent information from peripheral chemoreceptors and by various synaptic inputs from other brain nuclei. Objective: The present study sought to investigate the contribution of oxytocinergic modulation in the brainstem region to control the baseline respiratory activity and the ventilatory response to hypercapnia (HCVR) in both male and female mice. Methods: Male and female Oxt-cre mice with stainless steel cannula implanted into the 4th brain ventricle (4th V) were used for injection [beta-Mercapto-beta,beta-cyclopentamethylenepropionyl, O-Me-Tyr2, Orn8]-Oxytocin (a oxytocin receptor antagonist, 1 µg/µl, 1 µl), an oxytocin antagonist. Respiratory rates were measured in mice subjected to ambient air, and hypercapnic air. Results: Injection of [beta-Mercapto-beta,beta-cyclopentamethylenepropionyl, O-Me-Tyr2, Orn8]-Oxytocin (a oxytocin receptor antagonist, 9 mM, 100 nl) into the 4th V did not change baseline VE both in male (2 ± 0.76, vs. saline: 3 ± 0.68 µl/g/min) and female (5 ± 1.8, vs. saline: 5 ± 1.9 µl/g/min) mice. The injection of the antagonist into the 4th V did not change the HCVR (FICO₂ = 0.07) in female (11.8 ± 3.5, vs. saline + CO₂: 13.8 ± 6.1 µl/g min, $p = 0.035$), and in male (5.6 ± 3.4, vs. saline + CO₂: 8 ± 3.9 µl/g/min, $p = 0.004$) mice. However, the HCVR in female is higher than male mice (13.8 ± 6.1, vs. male: 8 ± 3.9 µl/min/g). Conclusion: These results demonstrate that the blocking of oxytocinergic receptor at the level of brainstem did not have a significant impact on the hypercapnic ventilatory response in both conscious male and female mice, suggesting that oxytocin signaling to the brainstem is not crucial to control breathing output. Support: FAPESP, CAPES and CNPq/PROEX Protocol: 5585060323</p>

Title	PHYSICAL EXERCISE PREVENTS NEURODEGENERATION IN CARDIORESPIRATORY NUCLEI AND BREATHING DEFICITS IN THE 6-OHDA MODEL OF PARKINSON'S DISEASE
Authors	PAMELA OJUORUN SANTOS MEDEIROS, LUIZ FERNANDO DE ARAUJO TRINDADE PEDRÃO, BÁRBARA FALQUETTO
Affiliations	Farmacologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disease characterized by the loss of dopaminergic neurons in the Substantia Nigra (SN). There are several motor symptoms, such as respiratory problems. It's also known that there is neurodegeneration in cardiorespiratory regions such as nucleus of solitary tract (NTS), retrotrapezoid nucleus (RTN), preBöttinger complex (preBötC), rostral ventral respiratory group (rVRG) and nucleus ambiguus (NA), noted in 6-hydroxydopamine (6-OHDA) PD animal model, causing a high loss in cardiorespiratory function. Objective: Evaluate the effects of the physical exercise (EX) preventing the neurodegeneration of cardiorespiratory nuclei and the cardiorespiratory deficits in 6-OHDA animals. Methods: 6-OHDA (24ug/ul) or vehicle was injected into male adult rat's striatum. EX was performed 12 days after PD induction (n=42), for 28 days. On the 40th day, the animals were submitted to the whole-body plethysmography, perfusion, and brain dissection to perform immunohistochemistry. All animals were submitted to tyrosine hydroxylase (TH)-immunoreactivity (ir) to evaluate SN and phox2b and ChAT-ir to evaluate cardiorespiratory nuclei degeneration. Two-way ANOVA followed by Newman Keuls1's was applied with $p < 0.05$. Results: 6-OHDA reduced TH+ neurons in SN and EX did not reverse it as expected, confirming the PD model (vehicle: $918,2 \pm 176,1$; 6-OHDA: $235,8 \pm 71,5$; vehicle + EX: $810,4 \pm 136,9$; 6-OHDA + EX: $189,5 \pm 46,0$ neurons, $F(1,33) = 194,2$; $p < 0,0001$). At normoxia, 6-OHDA animals showed reduced respiratory frequency (fR), prevented with PE (vehicle: $98,8 \pm 5,6$; 6-OHDA: $60,9 \pm 3,3$; vehicle + EX: $87,9 \pm 12,5$; 6-OHDA + EX: $85,9 \pm 9,3$ bpm, $F(1,33) = 35,53$; $p < 0,0001$). The same results were observed during hypercapnia for fR (vehicle: $150,1 \pm 17,9$; 6-OHDA: $125,3 \pm 4,0$; vehicle + EX: $159,1 \pm 13,3$; 6-OHDA + EX: $154,7 \pm 14,3$ bpm, $F(1,33) = 8,536$; $p = 0,0062$). Moreover, at normoxia, it was not observed changes in minute (VE) and in tidal volume (VT), neither at hypercapnia. It was observed a reduction in phox2b neurons in NTSc (vehicle: $135,55 \pm 20,15$; 6-OHDA: $52,37 \pm 7,98$; vehicle + EX: $124,82 \pm 23,52$; 6-OHDA + EX: $87,34 \pm 13,26$ neurons, $F(1,17) = 60,34$, $p < 0,0001$), NTSi (vehicle: $917,35 \pm 128,95$; 6-OHDA: $548 \pm 64,27$; vehicle + EX: $1009,55 \pm 229,01$; 6-OHDA + EX: $744,3 \pm 42,44$ neurons, $F(1,17) = 46,93$, $p < 0,0001$) and RTN (vehicle: $52,47 \pm 7,57$; 6-OHDA: $21,01 \pm 12,09$; vehicle + EX: $57,61 \pm 16,35$; 6-OHDA + EX: $44,44 \pm 4,9$ neurons, $F(1,13) = 23,05$, $p = 0,0003$) in sedentary groups and it was prevented with EX. Neurodegeneration was also seen in ChAT neurons in nucleus ambiguus, prevented with EX (vehicle: $61,2 \pm 10,7$; 6-OHDA: $34,5 \pm 7,6$; vehicle + EX: $74,9 \pm 14,3$; 6-OHDA + EX: $48,6 \pm 13,4$ neurons, $F(1,14) = 33,58$, $p < 0,0001$). Conclusion: The respiratory impairments and the neurodegeneration observed in medullary cardiorespiratory neurons in the PD 6-OHDA animal model were prevented by EX. Support: CAPES, 88887.684788/2022-00, FAPESP (2021/08562-4) Protocol: CEUA: 1342290421</p>

Title	Assessment of Pulmonary Function and Levels of Inflammatory and Immunological Biomarkers in Asthmatic Children and Adolescents Residing in the Municipality of Vitória, ES
Authors	MAIANE FERNANDES FERREIRA, MARIA EDUARDA DE SOUZA BARROSO, EDGAR HELL KAMPKE, LETICIA VERONÉS MARSAGLIA, HELLEN SILER VASCONCELLOS, JOSÉ GERALDO MILL, SILVANA SANTOS MEYRELLES
Affiliations	Laboratório de Fisiologia Integrativa, UFES
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epidemiological have indicated a high prevalence of asthma among Brazilian children and adolescents. Asthma manifests as a respiratory tract disease characterized by the excessive production of antibodies, such as IgE, chronic inflammation involving eosinophil and lymphocyte proliferation, elevated levels of Reactive Oxygen Species (ROS), and airway constriction in response to various stimuli, including allergens, pollution, physical exercise, and cold air. Objective: This study aims to assess the levels of inflammatory activity and ROS, markers of allergic response, and pulmonary function in children and adolescents diagnosed with asthma residing in the city of Vitória, ES. Methods: This is an analytical, observational, cross-sectional study involving a sample of 57 children and adolescents residing in the municipality of Vitória, ES. Participants both male and female, aged 6 to 15 years, were selected regardless of their clinical diagnosis of asthma. Patients were divided into two groups: Control group (n= 27) and Asthma group (n= 30). Pulmonary function in asthmatic patients was assessed using spirometry to measure Forced Expiratory Volume in the first second pre-bronchodilator (FEV1). Additionally, blood samples were collected to quantify the number of eosinophils (EOS) and levels of Immunoglobulin E (IgE). Additionally, levels of ROS, including superoxide and hydrogen peroxide, were assessed in blood cells using flow cytometry. This was achieved using fluorescent probes, specifically dihydroethidium (DHE) for superoxide and dihydrochlorofluorescein (DCF) for hydrogen peroxide. This study was approved by the Research Ethics Committee (CEP) under opinion number 3.546.535. Statistical analyses were conducted and visualized using GraphPad Prism version 9.0. Data were expressed as median [25%-75% percentile]. Data between groups were compared using the non-parametric Mann-Whitney test, with a level of statistical significance set a $p < 0.05$. Results: Children in the Asthma group exhibited a significant decrease ($p < 0.05$) in pulmonary function, with FEV1 measured at 1.520 [1.315 – 1.655], compared to control children, who demonstrated an FEV1 of 2.460 [1.670 – 3.070]. Similarly, in asthmatic children, levels of EOS 483 [200 – 946.8] and IgE 638.5 [212 – 1,201] were significantly higher ($p < 0.05$) compared to the control group, which had EOS 237 [157 – 410] and IgE 138 [49.4 – 480]. Regarding ROS results, we observed a significant increase ($p < 0.05$) in DCF levels 3.651 [2.673 – 4.570] in asthmatic children compared to non-asthmatic children 2.849 [1.910 – 3.403]. However, we did not observe differences in DHE levels between the asthma group 1.257 [1.106 – 1.346] and the control group 1.129 [973 – 1.302]. Conclusion: The findings of this study underscore a complex interplay between inflammation, allergic response, and reduced pulmonary function in children and adolescents diagnosed with asthma, highlighting the necessity of a comprehensive approach in disease management. Thus, this research may serve as a steppingstone for future studies and aid in the formulation of public policies in the city of Vitória aiming disease control and improving disease monitoring. Finally, this study may help optimize healthcare services provided within the municipality. Support: Coordination for the Improvement of Higher Education Personnel (CAPES) Protocol: 3,546,535.00</p>



Title	OMEGA-3 TREATMENT PREVENTS FUNCTIONAL AND NEUROANATOMICAL RESPIRATORY CHANGES IN A PARKINSON'S DISEASE ANIMAL MODEL
Authors	TAINÁ OLIVEIRA MACEDO, NICOLE CASTRO MIRANDA, LAIS MARIA CABRAL, THIAGO DOS SANTOS MOREIRA, ANA CAROINA TAKAKURA
Affiliations	Farmacologia, USP, Fisiologia e Biofísica, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by the loss of dopaminergic neurons in the substantia nigra (SN), which leads to its classical symptoms. Alongside these symptoms, respiratory impairments have been observed, potentially associated with neuronal degeneration in the ventral respiratory column (VRC) of the brainstem. This degeneration can be triggered by increased oxidative stress and neuroinflammation in the VRC. Therefore, this study aims to investigate the potential of omega-3 fatty acids, known for their antioxidant and anti-inflammatory properties, in alleviating respiratory impairments in an animal model of PD. Objective: Investigate the potential of omega-3 fatty acids, known for their antioxidant and anti-inflammatory properties, in alleviating respiratory impairments in an animal model of PD. Methods: Adult male mice (C57BL/6 lineage, CEUA nº 8760150318) received bilateral injections of either 6-hydroxydopamine (6-OHDA) or vehicle into the striatum to induce the PD model. Five days after the injection, mice were treated with either omega-3 (85 mg/kg/day, for 10 days via gavage) or vehicle. Subsequently, respiratory parameters were measured using whole-body plethysmography, and immunohistochemistry was performed to evaluate neurodegeneration and neuroinflammation in the SN and specific regions of VRC: preBötzing Complex (preBötC) and retrotrapezoid nucleus (RTN). Results: As expected, animals injected with 6-OHDA exhibited a 76% of reduction of SN dopaminergic neurons (72 ± 5.42 vs. vehicle: 302 ± 4.16 neurons, $p < 0.0001$), 16% of neurokinin 1 receptor (NK1R) density reduction in the preBötC ($26 \pm 1.07\%$, vs. vehicle: $31 \pm 1.32\%$ of density, $p = 0.0337$), and 38% of reduction in phox2b-expressing neurons of the RTN (30 ± 2.85 vs. vehicle: 48 ± 1.32 neurons, $p = 0.0013$). Furthermore, there was a 37% of decrease in astrocyte density within the RTN (19 ± 1.91, vs. vehicle: $30 \pm 0.91\%$ of density, $p = 0.0012$), alongside a 17% of decrease in microglia density in the VRC (0.052 ± 0.001, vs. vehicle: $0.063 \pm 0.002\%$ of cell density, $p = 0.0393$). Additionally, a decrease in resting respiratory rate was observed (161 ± 4.3 vs. vehicle: 183 ± 8.4 breaths/min, $p = 0.0001$). Interestingly, the omega-3 treatment effectively prevented the degeneration of NK1R of preBötC (29 ± 0.71 vs. vehicle: $31 \pm 1.32\%$ of density, $p > 0.05$), phox2b neurons of the RTN (45 ± 2.98 vs. vehicle: 48 ± 1.32 neurons, $p > 0.05$), as well as astrocytes (24 ± 1.81 vs. vehicle: $30 \pm 0.91\%$ of density, $p > 0.05$) and microglia (0.062 ± 0.003 vs. vehicle: $0.063 \pm 0.002\%$ of cell density, $p > 0.05$) densities. Omega-3 treatment was also able to improve breathing impairment (185 ± 9.7 vs. vehicle: 183 ± 8.4 breaths/min, $p > 0.05$). Conclusion: Our findings highlight the potential of omega-3 treatment as a promising approach for attenuating the respiratory changes observed in an experimental model of PD. Support: FAPESP, CNPq and CAPES. Protocol: CEUA nº 8760150318</p>

Title	Gender-specific Respiratory and Neuroanatomical Impairments in a Mice Model of Parkinson's Disease
Authors	GIOVANNA MATOS RODRIGUES, YASMIN CESTARI AQUINO, THIAGO DOS SANTOS MOREIRA, ANA CAROLINA THOMAZ TAKAKURA
Affiliations	Departamento de Farmacologia, Universidade de São Paulo, Departamento de Fisiologia e Biofísica, Universidade de São Paulo
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's Disease (PD) is a neurodegenerative disorder characterized by dopaminergic neuron declines in the substantia nigra (SN), leading to motor impairments. Besides classical motor symptoms, PD can manifest non-typical symptoms including respiratory dysfunction. PD is observed to be twice as common in men as in women. Studies in male mice suggest that the respiratory deficits seen in PD may be caused by neural damage in the areas of the brain responsible for controlling breathing. Objective: Therefore, our aim was to investigate the influence of sex hormones on neuroanatomical and physiological aspects of respiratory function in PD. Methods: Adult C57BL/6 mice (18-25 g; male: 34 and female: 50; CEUA: 3325170822) were subjected to bilateral ovariectomy (OVX), orchietomy (ORX), or sham surgery. Following a two-weeks recovery period, PD's model was induced by bilateral injections of 6-hydroxydopamine (6-OHDA) or vehicle in the striatum. The efficacy of OVX and ORX was assessed by measuring the weight of the dry uterus and the seminal vesicles adjacent to the anterior portion of the prostate, respectively. Respiratory parameters were measured by whole-body plethysmography and neuroanatomical changes were investigated by immunohistochemistry. All data are presented as the mean \pm standard error of the mean and for each analysis $p < 0.05$ was considered statistically significant. Results: OVX mice that received 6-OHDA in the striatum showed a further reduction in the number of tyrosine hydroxylase-positive (TH+) neurons in the substantia nigra (30.8 ± 1.6 vs. sham+6-OHDA: 63.8 ± 2.4 neurons, $p=0.0014$), in the density of neurokinin 1 receptors (NK1r) in the pre-Bötzing Complex (28.3 ± 0.7 vs. sham+6-OHDA: $33.6 \pm 0.6\%$, $p=0.0060$), and in the number of phox2b-expressing neurons in the Retrotrapezoid Nucleus (35.0 ± 1.8 vs. sham+6-OHDA: 44.3 ± 1.2 neurons, $p=0.0399$). The reduction in resting respiratory frequency was even more pronounced (151.1 ± 2.4 vs. sham+6-OHDA: 161.0 ± 1.2 bpm, $p < 0.0001$). In OVX mice, a significant increase in estrogen receptor alpha was observed throughout the ventral respiratory column. Although ORX did not affect the number of neuronal profiles or the respiratory frequency, it did reduce the number of TH+ cells in the substantia nigra (272.8 ± 5.9 vs. sham: 306.6 ± 8.8 neurons, $p=0.0026$). Conclusion: Our results indicate that OVX enhances neurodegeneration in the substantia nigra, pre-Bötzing Complex, and Retrotrapezoid Nucleus, exacerbating the reduction in respiratory frequency induced by 6-OHDA, suggesting that estrogen plays a neuroprotective role. Support: FAPESP, CNPq and CAPES-PROEX. Protocol: CEUA protocol: 3325170822</p>

Title	Impaired arousal response to hypercapnia in a mouse model of Parkinson's disease
Authors	YASMIN CESTARI AQUINO, NICOLE CASTRO DE SOUZA MIRANDA, LUIZ MARCELO OLIVEIRA, THIAGO MOREIRA, JAN-MARINO RAMIREZ, ANA CAROLINA TAKAKURA
Affiliations	Farmacologia, USP, Fisiologia e Biofísica, USP, Center for Integrative Brain Research, SCRI
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's disease (PD) is marked by a gradual decline in dopaminergic neurons within the substantia nigra (SN). PD patients display classic and non-classic symptoms, such as respiratory deficits and sleep disorders. Arousal, especially during sleep, is crucial for maintaining homeostasis and responding to environmental challenges such as high levels of CO₂ (hypercapnia). Animal model of PD induced by 6-hydroxidopamine (6-OHDA) show a reduction in the resting respiratory rate during sleep, which correlates with neurodegeneration in a key area for central chemoreception (detection of CO₂) and respiratory control, such as the retrotrapezoid nucleus (RTN). Objective: Thus, our aim was to investigate potential changes in the arousal process induced by hypercapnia in 6-OHDA model. Methods: Adult C57BL/6 and Vglut2Ai6 mice (N=29; CEUA: 6641200919; 8760150318) were bilaterally injected with either vehicle or 6-OHDA into the striatum. Ten days later, electroencephalogram (EEG) and electromyography (EMG) recordings were conducted in one group of animals to assess arousal in response to hypercapnia during sleep. Meanwhile, the other group was exposed to a hypercapnic stimulus (7% CO₂; 3 hours) to evaluate neuronal activation in regions related to central chemoreception. For statistical analyses, data were tabulated, presented as mean ± standard error and, for each analysis, the statistical significance index was established at p < 0.05. Results: Our findings revealed a 77% decrease in the number of dopaminergic neurons in the SN of mice that received 6-OHDA (87.1 ± 15.8 vs. sham 380.5 ± 29.7 neurons, p < 0.0001). Moreover, PD animals showed a 40% reduction in fos-activated glutamatergic neurons in the RTN (15.4 ± 4 vs. sham 25.6 ± 3.1 neurons, p < 0.0001) and 34% reduction in fos-activated orexinergic neurons in the lateral hypothalamus (129.7 ± 30.7 vs. sham 196.2 ± 32.3 neurons, p = 0.0044). However, in these animals we observed an increase of 36% and 73% in fos-activated glutamatergic neurons in the nucleus of the solitary tract (236.2 ± 22.9 vs. sham 173.5 ± 10.7 neurons, p = 0.0001) and external lateral parabrachial nucleus (36.7 ± 3.6 vs. sham 21.2 ± 4.1 neurons, p < 0.0001), respectively. These animals also exhibited a 45% of delay in arousal under hypercapnic conditions compared to control animals during non-rapid eye movement sleep (137.5 ± 37.0 vs. sham 95.0 ± 31.9 seconds, p < 0.0001), and the threshold level of CO₂ required for their arousal was 40% higher (6.0 ± 1.2 vs. sham 4.3 ± 1.5 %, p < 0,0001). Conclusion: Therefore, our data suggest a possible impairment of the physiology of arousal in the PD animals induced by 6-OHDA. Support: FAPESP, CNPq, CAPES Protocol: 6641200919; 8760150318</p>

Title	Progesterone and etonogestrel with estradiol increase ventilatory responses to hypercapnia in female rats
Authors	VITORIA SILVA OLIVEIRA, BEATRIZ RODRIGUES APGAUA, ANA CLARA CAMPIDELI-SANTANA, MARISTELA DE OLIVEIRA POLETINI, RAPHAEL ESCORSIM SZAWKA, ROBERTA ARAÚJO-LOPES, GLAUBER DOS SANTOS FERREIRA DA SILVA
Affiliations	Fisiologia e Biofísica, UFMG
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Evidence points to the effects of progesterone on ventilatory responses to CO₂. Furthermore, the progestin desogestrel and its metabolite ETONogestrel (ETO) have a greater affinity for progesterone receptors than the endogenous hormone. Evidence also supports an excitatory role of ETO in respiratory control. ETO's higher affinity could accentuate the effect of increased ventilation in hypercapnic conditions.</p> <p>Objective: We hypothesize that hormonal replacement with progesterone and/or ETO enhances the ventilatory response to hypercapnia. Therefore, we tested the effects of hormonal replacement with progesterone alone (P4; 2.5 mg / 0.2 mL / animal, s.c.) and combined with estradiol (E2; 10 µg/0.1 mL/animal, s.c.), and additionally, we also tested the effects of ETO treatment in the hypercapnic ventilatory responses. Methods: OVX (200, 270g) female rats were divided into two groups: 1) received pre-treatment with E2 (n=10) and 2) received pre-treatment with oil (n=9). After that, both groups received a one-day and three-day treatment with P4. Ventilatory measurements were taken: 1) in diestrus, before treatment; 2) after pre-treatment, 3) 2h after 1-day treatment, and 4) one day after 3-day treatment. To test the effects of ETO we divided the animals (211, 298g) into five groups: 1) oil (n=8); 2) 0.25µg/0.1 mL/ animal (n=9); 3) 2.5µg/0.1 mL/ animal (n=9); 4) 250µg/0.1 mL/ animal (n=9); and 5) 250µg/0.1 mL/ animal + 10 µg/0.1 mL/animal E2 (n=8). The female rats were treated for 21 days and submitted to the whole-body plethysmography method at the end of the treatment. Moreover, immunohistochemistry for assessing progesterone receptors (nPR) was performed in OVX rats treated for 3 consecutive days with E2. Considering previous evidence, the nucleus of the solitary tract (NTS) was the predominant brainstem region assessed. All experiments were approved by animal ethics committee (#87/2018). Results: Our results show that treatment with P4+E2 significantly enhanced the ventilatory response to CO₂ (3-day P4 %VE 309.9±19.6; %FR 168.6±8.1), compared to female rats that received only P4 treatment (P4 + oil; %VE 237.5±12.3, %FR 136.6±6.2). No significant difference was observed in ventilatory parameters between the control and the different doses of ETO. However, the combination with estradiol (ETO + E2) significantly increased the ventilatory responses to CO₂ (% VE 294.3±9.02%). To investigate the putative mechanisms underlying this enhanced hypercapnic VE response, we tested the hypothesis that the progesterone receptor (nPR) is increased in the solitary tract nucleus (NTS), a well-known dorsal brainstem region involved in the central respiratory network. The results showed that animals treated with E2 did increase the expression of nPR in the NTS. Conclusion: In conclusion, in ovariectomized and intact rats, the replacement of P4 or ETO and estradiol respectively (but not P4 or ETO alone), promoted increased ventilatory response to CO₂, suggesting that both hormonal replacements modulate an excitatory response of the respiratory adjustments to hypercapnia. Additionally, we propose that estradiol is necessary to the effects of progesterone in the ventilatory responses to hypercapnia, and the NTS may play an important role in this process, considering the increased nPR in the NTS. Support: This project was funded by CNPQ and FAPEMIG. Protocol: 87/2018</p>

Title	The role of GSK3b in respiratory nuclei in Parkinson`s Disease.
Authors	ESTELA CORREIA LEANDRO DOS SANTOS, PAMELA OJUORUN SANTOS MEDEIROS, LUIZ FERNANDO DE ARAUJO TRINDADE PEDRÃO, BARBARA FALQUETTO
Affiliations	Departamento de Farmacologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introduction: Parkinson`s disease (PD) is a degenerative disease characterized by the loss of dopaminergic neurons in the Substantia Nigra (SN). Its motor symptoms are widely known as bradykinesia and dyskinesia, however it also presents non-classic motor symptoms, such as respiratory dysfunction. In animals injected with 6-OHDA into the striatum, a drug that allows the development of a mimetic model of idiopathic PD, there is a loss of neurons in respiratory nuclei such as the rostral ventral respiratory group (rVRG) and pre-Bötzing (preBötC) and significant loss of chemosensitive neurons in the retrotrapezoid nucleus (RTN) in mice. Studies demonstrate that oxidative stress is a major mechanism to explain these losses. The presence of free radicals leads to a response from immune cells in the central nervous system (CNS), activating microglia and astrocytes that respond by releasing pro-inflammatory agents that are often toxic to neurons. Evaluating the signaling pathways of this inflammatory response, there is the presence of GSK3-β, glycogen synthase kinase 3β, which when autophosphorylated on the Tyr216 residue (activated GSK-3β) has a close relationship with pro-apoptotic pathways. Therefore, its inhibition can protect dopaminergic neurons from the harmful agents of neuroinflammation, and thus can also protect the respiratory nuclei from degeneration in PD. Objective: Aim: To evaluate the participation of GSK-3β in cell death and survival pathways in the respiratory nuclei in the 6-OHDA model of PD in mice. Methods: Methods: 6-OHDA (10μg/μl) or vehicle was injected into the striatum of male mice (n=15, ~22g) and after 6 days they were euthanized, and the brainstem was removed and sliced in the microtome. The tissues were dissected, and the respiratory nuclei collected for Western Blot (WB). The mesencephalic region was divided into 30 μm thick sections, and the tissues underwent tyrosine hydroxylase (TH)-immunoreaction to evaluate the SN to confirm the PD model. Student T test was applied with p<0.05. Results: Results: 6-OHDA reduced TH+ neurons in SN confirming the PD model (6-OHDA: 143,5 \pm 27,1 vs. Vehicle: 475,83 \pm 81.8 neurons, T10=9,443; p>0,0001). The WB analysis show an increase in GSK3β in the RTN (6-OHDA: 1,25 \pm 0,14 vs. Vehicle: 0,86 \pm 0,30, T8=2,375; p=0,0449) and a reduction in rVRG + preBotC (6-OHDA: 0,60 \pm 0,28 vs. Vehicle: 0,92 \pm 0,30, T10=2,362; p=0,0398). Furthermore, analyses showed a reduction in pGSK-3βTyr216 in the rVRG + preBötC nuclei (6-OHDA: 0,67 \pm 0,20 vs. Vehicle: 1,03 \pm 0, 35; T13=2,418; p=0,0310), but not in RTN (6-OHDA: 1,53 \pm 0,77 vs. Vehicle: 1,03 \pm 0, 29; T9=1,576; p=0,1494). Conclusion: Conclusion: The GSK-3β showed a reduction in its levels in the rVRG + preBötC nuclei and an increase in the RTN after 6 days of PD induction, followed by the reduction also in pGSK-3βTyr216only in the rVRG + preBotC, which already has a known role in pro-apoptotic pathways. These findings indicate that the GSK-3β pathway might play a role in the PD` neurodegeneration of respiratory nuclei, with its involvement varying depending on the specific respiratory nuclei and the progression over time. Support: Financial support: FAPESP (2023/09695-3) Protocol: CEUA: 7992180820</p>

Title	Inhibition of glutamatergic interneurons of the lateral parafacial region of mice reduced the ventilatory response to hypercapnia
Authors	JULIANA REIS SOUZA, NATHALIA SALIM, RENATO WILLIAN M. SÁ, BENEDITO HONÓRIO MACHADO, DAVI JOSÉ DE ALMEIDA MORAES
Affiliations	Fisiologia e Biofísica, USP, Fisiologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The lateral parafacial region (pFL) contains excitatory neurons and interneurons with a population of glutamatergic neurons that are silent under resting, but become active at the end of expiration, simultaneously with active expiration, in response to hypercapnia/acidosis. However, the role of pFL glutamatergic interneurons in regulating pulmonary ventilation during hypercapnia is unclear. Objective: To evaluate the effects of pFL glutamatergic interneurons inhibition of mice on ventilatory parameters during resting and hypercapnia. Methods: Mice expressing Cre recombinase in glutamatergic neurons (VGLUT2) received unilateral injections into the pFL region of a Cre-dependent retrograde virus to express Flp recombinase, and a Cre- and Flp-dependent virus to express the inhibitory DREADDs (hM4D-Gi) only in glutamatergic interneurons. Using whole-body plethysmography, we measured respiratory frequency (fR), tidal volume (VT), pulmonary ventilation (VE), duration of respiratory cycle, inspiration (DI) and expiration (DE) at normocapnia and hypercapnia (7% CO₂) in conscious freely moving mice before and after activating hM4D-Gi (JHU 0.1 mg/kg). Results: We found a high number of glutamatergic interneurons (68 ± 11; n=18) in the pFL region. At normocapnia, JHU did not change the ventilatory parameters [(ΔfR: -2.4 ± 51 vs 0.2 ± 48cpm) (ΔVT: -1.3 ± 4 vs $-0.2 \pm 1$$\mu$L.g⁻¹) ($\Delta$VE: -39 ± 1198 vs $-71 \pm 607$$\mu$L.g⁻¹.min⁻¹) ($\Delta$Cycle duration: 5.3 ± 41 vs -1.9 ± 45ms) (ΔDI: 6.6 ± 14 vs 6 ± 20ms) (ΔDE: -1.3 ± 35 vs -1.6 ± 31ms)] or the respiratory variability (0.018 ± 0.023 vs 0.011 ± 0.011 cm²; p>0.9) of VGLUT2(cre/cre+hM4D-Gi) (n=18) and VGLUT2(cre/cre) mice (n=12). On the other hand, JHU injection reduced the hypercapnia-induced ventilatory responses of VGLUT2(cre/cre+hM4D-Gi) (n=18) mice when compared to VGLUT2(cre/cre) (n=9) [(ΔfR: 67 ± 69 vs 157 ± 41cpm; p=0.0003) (ΔVT: 3.8 ± 5 vs $11.9 \pm 4$$\mu$L.g⁻¹; p<0.0001) ($\Delta$VE: 2052 ± 2197 vs $5374 \pm 1773$$\mu$L.g⁻¹.min⁻¹; p<0.0001) ($\Delta$cycle duration: -46 ± 50 vs -107 ± 49ms; p=0.002) (ΔDI: -3.7 ± 16 vs -21 ± 19ms; p=0.011) (ΔDE: -42 ± 41 vs -86 ± 36ms; p=0.01)]. However, the reduction in breathing interval variability in response to hypercapnia was similar between VGLUT2(cre/cre+hM4D-Gi) and VGLUT2(cre/cre) mice (0.006 ± 0.007 vs 0.004 ± 0.003 cm²; p>0.9). Conclusion: The pFL glutamatergic interneurons are important for the ventilatory response of mice to hypercapnia. Support: FAPESP, CNPq and CAPES. Protocol: CEUA #1143/2022</p>

Title	“Role of BK channels in the respiratory response to CO ₂ /pH during development in mice”
Authors	BIANCA DE AVILA MARTINS, LUIS GUSTAVO ALEXANDRE PATRONE, MARIANA BERNARDES-RIBEIRO, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI
Affiliations	Departamento de Morfologia e Fisiologia Animal, UNESP, UNIVERSIDADE ESTADUAL PAULISTA JÚLIO DE MESQUITA FILHO
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Calcium-activated potassium (BK) channels are found in nearly all mammalian tissues and play a crucial role in suppressing action potential excitability and the release of signaling molecules contained in vesicles. In the central nervous system, BK channel also provides a negative feedback mechanism to regulate local increases in intracellular Ca²⁺ concentrations. In neurons, these channels regulate the time and duration of Ca²⁺ influx, thereby influencing the firing rate (FR). Our laboratory demonstrated the expression of BK channels in the Locus Coeruleus (LC), and their involvement in the response of LC neurons to hypercapnic acidosis which leads to an increase in intracellular Ca²⁺ levels and subsequently, an elevation in the FR and possibly an increase in noradrenaline release in neonate rats. However, in older animals, the density of BK channels increases in LC cells reducing CO₂/pH chemosensitivity. This increased density of BK channels acts as “braking pathway” by facilitating K⁺ outflux under hypercapnic acidosis, leading to neuronal hyperpolarization and subsequent reduction in FR. However, the influence of these channels on the respiratory response to hypercapnia is not yet known. Objective: The aim of this study is to investigate the participation of BK channels in the respiratory and metabolic control during exposure to normocapnic and hypercapnic air (7% CO₂), during development in mice in postnatal ages: P0-1, P6-7, P12-13. Methods: To this end thirty-two mice were used, 13 male and 19 female, divided in three different genotypes: knockout (KO; n=10), intermediate (HET; n=13) and wildtype (WT; n=9). Each animal was consistently monitored throughout its development. Ventilation (VE), tidal volume (VT) and respiratory frequency (fR) and O₂ consumption (VO₂) and respiratory equivalent (VE/VO₂) were recorded in mice (Ethics Committee Protocol CEUA/FCAV-UNESP: 9486/22), that were submitted to a plethysmography test, in a whole-body closed system to obtain these parameters. The respiratory and metabolic variables were compared between the groups by two-way ANOVA, comparing treatments (genotype) and the exposure condition (normocapnia or hypercapnia), with T-student tests. Results: Our data showed an increased VE in female KO mice of postnatal ages 6-7 compared to WT and HET group during hypercapnic exposure (WT: 4.04 ± 0.55 and HET: 3.70 ± 0.49 vs KO: 5.09 ± 0.33 mL.Kg⁻¹.min⁻¹), and in P12-13 (WT: 5.24 ± 0.72 and HET: 5.04 ± 0.68 vs KO: 6.74 ± 0.67 mL.Kg⁻¹.min⁻¹), possibly due to an increase in VT (WT: 0.0183 ± 0.0020 and HET: 0.0186 ± 0.0026 vs KO: 0.0219 ± 0.0021 mL.Kg⁻¹), also during hypercapnic exposure. As to metabolism, the female KO group increased its VO₂ in P12-13 (WT: 0.410 ± 0.0051 and HET: 0.0374 ± 0.0042 vs KO: 0.0493 ± 0.0061 mL.g⁻¹.min⁻¹) and showed a higher VE/VO₂ in P0-1 when compared to other groups (WT: 46.7 ± 7.6 and HET: 58.9 ± 10.7 vs KO: 70.2 ± 29.5) during hypercapnic exposure. The data didn’t show other significant results concerning male groups or other variables. Conclusion: These findings suggest that BK channels play an important role in ventilatory responses elicited by CO₂ during development in females, but not in males. Support: CNPq and FAPESP. Protocol: 9486/22</p>

Title	Ventilatory Responses To Hypercapnia After Recurrent Seizures In Adult Rats: A State-Dependent Study
Authors	DAFNE MONTEIRO DE CARVALHO FREIRE, HANNA LURY UMEZU, GLAUBER DOS SANTOS FERREIRA DA SILVA, VICTOR RODRIGUES SANTOS
Affiliations	Departamento de Fisiologia e Farmacologia, UFMG, Morfologia, UFMG
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy is a highly prevalent disease, affecting approximately 50 million people, being one of the most common neurological diseases in the world (WHO, 2024). Epilepsy is characterized by recurrent and spontaneous seizures and is a risk factor for premature death. Convulsive seizures are characterized by abnormal and excessive neuronal activity, which can spread to other brain regions. Respiratory changes during ictal events (seizures) are well described in the literature, however, changes in the post-ictal period and in the case of chronic recurrent seizures are not yet well understood. Objective: The present work seeks to study the consequences of recurrent seizures on ventilatory responses to hypercapnia, and possible changes in the CO₂ chemoreception in the different phases of the sleep-wake cycle. Methods: Adult male Wistar rats (160-390g) were used, and the seizures were induced by a chemical model with Pentylentetrazole (PTZ, Sigma-Aldrich). The PTZ (GABAA antagonist) is widely used and induces severe seizures (after sensitization) by recurrent application (i.p.) of subconvulsant doses. The PTZ was given at a dose of 40 mg/kg (dissolved in 0.9% sterile saline) on alternate days until the 10th dose. To assess the sleep-wake state of the animals, cortical electroencephalogram (EEG) and neck electromyogram (NeckEMG) electrodes were surgically implanted. During and after the PTZ injection protocol, the ventilatory response of all animals to hypercapnia (7% CO₂) was analyzed (in a state-dependent manner) using whole-body plethysmography. Data are expressed as mean ± SEM. Results: All animals presented ventilatory response to CO₂. However, the results indicate that repeated seizures elicited a reduced V_e response to hypercapnia during wakefulness (243.76 ± 14.09) as well as during NREM sleep (273.5 ± 19.79), compared to control group (335.1 ± 10.5; 373.78 ± 19.8). During NREM sleep, there is a decrease in both respiratory frequency (Rf) and tidal volume (VT) (144.8 ± 6.18; 186.38 ± 7.54, respectively), while during wakefulness we can observe a significant decrease only in RF (131.37 ± 5.73). There was also an increase in inspiratory duration (Ti) and expiratory duration (Te) during sleep in hypercapnia (77.75 ± 3.14; 64.77 ± 3.76, respectively), but especially during wakefulness (95.17 ± 2.97; 63.51 ± 3.16), an indicator of independent mechanisms of the respiratory control in different phases of sleep-wake cycle. Conclusion: In conclusion, the results suggest that chronic recurrent seizures induced by PTZ caused a change in the animals` ventilation pattern and promoted an attenuated response to hypercapnic stimulus in both sleep-wake phases. Support: FAPEMIG; CNPq; CAPES Protocol: CEUA 279/2022</p>



14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	Oxytocinergic signaling contributes to breathing regulation in the retrotrapezoid nucleus
Authors	PHELIPE EDUARDO SILVA, ANA CRISTINA TAKAKURA, DANIEL K MULKEY, THIAGO SANTOS MOREIRA, EMMANUEL VERISSIMO DE ARAUJO
Affiliations	Departamento de fisiologia e biofísica, USP, Departamento de farmacologia, USP, Department of Physiology and Neurobiology, UCONN
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The RTN is a small group of brainstem neurons that are activated by elevations in CO₂ levels and regulates several aspects of the breathing cycle. Evidence also indicates that RTN neuronal activity can be modulated by several peptidergic signaling; however, the extent to which oxytocinergic signaling contributes to chemoreception and breathing regulation at the RTN level is not clear. Objective: evaluated whether oxytocinergic signaling within the RTN region influences breathing activity in vitro and in vivo.</p> <p>Methods: Male or female C57B6/J, Phox2b-dtomato or Oxt-cre, Ai32 mice [P7-11 (neonate) or P100 (adult)] were used (CEUA-ICB/USP: nº 9750170720). Results: In brain slices, cellattached recordings of membrane potential of RTN chemosensitive cells show that the oxytocin agonist (TGOT: 2 nM) produced an increase in the firing rate (3.93 ± 0.33 vs. baseline: 1.84 ± 0.32 Hz). The increase in firing rate elicited by TGOT was retained in the presence of synaptic blockade (2.04 ± 0.32 vs ΔTGOT: 1.82 ± 0.19 Hz). In vivo, TGOT (1 μM, 30 nL) injection or optogenetic stimulation of oxytocinergic terminals at the RTN region produced an increase in intercostal electromyography (IntEMG) amplitude (TGOT: 16.3 ± 10.9 vs. saline: $2.7 \pm 4.2\%$ and optogenetic stimulation: $18.7 \pm 8.3\%$ of baseline) without changing IntEMG frequency. Conclusion: Our data suggest that oxytocinergic signaling plays an excitatory effect relevant to breathing activity in the RTN region. Support: FAPESP, CNPq, CAPES-PROEX Protocol: CEUA-ICB/USP: nº 9750170720</p>



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14 a 17 de Setembro de 2024
 Hotel Glória Caxambu Resort & Convention

Title	Are long COVID symptoms related to respiratory dysfunction? An observational study
Authors	GRAZELLE MARIA SILVA PEREIRA DE MORAES, JESSICA FABIA POLESE, JOSÉ GERALDO MILL
Affiliations	Programa de Pós Graduação em Ciências Fisiológicas, Universidade Federal do Espírito Santo
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Long COVID is a condition that appears three months after a history of COVID-19 infection, with symptoms that last at least two months and cannot be explained by an alternative diagnosis. Dyspnea and fatigue are among the most common symptoms. (Lancet Infect Dis. 22:102, 2022) Objective: The aim of this study was to investigate potential lung and respiratory muscle dysfunction in participants of the ELSA-Brazil study with and without a history of COVID-19 infection. Methods: An observational and cross-sectional study was carried out during the 4th wave of exams in ELSA-Brazil participants attending the Investigation Center of Vitória, ES. Participants with or without COVID-19 history were invited to respond to a structured questionnaire to obtain data of previous comorbidities and history of clinical complaints. Respiratory function was assessed with spirometry and respiratory muscle strength with manovacuometry. Data are reported as percentage and mean \pm standard deviation. Means were compared with the two-tailed Student t-test for independent groups. Chi-square test was performed to compare dichotomous variables. Results: Total participants were 121 with an age mean of 64.6 years, 56.7% were female and 94.2% were non-smokers. History of previous COVID infection was related by 79 individuals (65.2%). The prevalence of respiratory symptoms in the COVID group were fatigue (39.2%), sleep disturbance (27.8%) and dyspnea (10.9%). The frequency of these symptoms in the control group was 26.2%, 33.3% and 11.9%, respectively ($P>0.05$). In the COVID group, the maximum inspiratory pressure was 92.67 ± 22.7 cmH₂O and in the control group was 90.8 ± 28.6 cmH₂O ($P>0.05$). The mean percentage of expected forced vital capacity in spirometry in the COVID group was $97 \pm 0,12\%$ and in the control group was $92 \pm 0,13\%$ ($P>0.05$). Conclusion: The data showed that in the ELSA-Brasil participants, complaints of fatigue, dyspnea and sleep disorders were unrelated to previous COVID infection. Moreover, these complaints are not related to respiratory dysfunction or weakness of the respiratory muscles. Support: This work was supported by grants from Ministry of Health/Decit and CNPq and a scholarship to GMSP Moraes by FAPES. Protocol: 60070222.8.0000.5060</p>



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Title	Cholinergic neuronal stimulation in the LDTg alleviates respiratory and sleep disruptions in a mouse model of Parkinson's disease
Authors	NICOLE CASTRO MIRANDA, LUIZ M. OLIVEIRA, THIAGO S. MOREIRA, FRANCK KALUME, JAN-MARINO RAMIREZ, ANA CAROLINA TAKAKURA
Affiliations	Farmacologia, USP, Center for Integrative Brain Research, SC, Fisiologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's disease (PD) is a neurodegenerative disorder marked by the loss of dopaminergic neurons in the substantia nigra compacta (SNpc). It manifests through both classical and non-classical symptoms, including respiratory instability and sleep disturbances. The laterodorsal tegmental nucleus (LDTg) has emerged as a crucial region for sleep regulation and potentially respiratory control. It houses, a combination of cholinergic, glutamatergic, and GABAergic neurons. Objective: We hypothesized that activating cholinergic neurons in the LDTg could ameliorate sleep and respiratory disruptions in a murine model of PD. Methods: Adult mice (CEUA: 6641200919 and 8760150318; SCRI: 18819) that express the fluorescent green protein in cholinergic cells (ChATcre Ai6) received bilateral injections of AAV-hM3Dq-mCherry or AAV-mCherry vectors into LDTg. Ten days later, animals underwent nigrostriatal injections of either vehicle or 6-hydroxydopamine (6-OHDA, 10 $\mu\text{g}/\mu\text{l}$) to induce PD model. This was followed by the implantation of electroencephalogram (EEG) and electromyography (EMG) electrodes eight days later. Results: In mice injected with 6-OHDA, there was a 80% reduction in the number of dopaminergic neurons in the SNpc (PD: 83 ± 14 vs. Control: 425 ± 28 neurons, $p < 0.0001$) and a 28% reduction in cholinergic neurons in the LDTg (PD: 433 ± 34 vs. Control: 604 ± 30 neurons, $p < 0.0001$). This decline correlated with a decreased occurrence of apneas and sighs during wakefulness, a 17% decrease in respiratory frequency (PD: 158 ± 13 vs. Control: 190 ± 12 breaths/min, $p = 0.0014$) during non-rapid eye movement sleep (NREMs), and a 26% decrease in respiratory frequency (PD: 140 ± 6 vs. Control: 188 ± 15 breaths/min, $p < 0.0001$) during in rapid eye movement sleep (REMs). Additionally, there was a fivefold increase in NREMs apneas and a sixfold increase in REMs apneas. These mice also exhibited reduced wakefulness time (PD: 102 ± 13 vs. Control: 121 ± 15 minutes, $p = 0.0481$) and increased total sleep time (PD: 194 ± 15 vs. Control: 176 ± 12 minutes, $p = 0.0483$) during 6 hours of recording. Selective pharmacogenetic stimulation of ChAT+ neurons in the LDTg rescued respiratory frequency during NREMs (PD mice, CNO: 176 ± 14 vs. vehicle 189 ± 20 breaths/minute, $p = 0.810$) and REMs (PD mice, CNO 162 ± 22 vs. vehicle: 188 ± 39 breaths/minute, $p = 0.1724$) and reduced apneas, as well as sighs during wakefulness in 6-OHDA mice. Interestingly, during the selective pharmacogenetic stimulation in control animals (i.e. vehicle in the nigrostriatal pathway), we observed a more than twofold increase in wakefulness time compared to the same group without cholinergic neuron stimulation in the LDTg (CNO: 276 ± 17 vs. saline: 125 ± 13 minutes, $p < 0.0001$), resulting in a concurrent decrease in total sleep time and these same animals did not exhibit REMS events. Conclusion: This study reveals neurodegeneration in the LDTg in the mouse model of PD induced by 6-OHDA, impacting normal respiratory frequency and sleep patterns. Selective stimulation of the remaining cholinergic LDTg neurons results in the normalization of respiratory parameters and sleep pattern, indicating a fundamental role in modulating respiration and sleep in this experimental model. Furthermore, it alters entire sleep architecture in control animals, underscoring the essential role of the LDTg in regulating REM sleep. Support: FAPESP, CAPES-PROEX, CNPq and NIH. Protocol: CEUA: 6641200919 and 876015031</p>

Title	NADPH Oxidase, Apocynin, And Its Effects On Apoptotic And Survival Pathways In The 6-OHDA Rat Model Of Parkinson's Disease
Authors	LUIZ FERNANDO DE ARAUJO TRINDADE PEDRÃO, PAMELA OJUORUN SANTOS MEDEIROS, ESTELA CORREIA LEANDRO SANTOS, BARBARA FALQUETTO
Affiliations	Farmacologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's disease (PD) is a neurodegenerative disease characterized by the death of dopaminergic neurons in the Substantia Nigra (SN). It presents motor symptoms, such as dyskinesia, postural instability and respiratory problems. It is known that the 6-OHDA animal rat model presents neurodegeneration in respiratory control regions such as nucleus of solitary tract (NTS), retrotrapezoid nucleus (RTN), preBötzing complex (preBötC) and rostral ventral respiratory group (rVRG), which causes loss in ventilatory function. Oxidative stress seems to be the main cause of this impairment in breathing and previous work have shown that apocynin (APO) prevented respiratory nuclei degeneration and breathing dysfunction in PD model. Aim: Evaluate the effects of the treatment with APO on NOX expression and in the death and survival signaling of respiratory nuclei and respiratory deficits in 6-OHDA animals. Objective: Evaluate the effects of the treatment with APO on NOX expression and in the death and survival signaling of respiratory nuclei and respiratory deficits in 6-OHDA animals. Methods: 6-OHDA (24µg/µl) or vehicle was injected into male adult rat's striatum. Animals were treated with APO in drinking water for 10 days, starting on the 20th day after PD induction. On the 30th day, the animals were euthanized, their brains were sliced in microtome, and their brainstem was dissected to extract respiratory neurons and perform Western Blot. All animals were submitted to tyrosine hydroxylase (TH)-immunoreactivity (ir) to evaluate SN and confirm PD model. Two-way ANOVA followed by Newman Keuls post-hoc was applied with $p < 0.05$. Results: 6-OHDA reduced TH+ neurons in SN and APO did not reverse it as expected, confirming the PD model (vehicle: $755,49 \pm 141,55$; 6-OHDA: $207 \pm 62,24$; vehicle + APO: $711,43 \pm 97,52$; 6-OHDA + EX: $210,75 \pm 80,63$ neurons, $F_{1,26} = 213,7$, $p < 0.0001$). Our ELISA protocol showed a reduction NOX2 expression of the rVRG + preBotC nuclei in the 6-OHDA group, and treatment with APO prevented it (Vehicle: $0,2768 \pm 0,0711$; 6-OHDA: $0,4060 \pm 0,0647$; Vehicle + APO: $0,2284 \pm 0,0686$; 6-OHDA + APO: $0,2960 \pm 0,0723$, $F_{1,13} = 0,8363$, $p = 0,0119$, $F_{1,13} = 5,517$, $p = 0,0353$), but not in the RTN (Vehicle: $0,2027 \pm 0,0808$; 6-OHDA: $0,1925 \pm 0,0757$; Vehicle + APO: $0,1876 \pm 0,0426$; 6-OHDA + APO: $0,2592 \pm 0,0582$, $F_{1,21} = 1,316$, $p = 0,2643$). Also, in the rVRG + preBotC, we saw alterations in the expression of Akt1, GSK3β-p (Ser9), and GSK3β, which were prevented by the treatment with APO ($p < 0,05$). Finally, in the RTN, we saw altered expression of Bcl-2, GSK3β and β-catenin, with prevention after treatment with APO ($p < 0,05$) Conclusion: Survival signaling is important in the respiratory neurodegeneration in 6-OHDA model, and treatment with APO can prevent it, revealing that NOX2 is valuable in the neurodegeneration of respiratory nuclei in the 6-OHDA model. Support: CAPES, 88887.940799/2024-00; FAPESP, 2019/00065-1; 2021/12538-1 Protocol: 2040200319</p>

Title	Impairment of the olfactory system increases the hypercapnic ventilatory response in conscious mice
Authors	PHELIPE EDUARDO SILVA, GEORGE K. TAMARU, EMMANUEL V. ARAUJO, THIAGO S. MOREIRA, ANA C. TAKAKURA
Affiliations	Fisiologia e Biofísica, USP, Farmacologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Olfactory epithelium (OE) GC-D+ neurons project axons to the so-called necklace glomeruli in the caudal portion of the olfactory bulb (OB), being responsible for the CO₂ olfactory detection. This system serves as a vital indicator of danger or food sources and influences innate olfactory preferences and learning. In addition, it has been described that neurons located in the OB also express the peptide neuromedin B (Nmb). Nmb modulates distinct biological processes through discrete brain regions or circuits, and globally these peptidergic systems may serve in an integrative or homeostatic function. However, understanding CO₂ olfactory detection and its secondaries responses such as breathing activity remains limited. Objective: In the present study, we aim to investigate if impaired olfactory neurons produced a significant change in the hypercapnic ventilatory response (HCVR). Methods: Olfactory neurons impairments were achieved pharmacologically with the injection of GABA-A agonist muscimol (2 mM) in the OB or OE or pharmacogenetically by the injection of the AAV8 vector encoding the inhibitory chemogenetic actuator hM4D(Gi) in a cre-recombinase dependent manner (Nmb-cre) mice. Breathing parameters were measured by whole-body plethysmography in conscious unrestrained C57BL/6 or Nmb-cre mice. Results: Muscimol in the OB (VE: 320 ± 63 vs. saline: 259 ± 44%) or in the OE (VE: 491 ± 71 vs. saline: 351 ± 50%) both produced a higher HCVR in conscious mice. Chemogenetic inhibition of Nmb neurons in the OB also produced a higher HCVR (VE: 403 ± 67 vs. saline: 217 ± 15%) compared to saline injected mice. Conclusion: Our data suggest that the olfactory system plays an inhibitory role in central respiratory chemoreception, as its impairment intensifies CO₂ ventilatory responses response in conscious mice. Support: Financial support: FAPESP, CNPq, CAPES-PROEX Protocol: CEUA: 8033310719</p>

Title	EFFECTS OF HYPOXEMIA AND HYPEROXEMIA IN A FOCAL ISCHEMIC STROKE MODEL
Authors	CYNTHIA DOS SANTOS SAMARY, PEDRO LEME SILVA, ISADORA ANTUNES BOTELHO, GISELLE CARVALHO DE SOUSA, PEDRO HENRIQUE LIMA CONCEIÇÃO, RAQUEL FERREIRA DE MAGALHÃES SACRAMENTO, PATRÍCIA RIEKEN MACEDO ROCCO
Affiliations	Laboratório de Investigação Pulmonar, UFRJ
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Patients with ischemic stroke admitted to the intensive care unit often require mechanical ventilation and supplemental oxygen. There is an intense discussion about the safe target of arterial oxygen partial pressure (PaO₂). Mortality has a “U” shaped relationship with PaO₂, where there is a contribution from both hypoxemia and hyperoxemia to high lethality. However, the mechanisms involved in cerebral and pulmonary damage after exposure to different concentrations of oxygen in stroke are poorly explored.</p> <p>Objective: To compare the degree of brain and lung inflammation after exposure to different levels of oxygen in a focal ischemic stroke model. Methods: 16 male Wistar rats (CEUA-131/23) were induced to stroke, through thermocoagulation of pial blood vessels that cover the somatosensory, motor and primary sensorimotor cortices. 24 hours after stroke, they were randomly allocated into four groups (n=4/group): 1) normoxia (NORMO: PaO₂= 80-120 mmHg); 2) hypoxia (HYPO: PaO₂ < 80 mmHg); 3) moderate hyperoxia (MOD: PaO₂= 121-299 mmHg); 4) severe hyperoxia (SEV: PaO₂ ≥ 300 mmHg) then, mechanically ventilated for two hours, with positive end-expiratory pressure (PEEP) of 1 cmH₂O and tidal volume (TV) of 6ml/kg. PaCO₂ was controlled through respiratory rate. Respiratory mechanics and gas exchange data were acquired at the beginning (INITIAL) and at the end (FINAL) of the experiment. At FINAL, the lungs, brain and plasma were removed for further analysis. Results: The NORMO, HYPO, MOD and SEV groups demonstrated the following PaO₂ at FINAL: 98±16mmHg, 56±5mmHg, 217±55mmHg and 355±28mmHg, p<0.001, respectively, with no differences in the other blood gas variables. Airway peak (Ppeak) and plateau (Pplat) pressures increased in all groups over time (p<0.001). At FINAL, there were no differences in Ppeak and Pplat, between the groups. Mean arterial pressure was similar between groups. Hematocrit reduced in all groups over time (p<0.001), but without differences between groups at FINAL. Conclusion: In the present study, the oxygenation target was achieved, however, according to our preliminary data, there were no significant differences in respiratory mechanics, hemodynamics and gas exchange. Histological investigation and inflammatory markers will be analyzed in brain and lungs. References: Robba C, Battaglini D, Cinotti R, Asehnoune K, Stevens R, Taccone FS, et al. Individualized Thresholds of Hypoxemia and Hyperoxemia and their Effect on Outcome in Acute Brain Injured Patients: A Secondary Analysis of the ENIO Study. Neurocrit Care. 15 de junho de 2023. Crit Care Med. setembro de 2017;45(9):1464–71. Support: Financial Support: This project has financial support from the Coordination for the Improvement of Higher Education Personnel (CAPES), the National Council for Scientific and Technological Development (CNPq) and the Carlos Chagas Filho Research Support Foundation of the State of Rio de Janeiro (FAPERJ). Protocol: (CEUA-131/23)</p>



Title	THE DESCENDING MOTOR COMPONENT OF THE CENTRAL COMMAND DOES NOT INTERACT WITH THE MUSCLE METABOREFLEX FOR VENTILATION REGULATION DURING RHYTHMIC EXERCISE IN HEALTH HUMANS
Authors	FELIPE SILVA GOMES, THIAGO RIBEIRO LOPES, RICHARD M. BRUCE, BRUNO MOREIRA SILVA
Affiliations	Department of Physiology, Federal University of São Paulo, School of Basic and Medical Sciences, Kings College London
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The muscle metaboreflex effect on pulmonary ventilation (\dot{V}_E) regulation is more apparent during exercise than rest, possibly because it interacts with other mechanisms regulating \dot{V}_E during voluntary exercise, such as central command Objective: We investigated whether one part of central command, the descending component of motor execution, and the muscle metaboreflex interact synergistically to regulate \dot{V}_E. Methods: Thirteen healthy adults (9 men) completed four experiments in random order under isocapnia. The muscle metaboreflex was activated by rhythmic handgrip exercise at 60% maximal voluntary contraction (MVC) force with the dominant hand. Then, the muscle metaboreflex remained active during a 4-minute recovery period via post-exercise circulatory occlusion (PECO), or it was inactivated, maintaining free blood circulation to the dominant upper limb. During the last 2-minutes of the handgrip exercise recovery, participants either performed rhythmic voluntary plantar flexion with the dominant leg at 30% MVC torque to generate descending motor output or the dominant leg's calf muscles were involuntarily activated by electrical stimulation at a similar torque level, (i.e. without descending motor output). Results: \dot{V}_E increased to a similar level during handgrip exercise in all conditions (≈ 22 L/min, $P = 0.364$). PECO maintained \dot{V}_E elevated above recovery with free blood circulation (≈ 17 L/min vs. ≈ 13 L/min, $P = 0.009$). However, voluntary and involuntary plantar flexion with or without PECO evoked similar \dot{V}_E responses ($\Delta \approx 4$ L/min, $P = 0.311$). Conclusion: The descending component of motor execution of central command do not interact with the upper limb muscle metaboreflex for pulmonary ventilation regulation during exercise. Support: The Coordination for the Improvement of Higher Education Personnel (CAPES) funding covered consumables costs. FGS received scholarships from CAPES and The São Paulo Research Foundation (FAPESP; processes: 22/10295-7 and 23/07135-0). FAPESP funding covered equipment maintenance costs (process: 2023/12845-7). BMS received a scientific production award from the National Council for Scientific and Technological Development (CNPq, process: 307610/2022-5). Protocol: 58027522.7.0000.5505</p>

Title	Investigation into the Impact of Caffeine on Respiratory Changes Observed in a Murine Model of Parkinson's Disease
Authors	RAKHEL DAYANNE DAMASCENO SILVA, NICOLE C. MIRANDA, LAÍS M. CABRAL, LUARA A. BATISTA, THIAGO S. MOREIRA, ANA CAROLINA TAKAKURA
Affiliations	Departamento de Farmacologia, Universidade de São Paulo, Departamento de Fisiologia, Universidade de São Paulo
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson's disease (PD) is defined by the progressive degeneration of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Beyond the classical symptoms, PD presents additional challenges, including respiratory disorders. Addressing these non-classical symptoms, particularly respiratory issues, still requires viable pharmacological interventions. Previous studies have underscored caffeine, an adenosinergic blocker, for its potential to reduce SN lesions in experimental models of PD. Moreover, activation of adenosine receptors in brainstem regions associated with respiratory regulation has been shown to impact respiratory rate, further supporting the use of caffeine in PD treatment. Objective: Our aim is to examine whether caffeine administration can prevent respiratory impairments observed in a PD model induced by 6-hydroxydopamine (6-OHDA). Methods: Experiments were conducted in adult male C57/BL6 mice (18-25g, N = 28) and approved by the Animal Experimentation Ethics Committee of the Institute of Biomedical Sciences, University of São Paulo (CEUA: 3311170423). Animals were anesthetized with 2.5% isoflurane to undergo bilateral injections of 6-OHDA (10 µg/µl) or vehicle into the striatum. Five days post-induction, mice received daily intraperitoneal injections of caffeine (0.3 mg/kg) or vehicle for 5 consecutive days. Following the treatment period, whole-body plethysmography was conducted to evaluate respiratory parameters. Results: The findings revealed a reduction of over 70% in the number of dopaminergic neurons in the SNpc among animals receiving 6-OHDA injections. However, caffeine treatment prevented the reduction in respiratory rate (189±6 vs. 6-OHDA+vehicle: 158±2.6 breaths/min, p = 0.0002), the decrease in the number of phox2b neurons in the retrotrapezoid nucleus (50±4 vs. 6-OHDA+vehicle: 42±4 neurons, p = 0.2994), and the decline in the density of neurokinin 1 receptors in the pre-Böttinger complex (24.55±0.24 vs. 6-OHDA+vehicle: 22.37±0.65%, p = 0.0401) observed in this experimental model. No changes in these parameters were noted in control animals receiving caffeine treatment. Conclusion: These findings highlight the therapeutic potential of caffeine under subchronic conditions in preventing respiratory changes observed in the PD model. Support: FAPESP, CNPq, CAPEX-PROEX Protocol: 3311170423</p>

Title	PREDICTIVE VARIABLES ASSOCIATED WITH MORTALITY IN COVID-19 PATIENTS UNDER INVASIVE MECHANICAL VENTILATION: AN RETROSPECTIVE OBSERVATIONAL COHORT STUDY
Authors	SAMANTHA SILVA CHRISTOVAM, VICTÓRIA MARQUES BARBOSA, ISADORA ANTUNES BOTELHO, LEONARDO DOS SANTOS DE ASSUMPÇÃO, CAMILA MARINELLI MARTINS, GABRIEL GOMES MAIA, FERNANDO SILVA GUIMARÃES, PATRICIA RIEKEN MACEDO ROCCO, PEDRO LEME SILVA, CYNTHIA DOS SANTOS SAMARY
Affiliations	Laboratório de Investigação Pulmonar, UFRJ, Departamento de Fisioterapia Cardiorrespiratória e Musculoesquelética, Faculdade de Fisioterapia,, UFRJ, AAC&T Consultoria de Pesquisa LTDA, Curitiba, Brasil., AAC&T, Hospital Universitário Pedro Ernesto, UERJ
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Patients with COVID-19 can progress to endotracheal intubation and invasive mechanical ventilation (IMV) at intensive care unit (ICU). Under IMV, some patients may survive or not, though it depends on several variables which can gathered either at hospital or during hospitalization. Objective: The objective of the present retrospective cohort study was to gather and analyze predictive variables associated to death in mechanically ventilated COVID-19 patients. Methods: This is a retrospective observational cohort study carried out in 2 intensive care units located at two university hospitals (CAAE: 31062620010015259). Data was gathered at hospital admission and first day of IMV. At hospital admission, data about demographic data, lung damage on chest computed tomography (CT), co-morbidities, Simplified Acute Physiology Score (SAPS)-III, hemodynamics, respiratory function, blood gas analysis, and red blood cells (RBC)s were gathered. At first day of IMV, data about febrile status, hemodynamic, respiratory function, blood gas analysis and RBCs were collected. Additionally, the use of corticosteroids, the rate pulmonary complications, the ICU and hospital length of stay, days until IMV, and time under IMV were also gathered. Differences between groups were assessed using either t-test or Mann-Whitney test. For proportions, chi-squared or Fisher's exact test were used ($p < 0.05$). Results: 357 patients were screened and 109 were eligible, 58 non-survivors (NS) and 51 survivors (S). At hospital admission, male patients died more (65%) than female (40%). The rate of chronic kidney disease was higher in NS (25%) compared to S (2%). RBCs (10.80 ± 2.84 g/dL vs. 12.64 ± 2.35 g/dL) and lymphocytes (292.31 ± 8.40 mL vs. 635.76 ± 471.25 mL) were lower in NS than S ($p = 0.001$, and $p < 0.001$, respectively). Additionally, creatinine (2.70 ± 2.61 mg/dL vs. 1.40 ± 1.58 mg/dL) and urea (89 ± 66.37 mg/dL vs. 47.60 ± 42.15 mg/dL) were higher in NS than S ($p < 0.001$ for both). At first day of IMV, the rate of febrile status was higher in NS (60%) than S (40%) ($p = 0.045$). Diastolic blood pressure (64.46 ± 14.6 mmHg vs. 72.26 ± 13 mmHg), RBCs (10.50 ± 3 g/dL vs. 12.35 ± 2.17 g/dL), lymphocytes (182 ± 428.22 mL vs. 583.16 ± 699 mL) were lower in NS than S ($p < 0.001$ for all). Additionally, blood phosphate (6 ± 2.44 mg/dL vs. 4.21 ± 1.47 mg/dL), creatinine (2.70 ± 2.04 mg/dL vs. 1.22 ± 0.86 mg/dL) and urea (101 ± 52.34 mg/dL vs. 52.4 ± 37 mg/dL) were higher in NS than S ($p < 0.001$ for all). Plasma bicarbonate (19.11 ± 3.22 mEq/L vs. 23.45 ± 4.50 mEq/L) was lower in the NS than S ($p = 0.005$). Interestingly, the use of corticosteroid was associated to low rate of mortality. Respiratory system mechanics at first day of IMV did not predict death. The ICU [median (interquartile range) 8.5 (10.8) vs 21 (23.3)] and hospital [12 (20.3) vs 34 (31)] length of stay of NS were higher than S ($p = 0.027$, and $p = 0.005$, respectively). On the other hand, the days until IMV was higher in NS than S [2(2) vs 1(2), $p < 0.001$] and time under IMV did not differ. Conclusion: The present retrospective cohort study showed that male patients and chronic kidney disease, decreased levels of RBCs and lymphocytes and high levels of creatinine and urea were associated with death at hospital admission. At first day of IMV, in addition, febrile status, decreased diastolic blood pressure and bicarbonate levels were also associated with death. The use of corticosteroid whether at hospital admission or during hospital stay may decrease the risk of death. Support: This project has financial support from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), the National Council for Scientific and Technological Development (CNPq) and Carlos Chagas Filho Foundation for Research Support in the State of Rio de Janeiro (FAPERJ). Protocol: CAAE: 31062620010015259</p>

Title	FUNCTIONAL AND HISTOLOGY CHANGES IN BRAIN AND LUNG DURING EXPERIMENTAL PULMONARY ARTERIAL HYPERTENSION
Authors	VICTÓRIA MARQUES BARBOSA, RENATA TRABACH SANTOS, ELLEN CHRYSTINE DOS REIS TELÁCIO, RODRIGO GONZAGA VERAS, SAMANTHA SILVA CHRISTOVAM, NAZARETH DE NOVAES ROCHA, MARIA CAROLINA BARBOSA DA SILVA, FELIPE SIMOES LEMOS, TATIANA MARON-GUTIERREZ, CYNTHIA DOS SANTOS SAMARY, PEDRO LEME SILVA
Affiliations	Laboratório de Investigação Pulmonar, UFRJ, Laboratório de Imunofarmacologia, FIOCRUZ, Departamento de Fisioterapia Cardiorrespiratória e Musculoesquelética, UFRJ
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Pulmonary arterial hypertension (PAH) is a progressive disease characterized by an increase in mean pulmonary arterial pressure above 20 mmHg at rest due to a reduction in the cross-sectional and restriction of blood flow in the pulmonary circulation. PAH patients often present anxiety, depression and cognitive deterioration and the current literature focus on the reduction of oxygen delivery in the brain. However, the lung can interact with the brain by several mechanisms, mainly at pathological conditions. Herein, we further expanded the likely mechanisms which may contribute to the clinical presentation of PAH pathophysiology in terms of brain-lung axis. However, the pathophysiology of the interaction between PAH and neurological alterations need to be clarified. Objective: To evaluate neurological and cardiovascular functions as well as brain and lung histological changes during the experimental monocrotaline-induced PAH in rats. Methods: The study was approved by the animal ethics committee (CEUA 082-22). Twenty-one male Wistar rats (body weight: 241±29g) were randomly assigned to two groups: 1) control group (CTRL, n=7); 2) PAH group (n=14). PAH group received 60 mg/kg of monocrotaline intraperitoneally, while CTRL group received saline intraperitoneally. On day 14, object recognition (OR) and open field tests were performed, as well as echocardiography. One day after, the rotarod test was performed. On day 28, echocardiography and invasive right ventricle systolic pressure (RVSP) were performed, followed by animal exsanguination. After careful removal of the heart, the right ventricular hypertrophy (RVH) index was measured, and the brain and lungs were removed for histological analysis. Brain immunofluorescence for glial fibrillary acidic protein (GFAP, an astrocyte marker), and ionized calcium-binding adapter molecule 1 (Iba-1, a microglial marker) were done. Results: At day 14, the PAT/PET index, obtained by echocardiography, reduced in PAH compared with CTRL group (0.24±0,23 vs 0.45±0,03, p=0.001; respectively). Both the RVSP (78±5 mmHg vs 32±7 mmHg, p<0.001) and the RVH index (0.51±0.15 vs 0.22±0.06, p=0.001) were higher in PAH than CTRL groups. PAH showed higher pulmonary vascular collagen deposition and smooth muscle proliferation than CTRL group. The rotarod test did not differ between PAH and CTRL groups (277±27 vs 279±87, p=0.964; respectively), suggesting that the motor skill was preserved. Although the total distance did not differ between PAH and CTRL groups (18±3m vs 12±4m, p=0.058; respectively), the number of entries in the center of the box was lower in PAH than CTRL groups (3±1 vs 8±5, p=0.049; respectively), suggesting high anxiety degree in PAH animals. OR did not differ between PAH and CTRL groups (49±10% vs 63±8%, p=0.054; respectively). GFAP and Iba-1 markers were higher in PAH than CTRL groups in a brain region near the hippocampus. Moreover, the microglia morphology was associated with hyper-ramification and increased microglial process length and branching. Conclusion: In the present monocrotaline-induced PAH in rats, the neurological impairment was related to high anxiety degree associated with increased markers of astrocytes and microglia activation. The pathophysiology of PAH must be extended to other organs in an integrative point-of-view. Here, we provide preclinical evidence that the brain-lung axis during PAH is not only related to low oxygen delivery. Support: This project has financial support from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), the National Council for Scientific and Technological Development (CNPq) and Carlos Chagas Filho Foundation for Research Support in the State of Rio de Janeiro (FAPERJ). Protocol: 082-22</p>



Title	Role of inhibitory neurons of the Locus Coeruleus in the hypercapnic ventilatory response in unanesthetized mice
Authors	PATRICK APARECIDO DA SILVA PEREIRA, OCTÁVIO AUGUSTO DE CARVALHO MAIA, ANA CAROLINA THOMAZ TAKAKURA, THIAGO DOS SANTOS MOREIRA
Affiliations	Fisiologia e Biofísica, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The Locus Coeruleus (LC) represents an important neuronal group of cells located in the dorsolateral pons. The LC is the major noradrenergic nucleus with projections throughout the brain, controlling various functions, including central respiratory chemoreception. In addition to excitatory neurons, the LC also harbor a population of inhibitory neurons, whose participation plays a crucial role in the functioning of this region. Objective: Therefore, the aim of the present study was to investigate the role of inhibitory modulation as an important mechanism to avoid inappropriate responses during high levels of CO₂ (hypercapnic ventilatory response, HCVR). Methods: To teste possibility, we used male and female VGat-cre, Ai6 mice (CEUA #2190120723). Through a delivery system the animals received bilateral injections of the AAV-hSyn-DIO-hM3D(Gq)-mCherry vector in the LC region. After three weeks, respiratory parameters were analyzed using whole-body plethysmography. Results: To teste possibility, we used male and female VGat-cre, Ai6 mice (CEUA #2190120723). Through a delivery system the animals received bilateral injections of the AAV-hSyn-DIO-hM3D(Gq)-mCherry vector in the LC region. After three weeks, respiratory parameters were analyzed using whole-body plethysmography. Under baseline conditions (normoxia: FiO₂ = 0.21), intraperitoneal (ip) administration of CNO (1 mg/kg, 0.2 mL/animal) did not change baseline respiratory frequency (fR) (p = 0.29), tidal volume (VT) (p = 0.74), and ventilation (VE) (p = 0.85). After CNO injection, the increase in fR (220 ± 22 vs. saline: 322 ± 13 bpm), VT (8.8 ± 2.2 vs. saline: 13.57 ± 1.9 µl/g), and VE (1839 ± 630 vs. saline: 4209 ± 693 µl/g/min) elicited by hypercapnia (FICO₂ = 0.07) were reduced in animals that had GABAergic neurons transfected in the LC region. Conclusion: However, activation of GABA neurons in the LC region was not able to attenuate the increase in VE (1367 ± 218 vs. saline: 1557 ± 177 µl/g/min) produced by hypoxia. Our data showed that selective activation of GABA neurons in the LC region was able to attenuate the HCVR, suggesting that inhibitory pathways in the LC should control the activity of excitatory (catecholaminergic) neurons that would be involved in controlling ventilation during high levels of CO₂. Support: FAPESP, CNPq, and CAPES-PROEX. Protocol: #2190120723</p>



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Title	EXCITATION OF SOMATOSTATINERGIC INTERNEURONS OF THE LATERAL PARAFACIAL REGION OF MICE DURING NORMOCAPNIA AND HYPERCAPNIA
Authors	NATHALIA SALIM, RENATO MARTINS, DAVI JOSÉ DE ALMEIDA MORAES
Affiliations	Fisiologia, USP, Fisiologia e Biofísica, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The lateral parafacial region (pFL) generates active expiration and contains inhibitory neurons and interneurons (with local projections), and a subset of these neurons express the somatostatin peptide (Sst). The inhibition of Sst-positive neurons in the parafacial region increases ventilation and a portion of these neurons is intrinsically inhibited by hypercapnia. However, the role of pFL Sst-positive interneurons in regulating ventilation during normocapnia and hypercapnia is unclear. Objective: To evaluate the phenotype of pFL Sst-positive neurons. To evaluate the contribution of pFL Sst-positive interneurons in controlling ventilation of mice during normocapnic and hypercapnic conditions. Methods: We crossed Sst-ires-Flp knock-in, Ai65F, Vgat-ires-Cre knock-in and Ai6 mice to express GFP in inhibitory and tdTomato in Sst-positive neurons. We also used Sst-IRES-Cre knock-in mice and injected unilaterally a Cre-dependent retrograde virus to express the Flp recombinase, followed by a Cre- and Flp-dependent virus to express the excitatory Designer Receptors Exclusively Activated by Designer Drugs (hM3D-Gq) in the pFL Sst-positive interneurons. Respiratory frequency (fR), tidal volume (VT), ventilation (VE), duration of the respiratory cycle, inspiration (DI) and expiration (DE), and respiratory variability at normocapnia and hypercapnia (7% CO₂) were evaluated before and after activation of hM3D-Gq receptors (JHU; 0.1 mg/kg) in the pFL Sst-positive interneurons. Data are expressed as mean ± standard deviation. Results: We found that ~ 27% of inhibitory neurons (Vgat/GFP-positive) of the pFL region co-express Sst (tdTomato) (n=2). We also found a significant abundance of Sst-positive interneurons (74.38 ± 9.8) in the pFL region (n=13) after virus injections. JHU reduced VT (Δ: 0.38 ± 1.18 vs. -2.1 ± 2.51 μL.g⁻¹; p= 0.002) and VE (Δ: 192.1 ± 238.9 vs. -418.7 ± 756.6.1 μL.g⁻¹.min⁻¹; p= 0.008) of the Sst(cre/cre + hM3D-Gq) (n= 13) group compared to the Sst(cre/cre) (n=14) group during normocapnia. However, the administration of JHU did not affect the other ventilatory parameters or the respiratory irregularity during normocapnia. JHU administration reduced the hypercapnia-induced responses of fR (Δ: 130.5 ± 27.2 vs 74 ± 50.42 cpm; p= 0.002) and duration of the respiratory cycle (Δ: -131.8 ± 49.59 vs. -82.52 ± 58.23ms; p= 0.03) in the Sst(cre/cre + hM3D-Gq) (n=13) compared with the Sst(cre/cre) (n=12) group. JHU administration did not affect the other ventilatory parameters or the changes in respiratory irregularity in response to hypercapnia in both groups. Conclusion: pFL Sst-positive neurons of mice are inhibitory. pFL Sst-positive interneurons control the ventilatory parameters of mice during normocapnia and hypercapnia. Support: FAPESP, CNPq, CAPES and FAEPA. Protocol: CEUA 1142/2022</p>



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Title	Effect of the estrous cycle on the behavioral and respiratory responses to CO2 in mice
Authors	BEATRIZ DOMINQUINI MORAES, MARIANA BERNARDES RIBEIRO, LUIS GUSTAVO PATRONE, ELISA MAIOQUI FONSECA, ALANA TERCINO FRIAS, KAOMA S COSTA SILVA, RAPHAEL E. SZAWKA, KÊNIA C. BÍCEGO, HÉLIO ZANGROSSI JÚNIOR, ROBERTA ARAUJO-LOPES, LUCIANE HELENA GARGAGLIONI
Affiliations	Departamento de Morfologia e Fisiologia Animal, UNESP/FCAV, Departamento de Farmacologia, USP/FMRP, Departamento de Fisiologia e Biofísica, ICB UFMG
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Panic Disorder (PD) is a psychological disorder characterized by the occurrence of panic attacks, which are triggered by an abnormal sensitivity of brain chemoreceptors to CO₂. The prevalence of PD is 2–4 times higher in women compared to men, and hormonal changes during the menstrual cycle may play a role in the occurrence of panic attacks, as changes in respiratory function during different phases of the cycle appear to be influenced by levels of circulating progesterone. However, the impact of the estrous cycle on behavioral and respiratory responses to CO₂ in animal models remains unknown. Objective: To investigate the effect of the estrous cycle on the ventilatory and behavioral responses to CO₂ in mice. Methods: 73 female C57BL/6 mice (20-25 g, 11-12 weeks; CEUA protocol n° 1594/2021) in proestrus, estrus, metestrus or diestrus were exposed to atmospheric air (control group) or a gas mixture of 20% CO₂, 21% O₂ and N₂ balance to induce panic-like behaviors. Their escape behaviors (jumping, running and freezing), brain monoamines, and plasma levels of 17β-estradiol and progesterone (P₄) were measured. Pulmonary ventilation (V̇_E), respiratory frequency (f_R), tidal volume (V_T), oxygen consumption (V̇_O₂), and body core temperature (T_B) were also measured during normocapnia followed by CO₂. The respiratory equivalent was evaluated by calculating the V̇_E/V̇_O₂. Behavioral, hormonal and neurochemical data were analyzed by a two-way ANOVA, and ventilatory parameters using repeated two-way ANOVA, followed by Tukey post hoc testing. The significance level was set to p<0.05. Results: All females exposed to 20% CO₂ showed escape behaviors [number of jumps–F(1,65)=6.226, p<0.05; running episodes–F(1,65)=93.341, p<0.001; time in freezing–F(1,65)=201.417, p<0.001], without cycle effect. Hypercapnia caused an increase in V̇_E with cycle effect [cycle–F(3,62)=5.009, p<0.05; CO₂ challenge–F(1,62)=561.182, p<0.001; cycle × CO₂ challenge–F(3,62)=0.955, NS], due to an increase in V_T [cycle–F(3,62)=4.528, p<0.05; CO₂ challenge–F(1,62)=556.073, p<0.001; cycle × CO₂ challenge–F(3,62)=1.447, NS], with no changes in f_R. There was an attenuation of CO₂-induced hyperventilation in females during estrus and diestrus compared to proestrus (estrus: p=0.031; diestrus: p=0.030), and females in estrus also showed lower V_T than those in proestrus and metestrus under hypercapnic conditions (p<0.05). All females showed lower T_B during hypercapnia (p<0.001), without effect of the estrous cycle. Exposure to 20% CO₂ also caused a reduction in V̇_O₂ in estrus and metestrus phases only (estrus: p=0.013; metestrus: p=0.009), and an increase in V̇_E/V̇_O₂ for all females (proestrus: p=0.018; estrus: p=0.002; metestrus: p<0.001; diestrus: p=0.029), which was higher in metestrus phase compared to diestrus (p=0.018). Hypercapnia also increased the concentration of plasma P₄ (p<0.001) and central DOPAC (p<0.05) in all estrous cycle phases. There was a cycle effect on brainstem serotonin, with females in estrus showing a higher concentration than females in the metestrus and diestrus phases [cycle–F(3,49)=3.058, p<0.05; CO₂ challenge–F(1,49)=0.000, NS; cycle × CO₂ challenge–F(3,49)=0.201, NS]. Conclusion: Our data suggest that hypercapnia induces panic-related behaviors and ventilatory changes that lead to an increase in P₄ secretion in female mice, likely originating from the adrenals. The estrous cycle interferes in the ventilatory and metabolic responses to CO₂ in mice. Support: FAPESP and CNPq Protocol: 1594/2021</p>

Title	ADMINISTRAÇÃO DA METACOLINA POR VIAS INTRATRAQUEAL E INTRAPERITONEAL: UMA COMPARAÇÃO PARA ESTUDOS DE MECÂNICA VENTILATÓRIA
Authors	RICARDO MURILO PEREIRA EMÍDIO, ROSELI SONCINI
Affiliations	Departamento de Fisiologia, UNIFAL
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O estudo da mecânica ventilatória aliada a utilização de fármacos broncoconstritores e suas respectivas vias de administração, representam uma peça chave para o entendimento das mudanças nas funções pulmonares. Objective: Este estudo investiga o impacto das vias de administração intratraqueal (i.t.) e intraperitoneal (i.p.) do fármaco broncoconstritor metacolina (MCh) em um dos parâmetros de mecânica ventilatória em camundongos fêmeas, com o objetivo de determinar se há diferenças significativas entre essas duas vias. Methods: Foram utilizados 22 camundongos fêmeas da linhagem Swiss para medir a resistência das vias aéreas (Raw, cmH₂O.s/mL). Os animais foram separados em dois grupos: um grupo composto por 12 camundongos que receberam salina seguida de metacolina (MCh) por via i.t. através de aerossolização, e outro grupo composto por 10 camundongos que receberam salina seguida de MCh por via i.p. As avaliações realizadas para tal comparação foram: A: Salina i.t. x MCh i.t.; B: Salina i.p. x MCh i.p.; C: Salina i.t. x Salina i.p.; D: MCh i.t. x MCh i.p.; e E: Variação percentual [(Valor MCh, Valor Salina)/Valor Salina x 100] entre i.t. e i.p. Results: Os resultados mostraram que houve uma diferença significativa entre Salina i.t. e MCh i.t. em todos os tempos analisados, com a maior diferença observada aos 35 segundos após a administração de MCh (0,42 ± 0,010 vs 1,14 ± 0,092). Também foi observada uma diferença significativa entre Salina i.p. e MCh i.p. (0,65 ± 0,028 vs 1,55 ± 0,284). Não houve diferença significativa entre Salina i.t. e Salina i.p. Já na comparação entre MCh i.t. e MCh i.p., houve uma diferença significativa com o pico aos 55 segundos após a administração de MCh (1,05 ± 0,072 vs 2,00 ± 0,233). A maior variação percentual ocorreu aos 10 segundos, porém, não foram observadas diferenças significativas entre as vias de administração nos demais tempos. Conclusion: Sendo assim, pode-se presumir que as vias de administração intratraqueal e intraperitoneal não geraram variações significativas na resistência das vias aéreas na maioria dos tempos analisados, neste estudo com camundongos fêmeas. Support: Sem financiamento Protocol: Comitê de Ética de Uso Animal</p>

Title	Comparação da ativação microglial induzida por CO₂ e LPS em camundongos
Authors	ISABELA XAVIER MEDALHA, BEATRIZ FELIX GONÇALVES DE OLIVEIRA, LUIS GUSTAVO PATRONE, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI
Affiliations	Departamento de Morfologia e Fisiologia Animal, UNESP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O ataque de pânico é uma condição marcada por intensa angústia e ansiedade, na qual o paciente desenvolve sintomas respiratórios como falta de ar, hiperventilação e sensação de sufocamento. Estudos sugerem uma provável conexão entre desafios respiratórios e transtornos de pânico. O locus coeruleus (LC) é uma região quimiossensível capaz de gerar respostas emocionais e físicas durante episódios de estresse, além de importante participação na resposta ventilatória ao CO₂. As respostas pró-inflamatórias da micróglia contribuem para a detecção de um desequilíbrio homeostático, como a inalação de CO₂. Contudo, ainda não é conhecido se a ativação microglial induzida por 20% CO₂ (simulação do alarme de sufocamento) se assemelha à ativação microglial por desafio imune (LPS). Objective: Portanto, o presente estudo investigou a ativação da micróglia no LC de camundongos em resposta à hipercapnia e durante ao desafio imunológico. Methods: Foram utilizados camundongos machos adultos C57BL/6 (20-25g) (comitê de ética: n° 7674/23). Os animais foram colocados em câmara de 5 L e expostos a ar ambiente ou mistura gasosa contendo 20% CO₂, 21% O₂ e N₂ balanço por 15 min, para induzir respostas comportamentais de pânico. Para a indução de resposta imunológica, os animais receberam tratamento i.p. de LPS (1 mg/kg; E. coli sorotipo 0127:B8, Sigma, 0,1 mL/10 g) ou salina (0,1 mL/10 g). A avaliação morfológica da micróglia do LC foi realizada em três intervalos de tempo (1, 6 e 24 h) após o tratamento i.p. ou exposição hipercápnica. Fatias contendo a região do LC foram obtidas através de um criostato, e o protocolo de imunohistoquímica para Iba-1 foi realizado. Os grupos foram divididos em: grupo salina (n = 2, 3 e 2) e LPS (n = 2, 3, 3) e grupo normocapnia (n = 4, 4, 5) e 20% CO₂ (n = 4, 4, 5). Results: Os resultados parciais indicam que a resposta imunológica induzida por LPS resultou em diminuição na área de arborização em todos os intervalos de tempo comparando o grupo salina e LPS, sendo mais acentuada nos intervalos de 6 h (sal: 941,3 ± 25,9 vs LPS: 165,2 ± 7,2 μm²) e 24 h (sal: 937,7 ± 93,9 vs LPS: 203,4 ± 29,5 μm²). Paralelamente, a área do corpo celular apresentou um aumento significativo no grupo tratado com LPS nos intervalos de 6 h (sal: 12,5 ± 1,6 vs LPS: 22,2 ± 1,4 μm²) e 24 h (sal: 11,6 ± 0,4 vs LPS: 35,6 ± 4,0 μm²). Um aumento significativo foi observado no índice morfológico nos animais tratados com LPS, principalmente nos intervalos de 6 h (sal: 0,014 ± 0,0025 vs LPS: 0,128 ± 0,0032) e 24 h (sal: 0,013 ± 0,0006 vs LPS: 0,163 ± 0,0039). A densidade celular e espaçamento entre células vizinhas não foram alterados frente ao tratamento com LPS. Um padrão semelhante de resposta foi observado após o desafio com 20% CO₂, contudo, a resposta foi evidente somente 6 h após o estímulo. A hipercapnia promoveu uma diminuição da área de arborização (0% CO₂: 1012,9 ± 40,6 vs 20% CO₂: 300,0 ± 33,2 μm²), aumento do corpo celular (0% CO₂: 12,4 ± 0,8 vs 20% CO₂: 25,3 ± 2,2 μm²) e do índice morfológico (0% CO₂: 0,014 ± 0,0015 vs 20% CO₂: 0,094 ± 0,0031), e redução da densidade celular (0% CO₂: 0,0019 ± 0,00001 vs 20% CO₂: 0,0009 ± 0,00001 cels/μm²). Conclusion: Os dados morfológicos obtidos com o tratamento de LPS demonstram alterações microgliais a partir do intervalo de 1 h e duram até 24 h. Já a indução panicogênica do CO₂ promove alterações na morfologia da micróglia semelhantes somente no intervalo de 6 h, validando nosso modelo de estudo ao ataque de pânico. Support: FAPESP e CNPq. Protocol: 7674/23</p>

Title	NET measurement in the BALF of patients with interstitial lung disease: a possible biomarker in fibrosis?
Authors	JULIA RODRIGUES FERRAZ SILVA, BIANCA PEIXOTO PINHEIRO LUCENA, MAYCK MEDEIROS AMARAL DA SILVA, MONIQUE MARTINS MELO, NINA VISCONTI, MARCOS BETHLEM, CARLA CONCEIÇÃO DOS SANTOS, NADJA POLISSENI, FERNANDA CARVALHO DE QUEIROZ MELLO, MICHELLE CAILLEAUX, PEDRO LEME SILVA, FERNANDA FERREIRA CRUZ
Affiliations	Laboratorio de Investigação Pulmonar, UFRJ, Instituto de Doenças do Tórax da Universidade Federal do Rio de Janeiro, UFRJ
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: One of the mechanisms by which neutrophils act against microorganisms is the formation of neutrophil extracellular traps (NET). However, aberrant and prolonged NET release can cause permanent epithelial damage. The presence of neutrophilia in bronchoalveolar lavage fluid (BALF) in patients with interstitial lung disease (ILD) denotes a worse prognosis, however, how this occurs has not yet been completely elucidated. One of the pathways studied to try to elucidate a mechanism for the self-perpetuation of fibrosis is precisely the formation of NET. In a study published in January 2024, the NET measurement was associated with severity and worse survival in patients with idiopathic pulmonary fibrosis (IPF). Objective: In patients with ILD, evaluate whether there is a difference in NET measurement between patients with findings of fibrosis on chest tomography (TT) and those without such findings. Methods: Cross-sectional study with prospective allocation, carried out from May 2023 to May 2024. Patients undergoing ILD investigation, without diagnosis after anamnesis, laboratory data and TT, were referred for bronchoscopy with BALF collection. The material was processed following the guidelines of the ATS guideline, 2012. The NET measurement was evaluated through the quantification of free DNA in the BALF supernatant. Patients were divided into 2 groups: with CT findings of fibrosis (traction bronchiectasis, honeycombing and architectural distortion) and without these findings. Student's t-test was performed for independent samples and measures were taken to correct deviations from normality in the sample distribution. Results: 26 patients were recruited. 20 patients (74.1%) had TT with findings of fibrosis and 6 did not. The main diagnoses after multidisciplinary discussion in the fibrosis group in TT were: fibrotic non-specific interstitial pneumonia (NSIP), fibrotic hypersensitivity pneumonia (PH) and unclassifiable ILD. In the group without fibrosis, the main diagnosis was sarcoidosis. BALF neutrophilia greater than 5% was seen in 13 patients: 4 PH, 3 unclassifiable ILD, and 2 IPF. The results demonstrated that patients with fibrosis in TT had statistically higher NET values (M = 220.65; SD = 244.12) than patients without fibrosis (M = 47.65; SD = 22.25), with a size of high effect. The highest NET values were seen in fibrotic NSIP, fibrotic PH, and unclassifiable ILD. Conclusion: In a small sample, the NET measurement was higher in the group of patients with fibrosis in TT. NET's role in pulmonary fibrosis has been elucidated in recent years and in the few studies on it, there is an association with worse outcomes. It has the potential to be a useful biomarker for progressive fibrosis as well as a potential therapeutic target. This is an unprecedented study carried out in Brazil, in addition to being with a prospective allocation of patients, who will continue to be monitored at the IDT/UFRJ ILD outpatient clinic, being evaluated for the progression of fibrosis. Support: CAPES, FAPERJ e CNPQ Protocol: 66958223.9</p>

Title	Developmental changes in pulmonary ventilation of normotensive and spontaneously hypertensive rats
Authors	BEATRIZ NUNES VIEIRA, LETÍCIA R. MENDES, EMILSON DONIZETE PEREIRA JUNIOR, MILEDE H. SARAIVA PAES, DANIEL BRESEGHELLO ZOCCAL
Affiliations	Fisiologia e Patologia, UNESP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The quality of perinatal life can impact the formation of brain networks and affect the functioning of physiological systems in adulthood. Reduced oxygen availability during the postnatal period, as observed in infants with sleep-disordered breathing, is a risk factor for developing cardiorespiratory dysfunctions in adult life. Spontaneously hypertensive rats (SHR), an experimental model of neurogenic hypertension, exhibit breathing irregularities in adult life by mechanisms independent of elevated arterial pressure levels. Objective: This study tested the hypothesis that SHRs exhibit breathing irregularities and hypoxemia during postnatal life. Methods: We used head-out plethysmography to measure respiratory frequency (fR), tidal volume (VT), minute ventilation (Ve), inspiratory/expiratory time variability, oxygen consumption (VO₂), and peripheral oxygen saturation (SpO₂) in neonate (P0-12, males and females) normotensive (Holtzman) and SH rats (CEUA 02/2023). Statistical analyses: Student t-test. Results: At rest, we observed that SHR neonate animals (P0-2, n=9) exhibited hypoventilation (Ve/VO₂: 44.1±3.4 vs 29.9±6.7; P=0.0028) associated with hypoxemia (SpO₂: 93±5 vs 81±5%, P<0.0001) compared to NT animals (n=18). This decrease in ventilation was associated with a reduction in fR (130±15 vs 93±14 bpm, P<0.0001) and the presence of respiratory irregularities characterized by variable durations of inspiration and expiration (P<0.05). At ages of P4-6 (n=19/each group) and P10-12 (n=15-20), Ve was similar between NT and SHR groups; however, breathing irregularities were still present (P<0.05) as well as periods of oxygen desaturation (SpO₂: 90-99 vs 97-80 %, P<0.05). The hypoventilation, oxygen desaturation, and breathing irregularities of the SHR group were observed in males and females, indicating that, up to the P12 age, there is no influence of sex. Conclusion: Our study shows that SHR animals present respiratory irregularities and blood oxygen desaturations during the first two weeks of age that may compromise the development and maturation and promote long-term alterations in brain networks controlling cardiorespiratory functions. Support: FAPESP, CNPq Protocol: Feb-23</p>

Title	Effects of repeated cross-fostering on respiratory and behavioral response to hypercapnia and in CO ₂ -induced panic attacks
Authors	BEATRIZ FELIX GONÇALVES DE OLIVEIRA, LUANA TENÓRIO LOPES, ALANA TERCINO FRIAS, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI
Affiliations	Department of Animal Morphology and Physiology, UNESP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Respiratory symptoms and CO₂ hypersensitivity are hallmarks for studying panic disorder (PD). A validated risk factor linked to both PD and CO₂ hypersensitivity is childhood parental loss, encompassing loss/separation due to various events such as separation/divorce. Objective: This study aimed to evaluate the effects of the repeated cross-fostering (RCF) protocol in female mice (C57BL/6 strain) on respiratory and behavioral responses when exposed to 20% CO₂. All protocols were approved by the local ethics committee (CEUA protocol nº. 7674/23). FAPESP Protocol: 2023/07978-8. Methods: Female mice (control, n=10 and RCF, n=10, 12 weeks old, 20-25g) were placed in chamber where respiratory and behavioral responses such as escape (jumping/running) and time spent immobile (freezing) were recorded under normocapnia or 20% CO₂ during 15 min. Results: Our results demonstrate a similar increase in the ventilatory response (VE) of both groups due to CO₂ exposure (p<0.001), driven by an increase in tidal volume (VT) (p<0.001). No change in respiratory parameters were observed between groups. Oxygen consumption (VO₂) tended to increase in animals subjected to the RCF protocol exposed to hypercapnia compared to the control group (Normocapnia: VO₂ ACR: 0.0873 ± 0.0442 vs VO₂ control: 0.0826 ± 0.0190; Hypercapnia: VO₂ ACR: 0.1037 ± 0.0349 vs VO₂ control: 0.0687 ± 0.0354 mL·1.kg⁻¹·min⁻¹), which caused a trend to decrease the respiratory equivalent (VE/VO₂) of RCF females when compared to the control group (VE/VO₂ RCF: 123.5 ± 58.2 vs VE/VO₂ control: 181.7 ± 68.5). The respiratory data, although still preliminary, indicate a tendency for the RCF females hypoventilate during hypercapnia. The behavioral results indicate a trend to increase in the number of jumps in animals subjected to the RCF protocol and exposed to hypercapnia compared to the control group (Hypercapnia: RCF 23.0 ± 15.3 vs. control 7.8 ± 10.4). No significant differences were observed in freezing behavior (RCF 38.4 ± 3.8 vs. control 35.0 ± 3.5), running episodes (RCF 1.2 ± 2.2 vs. control 2.5 ± 1.9), or rearing behavior (RCF 0.6 ± 0.9 vs. control 0.8 ± 1.0) during CO₂ exposure. Conclusion: Therefore, our data suggest that RCF females tend to hypoventilate and to increase scape response during hypercapnia. Support: FAPESP and CNPq Protocol: 7674/23</p>

Title	SEXUAL DIFFERENCES IN THE PARTICIPATION OF LOCUS COERULEUS (LC) ASIC1a CHANNELS IN RESPIRATORY, METABOLIC AND BEHAVIORAL RESPONSES INDUCED BY CO ₂ .
Authors	LETÍCIA RODRIGUES PINHEIRO, LUIS GUSTAVO ALEXANDRE PATRONE, ALANA TERCINO FRIAS, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI
Affiliations	Departamento de Morfologia e Fisiologia Animal, Universidade Estadual Paulista "Júlio de Mesquita Filho" Unesp Jaboticabal (FCAV)
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Panic disorder (PD) is characterized by panic attacks, with behavioral changes and respiratory symptoms such as shortness of breath, hyperventilation and feeling of suffocation. Women are two to three times more likely to develop PD than men during the life, and sex can affect breathing control and susceptibility to some respiratory diseases. Some studies suggest a link between changes in chemosensitivity to CO₂/pH and PD, since episodes of hypoxia or hypercapnia can trigger panic attacks. ASIC1a channels respond to decreasing pH, which has been identified as relevant to CO₂-induced panicogenic responses. The locus coeruleus (LC) is a chemosensitive region that plays an important role in the ventilatory response to CO₂. However, the role of ASIC1a channels located in LC in CO₂-induced hyperventilation and panic remains unknown, as well as their differences regarding sex. Objective: The objective of the present study was to evaluate the participation of LC ASIC1a channels in the respiratory, metabolic and behavioral responses to 20% CO₂ exposure in male and female mice after intra-LC microinjection of Psalmotoxin-1 (Pstx-1; a selective blocker for ASIC1a channel). Methods: The experiments were carried out in male and female C57BL/6 mice (8 weeks old; Protocol CEUA/FCAV-UNESP: 3451/22), which underwent stereotactic surgery to implant guide cannulas directed to the LC and temperature sensor in the cavity abdominal. Seven days later, 50ng/0.1µL of Pstx-1 or saline was administered intra-LC. Ventilation was measured by whole-body plethysmography in a closed system. And Oxygen consumption by pull mode Behaviors related to panic attacks were recorded by a camera. The panic-like responses analyzed were number of jumps, freezing, running and rearing. Results: The results showed that ASIC1a channels in the LC are not involved in respiratory and metabolic responses in male mice from the control group (n=6) and Pstx-1 (n=6), but appear to participate in behavioral responses, since there is a decrease in the number of jumping in animals that received intra-LC administration of Pstx-1 (Saline: 9.33 ± 5.85 vs Pstx-1: 3.40 ± 3.85). In females, no changes between groups (control n=6 and Pstx-1 n=6) were observed in both respiratory and behavioral responses during CO₂ exposure, suggesting that the results found in the indicate that LC ASIC1a channels are not involved in respiratory control and behavioral responses under normocapnia and hypercapnia. Conclusion: Therefore, our data suggest that ASIC1a channels in LC do not participate in respiratory control under CO₂ challenge, but are involved in CO₂-induced panic behavior in males, demonstrating a specific sex-dependent response. Support: FAPESP (2020/01702-2), CNPq and Capes. Protocol: 3451/22</p>

Title	Inspiratory and expiratory muscle coordination during hypoxia and hypercapnia
Authors	LETÍCIA R. MENDES, BEATRIZ N. VIEIRA, ISABELA P. LEIRÃO, DANIEL B. ZOCCAL
Affiliations	Departamento de Fisiologia e Patologia, UNESP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Exposure to reduced oxygen (hypoxia) or elevated carbon dioxide levels (hypercapnia), as experienced in some pathological conditions, promotes rapid changes in respiratory muscle activity that increase pulmonary ventilation and gas exchange. However, it remains unexplored how inspiratory/expiratory pumping muscles and upper airway muscles are coordinated during conditions of hypoxia and hypercapnia and how these motor adjustments modify airflow to the lungs. Objective: The present study examined changes in inspiratory and expiratory motor activities and the corresponding alterations in airflow during hypoxia and hypercapnia. Methods: Electrodes were implanted in the diaphragm (DIA) and external intercostal (eIC) muscles (inspiratory), genioglossus (GG, upper airway), and abdominal (ABD) and internal intercostal (iIC) muscles (expiratory) of anesthetized adult male Holtzman rats (250-300 g). These animals were also equipped with a snout mask for exposure to gas mixtures and monitoring of nasal airflow. The experiments were conducted under anesthesia, and physiological parameters were recorded under resting conditions and during a 10-minute exposure to hypoxia (7% O₂) and hypercapnia (10% CO₂). All procedures were approved by the Institutional Ethics Committee (17/2020). Statistical analysis: one-way ANOVA followed by Bonferroni or Friedman post-tests. Results: Under resting conditions, DIA and eIC showed synchronized inspiratory bursts, GG exhibited abductor pre-inspiratory (pre-I) activity, and ABD and iIC were silent. The expiratory flow peaked during the first expiration stage. Hypoxia caused an initial increase in the respiratory frequency (fR) (resting: 88±11 vs 2nd-min: 113± 19 bpm, P<0.01), elicited a sustained increase in DIA (Δ: 25-41%) and eIC (Δ: 37-58%) burst amplitudes (P<0.05), and brought about phase-locked ABD (Δ: 60-120%) and iIC (Δ: 116-325%) expiratory bursts (P<0.05) during the initial six minutes of exposure. Moreover, hypoxia exposure reduced GG pre-I activity (Δ: -51-99%, P<0.05) and promoted an increase in airflow during the second stage of expiration (P<0.05). Under hypercapnic conditions, fR increased during the last 2 min of exposure (resting: 85±12 vs 10th-min: 97±14 bpm, P=0.0299), DIA (Δ: 45-56%) and eIC (Δ: 111-128%) burst amplitudes were higher throughout the exposure time (P<0.05), and ABD (Δ: 105-144%) and iIC (Δ: 219-255%) expiratory activities were higher during the last four minutes of exposure (P<0.02). Hypercapnia exposure did not change GG pre-I activity or expiratory airflow pattern. Conclusion: Hypoxia and hypercapnia exposures increase inspiratory and expiratory pumping activities. However, the expiratory (ABD and iIC) recruitment timing differs between gas conditions, occurring earlier under hypoxia than in hypercapnia. Hypoxia, but not hypercapnia, also depresses GG abductor activity, impacting the expiratory flow pattern. Our data indicate that respiratory motor coordination and the corresponding changes in pulmonary mechanics are different between hypoxia and hypercapnia. Support: FAPESP, CNPq, PROPE-UNESP Protocol: 17/2020</p>



Title	Effects of acute caffeine treatment on pulmonary ventilation of neonate spontaneously hypertensive rats
Authors	ANDRESSA BÁRBARA EVANGELISTA, MILEDE H. SARAIVA PAES, DANIEL BRESEGHELLO ZOCCAL
Affiliations	Department of Physiology and Pathology, Unesp
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: An excessive sympathetic drive is commonly observed in hypertensive patients and critically contributes to increasing arterial pressure levels. Reduced oxygen availability during postnatal life can promote long-term changes in sympathetic control, affecting blood pressure levels in adulthood. Our previous studies show that neonate spontaneously hypertensive rats (SHR), an experimental model of neurogenic hypertension, exhibit breathing irregularities and oxygen desaturations at rest, representing a risk factor for developing sympathetic overactivity in adult animals. Caffeine, a methylxanthine that blocks adenosine receptors, is commonly used in premature babies experiencing the apnea of prematurity.</p> <p>Objective: This study tested the hypothesis that caffeine (20 mg/kg, i.p.) can eliminate breathing irregularities and improve pulmonary ventilation in neonate SHRs. Methods: We used head-out plethysmography to measure respiratory frequency (fR), tidal volume (VT), minute ventilation (Ve), inspiratory/expiratory time variability, and oxygen consumption (VO₂) in neonate (P0-6, males and females) normotensive (NT, Holtzman rats) and SHRs (CEUA 02/2023). Statistical analyses: Student t-test. Results: Neonate SHRs (n=8) exhibited baseline hypoventilation (Ve/VO₂: 31.6±8.4 vs 19.6±10.6; P=0.0202) and reduced fR (134±20 vs 103±30 bpm, P=0.0233) compared to aged-matched NT animals (n=9). SHRs also displayed breathing irregularities characterized by variable durations of inspiration and expiration (P<0.05). Twenty to thirty minutes after systemic caffeine administration, Ve was elevated in NT and SHR groups (NT: 1301±366 vs 1681±313; SHR: 1073±451 vs 1291±537 ml/Kg/min, P<0.02) due to increases in VT (NT: 9.7±1.9 vs 12.6±1.6; SHR: 10.1±1.9 vs 12.4±2.3 ml/Kg, P<0.01). Caffeine injection did not modify fR in both groups and only increased VO₂ in the NT rats (44.6±13.1 vs 65.1±17.0 ml/Kg/min, P=0.035). Breathing irregularities were still present in SHR after caffeine injection. Vehicle injections (saline, n=3) did not promote alterations in the respiratory and metabolic parameters. Conclusion: Our findings show that acute systemic treatment with caffeine can stimulate breathing and increase pulmonary ventilation in neonate NTs and SHRs; however, it does not seem to improve fR and breathing regularity in hypertensive animals. Future studies will examine the effects of prolonged caffeine treatment on pulmonary ventilation and breathing regularity in neonate SHRs. Support: FAPESP, CNPq, PROPE-UNESP Protocol: Feb-23</p>

Title	Effects of chronic stress on ventilatory, metabolic and behaviour responses in adult male and female mice during inhalation of to 20%CO2
Authors	CAMILA MIGLIANO DE OLIVEIRA, ANGELA CRISTINA NICOLA, LUCIANE HELENA GARGAGLIONI, LUANA TENORIO-LOPES
Affiliations	Departamento de Morfologia e Fisiologia Animal, UNESP, FCAV
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: It is known that persistent exposure to stress that may takes place at early age, disrupts the function of the hypothalamus-pituitary-adrenal (HPA) axis, leading to a prolonged secretion of cortisol (the stress hormone). This neuroendocrine imbalance predisposes the development of psychiatric conditions, such as anxiety and panic disorder, in adulthood. These conditions are characterized by an increased chemosensitivity to CO₂, however, the cause for this alteration remains obscure. To develop an animal model to investigate these diseases, we combined two forms of stress exposition: chronic stress during the neonatal phase (maternal separation), with a single acute stress exposition at adulthood (CO₂ inhalation). We recently demonstrated that adult female (but not male) C57BL6 mice, previously exposed to neonatal maternal separation (NMS; P3-P12) have a significant reduction in ventilation, in response to the inhalation of 7% of CO₂. These responses are similar to symptoms observed in patients suffering from generalized anxiety disorder. Objective: Here, we aim to test if NMS exposed mice are more sensitive to panicogenic stimulus (through the inhalation of 20% of CO₂) in a sex-specific manner normocapnia and 20% CO₂ for 15 min. The experiment was recorded for behavior analysis (number of jumps, running, rearing, grooming and freezing). Methods: Male and female mice were subjected to the NMS protocol. From post-natal day 3 to 12, pups were separated from their mother and placed in an incubator for 3 h/day (separated from each other from 9:00 to 12:00 h). Control pups remained undisturbed. Mice were reared until adulthood and when they reached 8-10 weeks, the experiments were performed. The ventilatory response to hypercapnia (HcVR) was measured by whole-body plethysmography during Results: Both control and NMS animals (male and female) increased the HcVR when compared with normocapnia. Additionally, NMS caused a sex-specific difference in the HcVR. NMS male mice presented a higher ventilation due to an increased tidal volume in response to hypercapnia, compared to the control male group. No difference was observed in females. The previous exposition to NMS did not cause any significant effect on breathing frequency or temperature for both groups and sexes. Regarding behavior, in both male and female mice exposed to NMS, we observed a significant increase in the freezing response, running and rearing, during exposition to 20% CO₂ compared with normocapnia. However, there were no significant impact of stress when we compared control and NMS only during hypercapnia. Conclusion: Previous exposition to early stress increase respiratory chemosensitivity to 20% CO₂ and elicit panic-like behaviors only in adult male mice, making our model as a valuable tool to investigate pathological mechanisms present in PD. Support: CAPES – PrInt (Programa Institucional de Internacionalização) e FAPESP. Protocol: 9487/22</p>

Title	THE CHRONIC EFFECTS OF EXPERIMENTAL RADIATION-INDUCED PULMONARY FIBROSIS ON CARDIOPULMOARY INTERACTION AND KIDNEY CONGESTION: FOCUS ON INTEGRATIVE PHYSIOLOGY
Authors	LUCAS RODRIGUES DE MORAES, NAZARETH DE NOVAES ROCHA, MAICON LUIZ DE LIMA, TULA CELESTE WILMART GONÇALVES, RODRIGO JORGE VIANNA BARBOSA, KLARA DE SOUZA ROQUE, AMANDA PEREIRA DA CRUZ, RAQUEL FERREIRA DE MAGALHÃES SACRAMENTO, RODRIGO GONZAGA VERAS, SABRINA ARAÚJO FERREIRA, PEDRO HENRIQUE LIMA, VERA LUIZA CAPELOZZI, CAMILA MACHADO BALDAVIRA, SARAH APARECIDA DOS SANTOS ALVES, CELSO CARUSO NEVES, SERGIO AUGUSTO LOPES DE SOUZA, PEDRO LEME SILVA-
Affiliations	Laboratório de Investigação Pulmonar (LIP), UFRJ, UFRJ, Universidade Federal do Rio de Janeiro, CENABIO: Centro Nacional de Biologia Estrutural e Imagem, UFRJ, UFRJ, Departamento de Patologia, Faculdade de Medicina, USP, USP, Laboratório de Bioquímica e Sinalização Celular, Instituto de Biofísica Carlos Chagas Filho, UFRJ, UFRJ, Faculdade de Medicina, UFRJ, UFRJ
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Radiotherapy is widely used to treat chest tumors. However, it can lead to a specific type of pulmonary fibrosis (PF) in 5 to 50% of patients, even at healthy surrounding areas. PF is associated with irreversible remodeling of the lung extracellular matrix, resulting in impaired gas exchange and increased work of breathing. There are few case reports showing pulmonary arterial hypertension (PAH), and cor pulmonale but the pathophysiology is not clear. At clinical field, PF associated with PAH is very under-recognized and can result in high risk of death. Thus, it is necessary to understand how the pathophysiological process of radiation-induced PF occurs, making it possible to identify therapeutic targets.</p> <p>Objective: To temporally characterize a radiation-induced pulmonary fibrosis model in rats, focusing on cardiopulmonary and renal changes. Methods: The study was approved by the animal ethics committee (CEUA: 009/23). Thirty adult Wistar rats aged 8-10 weeks (390±22g) were randomized to receive 15Gy of radiation throughout the right lung (RAD, n=20); or were not expose to radiation (CTRL, n=10). After radiation, echocardiography and chest quantitative computed tomography (CT) were performed every 3 weeks in both groups. Invasive lung mechanics data, through an esophageal catheter, were obtained after 4 and 12 weeks the radiation exposure or not. At the end of the protocol, the animals were euthanized and the lungs were removed for collagen deposition and immunohistochemistry analysis for STAT3 and IL-6. Kidneys were also gathered and congestion score and collagen deposition were analyzed. Results: At chest CT, in the overall lung, there was a decrease in Hounsfield Units over time. The lung volume increased at 12th week compared with 3rd week (p=0.029). Interestingly, the chest CT impairment was more evident in the left compared to right lung, which was radiated. For instance, the left lung showed increased lung volume and weight at 12th compared with 3rd week (p<0.001 and p=0.004; respectively). Similar behavior was not observed in the right lung. At 12th week, P0.1, which is a marker of respiratory drive, was higher in RAD than CTRL (4.7±1.3cmH2O vs 2.9±1.5cmH2O, p=0.003; respectively). Lung compliance was lower in RAD than CTRL at 4th and 12th week (p=0.018 and p=0.039; respectively). At 12th week, clear signs of right ventricular (RV) overload were detected, according to reduction in pulmonary artery acceleration time to pulmonary artery ejection time (PAT/PET) in RAD compared with CTRL groups (0.34±0.06 vs 0.45±0.06, p<0.001; respectively). There was an increase in RV area in RAD group, which suggests concentric hypertrophy. Although, interventricular septum was higher in RAD than CTRL at 12th week, no changes were observed left ventricular ejection fraction. The lungs showed intense collagen deposition around the pulmonary vasculature, and increased STAT-3 and IL-6 quantification in RAD compared with CTRL group. Kidney showed signs of vascular congestion and collagen deposition between tubular cells. Conclusion: According to present data, likely, PF led pulmonary vascular remodeling and increased RV workload, which in turn may congest blood from distal toward central organs, as showed by renal congestion. The present radiation-induced pulmonary fibrosis model showed important changes in cardiopulmonary interaction and kidney, which are very unappreciated at clinical scenario. Support: This project has financial support from Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), the National Council for Scientific and Technological Development (CNPq) and Carlos Chagas Filho Foundation for Research Support in the State of Rio de Janeiro (FAPERJ). Protocol: 009/23</p>

Title	Efeitos biológicos do estiramento cíclico mecânico sob células epiteliais alveolares primárias oriundas de ratos jovens e idosos.
Authors	SABRINA SODRÉ DE SOUZA SERRA, LETÍCIA ALMEIDA DA SILVA, MONIQUE MARTINS MELO, MARIANNA RIBEIRO CABRAL, IRIS KRAUSE CONTRERAS, JOHNATAS DUTRA SILVA, MAYCK MEDEIROS, MAIRA REZENDE LIMA, CRISTINA MAEDA TAKIYA, YGOR SCHLEIER FRANCISCO DAS CHAGAS, ANTONIO CARLOS CAMPOS DE CARVALHO, JORGE MIGUEL CARONA FERREIRA, PATRICIA RIEKEN MACÊDO ROCCO, PEDRO LEME SILVA, FERNANDA FERREIRA CRUZ
Affiliations	Laboratório de Investigação Pulmonar, UFRJ, Laboratório de Imunopatologia, UFRJ, Laboratório de Eletrofisiologia Cardíaca Antonio Paes de Carvalho, UFRJ, Pulmonary Engineering Group, University Hospital Dresden
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A ventilação mecânica (VM) é a principal terapia de suporte utilizada em pacientes com insuficiência respiratória. No entanto, as forças biomecânicas geradas pela VM também podem causar danos ao pulmão, os quais configuram a Lesão Pulmonar Induzida pela Ventilação (VILI). É essencial compreender os mecanismos patogênicos envolvidos na VILI no nível celular, em especial as células alveolares que constituem grande parte do parênquima pulmonar. Nesse sentido, o estiramento cíclico mecânico in vitro das células alveolares simula os padrões da VM e permite análises bioquímicas e estruturais. Além disso, é importante destacar que a maior parte dos pacientes que requerem VM são idosos. Desta forma, o envelhecimento pode estar associado ao aumento da susceptibilidade e gravidade da VILI, além de uma maior taxa de mortalidade. Contudo, de forma paradoxal, a maioria dos estudos pré-clínicos sobre VILI representa apenas a população jovem e poucos estudam os efeitos biológicos da VM em células de animais idosos. Objective: Caracterizar a senescência celular e comparar os efeitos do estiramento cíclico mecânico no que tange à viabilidade celular e às alterações no citoesqueleto de células alveolares primárias oriundas de ratos Wistar jovens e idosos. Methods: Para isso, células alveolares foram extraídas do pulmão de animais jovens (2-3 meses) e idosos (20-22 meses) e cultivadas até a 3^a-4^a passagem (CEUA 031/21). A senescência celular foi avaliada por meio do ensaio de Beta-gal associada à senescência (SA-β-gal) e pela expressão dos marcadores de senescência p16, p21 e p53 através de RT-PCR. Após a validação de senescência, as células alveolares foram submetidas a um ensaio de estiramento cíclico mecânico por 4 horas, frequência de 0,25 Hz. Células alveolares não submetidas ao estiramento serviram como controle. A viabilidade celular foi acessada através dos ensaios de lactato desidrogenase (LDH) e de 3-(4,5-dimetiltiazol-2yl)-2,5-di- fenil brometo de tetrazolina (MTT) ao final do experimento. As alterações no citoesqueleto foram avaliadas através da marcação para faloidina e DAPI por imunofluorescência. Results: As células alveolares primárias de animais idosos apresentaram maior expressão dos marcadores de senescência p16, p21, p53 e SA-β-gal do que as células extraídas de animais jovens. A citotoxicidade foi maior nas células alveolares obtidas de animais idosos após o estiramento mecânico cíclico do que nas células alveolares não submetidas ao estiramento (0.124±0.055 vs 0.059±0.032, p=0.038; respectivamente). As análises qualitativas do citoesqueleto celular por imunofluorescência revelaram que as células idosas submetidas ao estiramento apresentaram mudanças na orientação dos filamentos de actina e um aumento de sua intensidade quando comparadas ao grupo idoso não-estirado. Além disso, há uma aparente diminuição nos filamentos de actina nas células alveolares obtidas de animais idosos quando comparadas ao grupo não estirado. Conclusion: As células alveolares de animais idosos apresentam maior expressão de marcadores de senescência do que as de animais jovens. Os resultados indicam que células epiteliais alveolares de animais idosos submetidas ao estiramento mecânico cíclico são mais suscetíveis à citotoxicidade do que o grupo não estirado. O estiramento mecânico cíclico é capaz de gerar mudanças no citoesqueleto de células jovens e idosas. Support: CNPq, CAPES, FAPERJ Protocol: CEUA 031/21</p>

Title	Cellular profile of bronchoalveolar lavage fluid of patients undergoing Interstitial Lung Disease investigation in the IDT/UFRJ cohort
Authors	ARTUR NEGRINI VICENTE, BIANCA PEIXOTO, MAYCK MEDEIROS, MONIQUE MARTINS MELO, CARLA LOREDO, MARCOS BETHLEM, NINA VISCONTI, NADJA POLISSENI, MICHELLE CAILLEAUX, FERNANDA MELLO, FERNANDA FERREIRA CRUZ
Affiliations	Laboratório de Investigação Pulmonar, Universidade Federal do Rio de Janeiro
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: The diagnosis of interstitial lung disease (ILD) involves several elements, such as anamnesis, chest tomography, spirometry (1). Another widely used tool is cellular analysis of bronchoalveolar lavage fluid (BALF). This technique is considerably simple to perform, however, despite the guideline published by the american thoracic society in 2012, the method lacks standardization and is still carried out only in few centers in Rio de Janeiro (2). The present work proposes to carry out a descriptive analysis of the BALF of patients undergoing ILD investigation referred to the IDT/UFRJ outpatient clinic. Objective: To describe the BALF cellularity of patients undergoing ILD investigation. Methods: Cross-sectional study with prospective allocation, carried out from May 2023 to May 2024. Patients undergoing ILD investigation were referred for bronchoscopy with BALF collection. All exams were performed by the same bronchoscopist. The BALF was collected through the syringe with suction control, avoiding airway collapse. The material was processed in less than 1 hour. Upon arrival at the laboratory, it was centrifuged. Cells were resuspended and a total cell count was performed via hemocytometer. Part of the cells were prepared for differential counting under the microscope, through cytocentrifugation, followed by fixation and staining with panoptic. The other part was processed for immunophenotyping the lymphocytes, using the flow cytometer, with the markers: CD3+, CD3+CD4+, CD3+CD8+ and, CD19+. Results: 27 patients were recruited. The median age was 65 years and duration of symptoms was 34 months. Environmental exposure and smoking were present in 55.6% and 66.7%. Medians of PSAP, FVC percentage and DLCO were: 26 mmHg, 77% and 51%. The main site of BALF was the right lower lobe (7 cases), followed by the right upper lobe and lingula (both 6 cases). The median instilled volume was 80 ml and return volume was 30 ml. Two samples were excluded from the analysis because they had more than 5% of epithelial cells. The medians of cell populations were: neutrophils 7.6%; lymphocytes 5.9%, macrophages 81.35% and eosinophils 1.2%. Lymphocytosis greater than 15% has been seen in patients with sarcoidosis (1), drug-induced pneumopathy (1), and organizing pneumonia (1). Neutrophilia greater than 5% was seen in 13 patients: 4 fibrotic hypersensitivity pneumonia (HP), 3 unclassifiable ILD, and 2 idiopathic pulmonary fibrosis. The CD4/CD8 ratio was greater than 3.5 in 6 patients, 4 of them with sarcoidosis. Main diagnoses after multidisciplinary discussion: sarcoidosis (7), HP (6), unclassifiable ILD (4), IPF (2). Conclusion: This is an unprecedented study in the IDT/UFRJ patient cohort. The presence of neutrophilia stands out, especially in patients with HP, which confers a worse prognosis. Patients have an average duration of symptoms of almost 3 years, a moderate reduction in DLCO and half of them presented with neutrophilia in the BALF, which raises the discussion that such patients arrive at the specialized service in more advanced stages, with predictors of severity. Support: Coordination for the Improvement of Higher Education Personnel (CAPES), the National Council for Scientific and Technological Development (CNPq) and Carlos Chagas Filho Foundation for Research Support in the State of Rio de Janeiro (FAPERJ). Protocol: 66958223.9.0000.5257</p>

Title	Ventilatory response to hypercapnia and hypoxia of mdx mice during sleep/wake states
Authors	LAÍSA TAÍS CABRAL RODRIGUES XAVIER, RENATO FERRETTI, MIRELA BARROS DIAS
Affiliations	Departamento de Biologia Estrutural e Funcional, UNESP campus de Botucatu
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Duchenne Muscular Dystrophy (DMD) is a disease related to mutations in the dystrophin gene, mostly affecting boys. Mdx mice, like DMD patients, lack dystrophin and have an analogous condition in the diaphragm. The ventilatory response to hypercapnia, but not to hypoxia, has been shown to be altered in these animals, but whether these changes are dependent on the sleep-wake cycle, is unknown. Objective: We aimed to evaluate the hypercapnic and hypoxic ventilatory response in mdx mice during wakefulness and NREM sleep. Methods: Unanesthetized adult (8-month-old) and elderly (18-month-old) mdx and C57BL10 mice were submitted to the whole-body plethysmograph method to measure pulmonary ventilation (\dot{V}_E), together with body temperature (T_b) during room air, hypercapnia (7% CO₂) and hypoxia (10% O₂). EMG and EEG were recorded only in 8-month-old animals. All procedures were approved by the Ethics Committee of Use of Animals (CEUA-IBB, UNESP, protocol no. 5769310822). Results: Hypercapnia respiratory response was attenuated in 18-month-old mdx mice compared to control ($\dot{V}_E = 3061 \pm 165$ (n = 8) vs. 4728 ± 297 ml kg⁻¹ min⁻¹ (n = 7); P = 0.0036, two-way ANOVA) but not in the hypoxia response ($\dot{V}_E = 2747 \pm 336$; n=3 vs. 1915 ± 394 mL g⁻¹ min⁻¹; n=3; P > 0.05; two-way ANOVA). 8-month-old mdx mice had the CO₂ response attenuated only during NREM sleep compared to control ($\dot{V}_E = 3860 \pm 341$ (n = 5) vs. 4881 ± 348 ml kg⁻¹ min⁻¹ (n = 3); P = 0.0214, two-way ANOVA). However, during hypoxia the responses did not change in awake mdx mice ($\dot{V}_E = 2347 \pm 384$; n = 4 vs. 2242 ± 259 mL g⁻¹ min⁻¹ (n = 4); P > 0.05) or during NREM sleep ($\dot{V}_E = 2875,1 \pm 412$; n = 3 vs. 2297 ± 209 mL g⁻¹ min⁻¹; n = 4; P > 0.05). Conclusion: We conclude that hypercapnic ventilatory responses are attenuated in 8-month-old mdx mice only during NREM sleep and in 18-month-old mdx mice, suggesting the onset of respiratory changes appears to occur during sleep. Support: This work was supported by National Council of Scientific and Technological Development (CNPq); fellowship to L.T.C.R. number 140547/2022-3. Protocol: All procedures were approved b</p>

Title	Association of Serum Biomarkers Obtained at Hospital Admission with Clinical Outcomes in COVID-19 Patients: A Secondary Cross-Sectional Analysis of a Randomized Clinical Trial
Authors	CAIO CÉSAR SOUZA DA CONCEIÇÃO, PATRICIA RIEKEN MACEDO ROCCO, FERNANDA FERREIRA CRUZ, EDSON ELIAS DA SILVA, HUGO CASTRO FARIAS NETO, CAMILA MARINELLI MARTINS, PEDRO LEME SILVA
Affiliations	LABORATÓRIO DE INVESTIGAÇÃO PULMONAR, UFRJ, Laboratório de Enterovírus, FIOCRUZ, Laboratório de Imunofarmacologia, FIOCRUZ, Consultoria em Pesquisa, AAC&T
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Although substantial pathophysiological advancements have been achieved within three years after the onset of the COVID-19 pandemic, there are still unresolved questions. One acknowledged gap is whether serum biomarkers obtained at hospital admission are associated with clinical outcomes in patients. This may help clinicians guide specific therapies and patient allocation in the ICU or not, according to specific serum biomarkers gathered at hospital admission. Objective: To evaluate the association of serum cytokines gathered at hospital admission in patients with COVID-19 pneumonia with clinical outcomes. Methods: This cross-sectional study evaluated patients primarily allocated to the placebo arm of a randomized multicenter clinical trial from 7 Hospital Units in Brazil (CAAE: 32258920.0.1001.5257). Demographic information was obtained at hospital admission as well as blood samples. Bio-Plex Multiplex immunoassays using luminex magnetic beads were used for the quantification of 48 human cytokine biomarkers. The primary outcome was clinical status improvement measured by hospital discharge, while secondary outcomes were the need for ICU admission, need for hospital admission, and death. Shapiro-Wilk test was performed to assess normality distribution, and Mann-Whitney U test was conducted to determine significant differences between biomarkers and clinical improvement. All analyses were considered significant when $P < 0.05$ and the analyses were performed in the R 4.0.4 environment (R Core Team, 2021). Results: 203 patients with COVID-19 pneumonia were analyzed, in which 64% were male. Patients were aged 40 up to 65 years old and 35% had a body mass index (BMI) higher than 30 kg/cm². 78% of the patients were discharged from the hospital, 14% needed ICU admission, and 2% were dead. Those patients who improved the clinical status compared to those who did not improve, presented increased levels of RANTES [median (interquartile interval), 242 (1239) vs 25 (520), $p=0.031$], b-NGF [13 (24.4) vs 10 (2.8), $p=0.007$], HGF [572 (1973) vs 18 (971), $p=0.048$], CTACK [362 (1389) vs 15 (464), $p=0.0445$], and PDGF-BB [838 (4620) vs 17 (1750), $p=0.034$] at hospital admission. In addition, PDGF-BB levels decreased according to advanced age and high BMI. In parallel, it was noticed that in the subgroup of patients who received corticosteroids (122 patients), and showed low levels of IL-1α, IL-16, IL-17 (and others) on D1, did not show clinical improvement, perhaps immunosuppressing too much. Conclusion: In this cross-sectional study, increased levels of RANTES, b-NGF, HGF, CTACK, and PDGF-BB measured at hospital admission were associated with clinical improvement measured by hospital discharge. Furthermore, PDGF-BB decreased according to advanced age and high BMI. These data highlight biomarker associations with disease severity, advanced age, and body mass index in COVID-19 patients. Recent results raise the question: is it worth giving corticosteroids when the level of inflammatory biomarkers is low? Further analysis is needed to investigate if this would be impairing clinical improvement. Support: CAPES, CNPq, FINEP, FAPERJ, INCT-RJ Protocol: CAAE: 32258920.0.1001.5257</p>

Title	Angiotensin-(1-7) exhibits anxiolytic and antidepressant effect in animal model of allergic asthma
Authors	STHÉFANIE CHAVES DE ALMEIDA GONÇALVES, JULIANA FABIANA GREGÓRIO, KAMYILLE SILVA FERRAZ, GISELLE SANTOS MAGALHÃES, SILVIA AMARAL ZEBRAL, LUCAS MIRANDA KANGUSSU, MARCO ANTÔNIO PELIKY FONTES, MARIA DA GLÓRIA RODRIGUES-MACHADO, RUBEN DARIO SINISTERRA MILLÁN, ANDREA SIQUEIRA HAIBARA, ROBSON AUGUSTO SOUZA DOS SANTOS, MARIA JOSÉ CAMPAGNOLE DOS SANTOS
Affiliations	Department of Chemistry, UFMG, Program in Medical Science, FCMMG, INCT Nanobiofar, Department of Physiology and Biophysics, UFMG, INCT Nanobiofar, Department of Morphology, UFMG
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Allergic asthma, a chronic respiratory condition characterized by airway inflammation and hyperresponsiveness, is often linked with anxiety and depression, complicating the overall well-being and disease progression. Angiotensin-(1-7) [Ang-(1-7)], a key component of the renin-angiotensin system, has demonstrated the ability to reduce airway remodeling, hyperreactivity, and inflammation in chronic asthma models. When administered into the central nervous system, Ang-(1-7) also exhibits anxiolytic and antidepressant effects. Objective: In this study, we evaluated whether Ang-(1-7) could attenuate emotional behaviors and inflammation in asthmatic mice. Methods: Male Balb/c mice, 8-10 weeks, were subjected to an experimental model of allergic asthma. The animals were separated into groups: control, asthmatic and treated with oral Ang-(1-7) included in cyclodextrin [60 µg/kg] or treated with intranasal Ang-(1-7) included cyclodextrin [30 µg/kg] or ICV (50 ng/h). Lung inflammation was assessed by histology, while anxiety-like behavior was assessed using the elevated plus maze and open field tests, while depression-like behavior was assessed using the tail suspension test. We also quantified c-Fos immunostaining in the paraventricular nucleus of the hypothalamus (PVN) and hippocampus. Additionally, we determined inflammatory parameters in the prefrontal cortex of the animals, through the measurement of TNF-α and IL-6, in addition to the anti-inflammatory parameter IL-10. Results: Treatment with either oral, intranasal Ang-(1-7) or ICV administration effectively mitigated anxiety- and depression-like behaviors in asthmatic rats. These effects were associated to a reduction in lung inflammation. Asthmatic animals exhibited decreased locomotor activity in the open field test. The reduction in mobility was significantly alleviated by treatments with Ang-(1-7) administered both orally, intranasally, or ICV. Both oral and intranasal treatments significantly reduced inflammatory cell infiltration in the lungs. Asthmatic animals exhibited a significant increase in c-Fos expression in the PVN and hippocampus, which was attenuated by oral administration of Ang-(1-7). Regarding inflammation in the central nervous system, asthmatic animals showed increased levels of TNF-α and IL-6, which was prevented by intranasal treatment with Ang-(1-7), but not by oral treatment. IL-10 levels were elevated in asthmatic animals, and were affected by peripheral Ang-(1-7) treatments. Conclusion: In summary, these results indicate that Ang-(1-7), administered by different routes (ICV, orally or intranasal), has combined anti-inflammatory, anxiolytic and antidepressant effects. These data emphasized the potential for the development of new formulations based on Ang-(1-7) for the treatment of inflammatory diseases. Support: Capes, Cnpq, Fapemig, and INCT Nanobiofar. Protocol: 290/2018</p>

Title	Inhibition of Locus coeruleus (LC) astrocytes via DREADD(Gi) attenuate panicogenic effects caused by CO2 exposure in mice.
Authors	ALANA TERCINO FRIAS, BEATRIZ FELIX GONÇALVES DE OLIVEIRA, KÊNIA CARDOSO BÍCEGO, LUCIANE HELENA GARGAGLIONI
Affiliations	Department of Animal Morphology and Physiology, UNESP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: In rodents, CO2 inhalation causes avoidance, freezing and endocrine changes that suggest the animals are experiencing a highly aversive situation, which resembles the triggering of a panic attack. In addition to neurons, glial cells such as astrocytes are involved in anxiety disorders. It is known that astrocytic dysfunction influences synaptic activity and can modulate neuronal circuits and behavior, in addition to detecting physiological changes in pH, activating neurons of the respiratory network. Several studies have suggested that astrocytes can respond to different stimuli and release gliotransmitters, which is a possible mechanism in the development and maintenance of mood disorders. Objective: To investigate the participation of locus coeruleus (LC) astrocytes in the neural control of breathing and in behavioral changes in physiological and pathological conditions, such as during a panic attack. Methods: Adult male C57BL/6 mice aged 10 weeks were used (CEUA: 5090/22). The injection procedure was performed by bilateral stereotaxic injection intra-LC of viral vector AAV-GFAP-DREADDs(Gi)mCherry After 28 days, mice were injected with clozapine N-oxide (CNO; 1mg/kg) or vehicle 30 min before exposure to 7% or 20% CO2. Behaviors related to panic attacks were recorded by a camera and analyzed following the parameters: number of jumps and freezing. Results: The results show that animals treated with CNO present a reduction in the number of jumps (vehicle: 29 +- 3.8, CNO: 7 +- 3.4) and an increased in percentage of freezing time (vehicle: 30.9 +- 3.2, CNO: 42.3 +- 2.2) when exposed to 20% CO2. Conclusion: Our data suggest that LC astrocytes exert an excitatory modulation on panicogenic behavior induced by CO2. Support: FAPESP (2022/05057-0; 2020/01702-2; 2023/97978-8), CNPq Protocol: 5090/22</p>

Title	Effects of similar cumulative power resulting from different combinations of respiratory variables on lung damage in experimental acute respiratory distress syndrome
Authors	CATHARINA MATOS DE OLIVEIRA, ADRINA LEME DA SILVA, RAQUEL F. MAGALHÃES, PEDRO H. LIMA CONCEIÇÃO, ANA CAROLINA M. DOS SANTOS, LAUREN T. THORTON, PHILIP S. CROOKE, CAMILA M. BALDAVIRA, VERA L. CAPELOZZI, FERNANDA FERREIRA CRUZ, CYNTHIA S. SAMARY, PEDRO LEME SILVA, JOHN J. MARINI, PATRICIA RIEKEN MACÊDO ROCCO
Affiliations	Laboratory of Pulmonary Investigation, UFRJ
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: We hypothesized that under the same cumulative power, resulting from combinations of different static and dynamic variables, a similar degree of damage to lung epithelial and endothelial cells as well as extracellular matrix would occur in acute respiratory distress syndrome (ARDS). Objective: Thus, the present study aims to investigate the effects of different combinations of tidal volume (VT) and respiratory rate (RR), which yield similar cumulative power, on lung function, histology, and molecular biology in experimental ARDS. Methods: Twenty-four hours after intratracheal administration of Escherichia coli lipopolysaccharide, 24 male Wistar rats were anesthetized and mechanically ventilated (positive end-expiratory pressure, 3 cm H₂O) with the combination of VT and RR enough to induce similar cumulative power (n = 6 per group): (A) VT=6 ml/kg, RR=140 breaths/min; (B) VT=12 ml/kg, RR=70 breaths/min; and (C) VT=18 ml/kg, RR=50 breaths/min. All groups were ventilated for 80 min. A control group, not subjected to mechanical ventilation (NV), was used for molecular biology analysis. Results: At the end of 80 min mechanical ventilation, respiratory system plateau and driving pressures, total and elastic mechanical power, alveolar collapse, lung overdistension, alveolar/interstitial edema, as well as biomarkers of lung inflammation (interleukin-6), lung stretch (amphiregulin) epithelial (surfactant protein-B) and endothelial cell damage (vascular cell adhesion molecule 1 and angiopoietin-2), and extracellular matrix (versican and syndecan) were higher in group C (combination of VT=18 ml/kg and RR=50 breaths/min) than A (VT=6 ml/kg and RR=140 breaths/min). Cumulative power did not differ between groups A, B and C, but with the time course of mechanical ventilation was more increased in groups B and C than A, and C than B. Conclusion: In the current experimental acute respiratory distress syndrome, our results demonstrate that it is not clinically defined mechanical power itself that is sufficient to cause VILI; rather, the way that its components are applied determines the injury potential of a given cumulative power value. Support: CAPES, FAPERJ, CNPq Protocol: CEUA CCS-069/23</p>

Title	Distinct Effects of Intravenous Bone Marrow-Derived Mesenchymal Stromal Cell Therapy on Ischemic and Non-Ischemic Lungs Following Ischemia-Reperfusion Injury
Authors	MILENA OLIVEIRA MOREIRA, JULIA RADICETTI SILVA, CAMILA B. MACHADO, VERA L. CAPELOZZI, MARIANA ALVES ANTUNES, PATRICIA R.M. ROCCO, FERNANDA F. CRUZ, PEDRO L. SILVA
Affiliations	Laboratório de Investigação Pulmonar, UFRJ, Departamento de Patologia, USP
Session	6-Fisiologia Respiratória
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Lung ischemia-reperfusion injury (IRI) can occur during lung transplants, cardiopulmonary bypass, and other thoracic surgeries. While much attention has been given to the direct effects of IRI on the ischemic lung, there is growing interest in understanding its impact on the contralateral lung—the lung not directly affected by ischemia. The pre-clinical efficacy of mesenchymal stromal cell (MSC) therapy following intravenous infusion has been promising, yet clinical studies have yielded only modest results. While most pre-clinical studies focus solely on the ischemic lung, it is crucial to evaluate both lungs after ischemia-reperfusion injury, considering various mechanisms involved. This study aimed to bridge this gap by assessing the acute effects of BM-MSC infusion before ischemic insult and evaluating both ischemic and non-ischemic lungs post-reperfusion. Objective: Evaluate the acute effects of mesenchymal stromal cell therapy in an unilateral ischemia-reperfusion experimental model Methods: Twenty-one male Wistar rats (403±23g) were anesthetized and mechanically ventilated with a protective strategy. After BASELINE data collection, the animals were randomized to 3 groups (n=7/group): 1) Sham; 2) ischemic-reperfusion (IR) and 3) intravenous BM-MSC infusion followed by IR. Ischemia was induced by complete clamping of the left hilum, followed by 1 hour of reperfusion after clamp removal. At the end of the experiment, the right and left lungs (non-ischemic and ischemic, respectively) were collected for immunohistochemistry and molecular biology analysis. (CEUA 005/20) Results: In the left lung, the tissue expression of IL-6 in BM-MSC was higher in SHAM and IR (p=0.003, p=0.045; respectively). Isoprostane was elevated in both IR and IR+MSC groups compared to Sham groups (p=0.042, p=0.002, respectively). Nrf2 and Catalase were higher in IR+MSC than IR (p=0.002, p=0.017, respectively). The tissue expression of VCAM-1 and Caspase-3 reduced in the BM+MSC compared to IR (p=0.011 e p=0.033, respectively). PECAM-1 and the gene expression of VE-cadherin was higher in BM+MSC than Sham (p=0.039, p=0.045, respectively). In the right lung, IL-6 also increased in BM+MSC compared Sham (p=0.009). Isoprostane was elevated in BM+MSC compared to both IR and Sham (p=0.015, p=0.007, respectively). Catalase was higher in BM+MSC than IR (p=0.015). The tissue expression of Caspase-3 was lower in Sham than IR and BM+MSC (p=0.033, p=0.009, respectively). Conclusion: This study demonstrates distinct effects of BM-MSC therapy on ischemic and non-ischemic lungs following ischemia-reperfusion injury. The findings underscore the importance of evaluating both lung types in ischemia-reperfusion studies, offering insights into the therapeutic potential of BM-MSC therapy in lung injury contexts. Support: CNPQ, FAPERJ Protocol: CEUA 005/20</p>

Title	PROTEOMIC PROFILE AND THERAPEUTIC EFFECTS OF EXTRACELLULAR VESICLES OBTAINED FROM HYPOXIA-PRECONDITIONED MESENCHYMAL STEM CELLS ON THE HEART OF EXPERIMENTAL PULMONARY ARTERIAL HYPERTENSION
Authors	CÁSSIA LISBOA BRAGA, MARIA EDUARDA DE SÁ FREIRE ONOFRE, CARLA MEDEIROS DA SILVA, NAZARETH DE NOVAES ROCHA, RODRIGO GONZAGA VERAS, DOUGLAS ESTEVES TEIXEIRA, BEATRIZ TOJA MIRANDA, MIRIA GOMES PEREIRA, CHRISTINA MAEDA TAKIYA, MONIQUE RAMOS DE OLIVEIRA TRUGILHO, PATRICIA RIEKEN MACÊDO ROCCO, FERNANDA FERREIRA CRUZ, PEDRO LEME SILVA, RENATA TRABACH SANTOS
Affiliations	Laboratório de Investigação Pulmonar, Universidade Federal do Rio de Janeiro, Laboratório de Bioquímica e Sinalização Celular, Universidade Federal do Rio de Janeiro, Laboratório de Cardiologia Celular e Molecular, Universidade Federal do Rio de Janeiro, Laboratório de Ultraestrutura Celular Hertha Meyer, Universidade Federal do Rio de Janeiro, Laboratório de Imunopatologia, Universidade Federal do Rio de Janeiro, Laboratório de Toxinologia, Fundação Oswaldo Cruz
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: During pulmonary arterial hypertension (PAH), the cardiac cells develop a hyperproliferative and apoptosis-resistant phenotype and the treatments focus on vasodilation. Although mesenchymal stem cells (MSCs) can halt the progression of PAH, there are limitations on the number of MSCs administered. Hypoxia preconditioning can induce bone marrow MSCs to release more and different extracellular vesicles (EVs) due to mechanism related to hypoxia-inducible factor. Objective: The aim was to evaluate the proteomic profile and therapeutic effect of EVs from normoxia and hypoxia preconditioned MSCs on cardiac tissue in experimental PAH. Methods: Bone marrow MSCs were isolated from male Wistar rats and submitted to normoxia (21%O₂) or hypoxia (1%O₂) for 48 hours. EVs were extracted from MSCs in each condition (EV-N and EV-H, respectively) by ultracentrifugation. Total proteins from EVs were isolated for mass-spectrometry analysis and proteomics. 48 male Wistar rats were randomly distributed into: 1) PAH group that received intraperitoneal monocrotaline (60mg/kg); 2) control group (CTRL) that received saline solution. On day 14, PAH was confirmed by echocardiography and the animals received treatments with EV-N and EV-H. On day 28, pulmonary acceleration time/pulmonary ejection time ratio (PAT/PET), right ventricular systolic pressure (RVSP) and right ventricular hypertrophy index (RVH) were analyzed. The rats were euthanized and the heart was collected for histological and molecular analyses. Results: Overall, 1019 proteins were identified in EVs, 614 proteins were shared between EV-N and EV-H, while 89 were only in EV-N and 316 only in EV-H. EV-H showed enrichment of biological processes related to PI3K-Akt signaling pathway, adrenergic signaling in cardiomyocytes, regulation of cell death and regulation of apoptotic process. EV-N showed enrichment of biological processes related to hypertrophic cardiomyopathy, dilated cardiomyopathy, regulation of cell death and negative regulation of cell death. PAT/PET ratio was lower in PAH than CTRL (0.25±0.01 vs 0.40±0.01, p<0.01), while it increased only in EV-H (0.30±0.01) compared to PAH. PSVD was higher in PAH than CTRL (39±2mmHg vs 22±2mmHg, p<0.01). Both EV-N and EV-H decreased PSVD (32±5mmHg and 29±4mmHg). RVH was higher in PAH than CTRL (0.56±0.07 vs 0.26±0.02). Both EV-N and EV-H decreased RVH (p<0.01 for both). C-myc, specific marker of myocardial injury, was higher in PAH than CTRL (2.72±0.89 vs 0.98±0.07, p<0.01). Both EV-N and EV-H decreased c-myc expression (p<0.01 for both). GSK3β, proliferative marker, was higher in PAH than CTRL (0.96±0.06 vs 0.24±0.04, p<0.01). Only EV-H decreased GSK3β levels. Conclusion: Both EVs reduced PSVD, RVH and c-myc expression. Only EV-N reduced apoptosis while only EV-H reduced GSK3β, and PAT/PET ratio. EVs obtained from hypoxia-preconditioned MSC have greater effect compared to normoxia on the cardiac structure-function in experimental PAH. Support: CAPES, FAPERJ, CNPq Finep e INCT Regenera Protocol: 043/22</p>

Title	Lithium Preserves Cognitive Function in Mice Undergoing Chemotherapy
Authors	IZABELA BOUERI SILVEIRA, ISADORA ZHONG LIANG FERREIRA FENG, MATHEUS DE FREITAS ITABORAHY, URI FLEGLER VIEIRA-MACHADO, THALITA M. VALVERDE, GUILHERME M. J. COSTA, DANIELA DE LAET-SOUZA, JENNIFER D. S. GUIMARÃES, MARIA ALESSANDRA FERREIRA MARTINS, JULIA MELISSA MARQUES, ALFREDO M. DE GOES, BARBARA EHRLICH, MARIA DE FÁTIMA LEITE
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Departamento de Morfologia, UFMG, Departamento de Bioquímica e Imunologia, UFMG, Department of Pharmacology, Yale University
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chemotherapy, while life-saving, often leads to chemotherapy-induced cognitive impairment (CICI), or `chemobrain,` affecting up to 75% of cancer patients with memory lapses, learning difficulties, and focus issues. Chemotherapeutic drugs impact the central nervous system despite the blood-brain barrier, and there are no approved treatments for CICI. This forces patients to reduce chemotherapy doses, compromising treatment efficacy. Microtubule-based chemotherapy agents, essential in breast cancer treatment, are particularly associated with neuropathy. Lithium shows promise in preventing chemotherapy-induced neuropathy caused by some chemotherapeutic drugs, such as paclitaxel. Objective: We aimed to explore whether lithium is able to prevent adverse events characteristic of chemobrain, such as memory loss, in a mouse model treated with monomethyl auristatin E (MMAE). Methods: To establish a model of chemobrain, seven to eight-week-old female C57BL/6 mice randomly assigned to 4 groups: control (saline), lithium chloride (12.8 mg/kg), MMAE (0.12 mg/kg) and lithium chloride (12.8 mg/kg) administered 1 hour before MMAE (0.12 mg/kg). Drug injections were given every other day for 8 days. To evaluate whether MMAE promotes anxiety-like behavior and cognitive impairment, along with the possible therapeutic effects of lithium, open-field exploration (OF), elevated plus maze (EPM) and novel object recognition (NOR) tasks were carried out over three consecutive days. To evaluate whether lithium impacts the antitumoral activity of MMAE, a mouse model of xenograft tumor was carried out. MDA-MB-231 cells were injected into the dorsal scapular area of mice. Two weeks post-implantation, chemotherapeutic treatment was initiated. Tumor volume was measured and normalized by mouse weight and PET-CT imaging. Results: OF and EPM results indicate MMAE injections did not cause anxiety-like behavior nor locomotor impairment in the animals with the protocol established ($p>0.05$ in comparison to saline). Novel Object Recognition Test shows that the saline group had a preference for the new object over the familiar ($p<0.001$). MMAE treatment caused impairment of short-term acquisition memory, demonstrated by the absence of preference for the new object in comparison to the familiar object in the group ($p>0.05$). Lithium administration is able to prevent this side-effect, maintaining the preference for the novel object, similarly in the saline group ($p<0.001$). The measurements of the xenograft tumor along the treatment showed that both MMAE and lithium+MMAE treatments were able to reduce the xenograft tumor, respectively in 43.56% and 69.38% below the initial tumor size ($p<0.05$; $p<0.001$), while the control group showed no statistical difference in tumor size during the treatment ($p>0.05$). Conclusion: Our findings suggest lithium as a potential therapeutic agent to mitigate the cognitive side effects of chemotherapy, improving patient quality of life without sacrificing treatment efficacy. Further research is warranted to explore the underlying mechanisms of lithium's neuroprotective effects and its potential clinical application. Support: CNPq, FAPEMIG, CAPES, INCT-NanoBioFar, Rede-FAPEMIG. Protocol: 201/2023</p>



Title	Ketamine attenuates changes in emotional behavior and oxidative imbalance in the maternal immune activation model: emphasis on the cerebellum
Authors	MAYARA VICTÓRIA DE SOUZA BARBOSA, ELIFRANCES GALDINO DE OLIVEIRA, DIÓGENES AFONSO DE LIMA, JOSÉ CARLOS DA SILVA JÚNIOR, SEVERINA CASSIA DE ANDRADE SILVA, JONATA HENRIQUE DE SANTANA, OSMAR HENRIQUE DOS SANTOS JUNIOR, EDUARDO CARVALHO LIRA, CLAUDIA JACQUES LAGRANHA, FILIPE SILVEIRA DUARTE, DAYANE APARECIDA GOMES
Affiliations	Departamento de Fisiologia e Farmacologia, Universidade Federal de Pernambuco, Núcleo de Educação Física e Ciências do Esporte, Universidade Federal de Pernambuco
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Maternal immune activation (MIA) during pregnancy results in structural and functional changes in the nervous system that directly affect behavior. Therefore, MIA is considered a risk factor for the development of psychiatric disorders such as autism and schizophrenia. Because of its involvement in cognition, emotional and autonomic function, and anxiety, the cerebellum has received attention in psychiatric disorders. Given the modulatory effects of ketamine on the nervous and immune systems, we tested its potential to attenuate the dysfunctions caused by MIA in behavior, oxidative balance and cytokine expression in cerebellum. Objective: To investigate the emotional behavior, oxidative balance and cytokine gene expression in the cerebellum of the offspring exposed to MIA and to evaluate the ability of ketamine to reverse the observed alterations. Methods: To induce MIA, pregnant females were given saline or LPS (100 µg/kg/day; on gestational days 15 and 16). Male offspring exposed or not to MIA received saline solution or ketamine (20 mg/kg/day from the postnatal day 36 to the 50). On the postnatal day 62, the offspring were evaluated for anxiety-like behavior and social interaction, and the cerebellum was collected for analysis of oxidative balance and gene expression of the cytokines. Ethical approval protocol nº004/2021.</p> <p>Results: In the open field, in center time (s), the MIA showed a reduction compared to CRTL (CRTL: 98.94±8.86; MIA: 63.90±7.17; p=0.0267) and MIA+KET an increase compared to MIA (MIA+KET: 98.62±10.03; p=0.0391). In the center entries, MIA showed a reduction compared to CRTL (CRTL: 79.67±4.85; MIA: 56.27±5.24; p=0.0149) and MIA+KET an increase compared to MIA (MIA+KET: 77.70 ±3.99; p=0.0402). In the social interaction test, there was a reduction in interaction time in the MIA compared to the CRTL (CRTL: 228.56±31.58; MIA: 136.10±12.68; p=0.0369). MIA+KET showed an increase in social interaction compared to MIA (MIA+KET: 277.33±20.02; p=0.0005) and KET (KET: 183.01±26.97; p=0.0311). Regarding oxidative stress in the cerebellum, MIA compared to CRTL showed an increase in MDA (CRTL: 2.19±0.05; MIA: 3.06±0.21; p=0.0198) and carbonyls (CRTL: 7.42±1.18; MIA: 19.85±2.72; p=0.0192) and reduced SOD activity (CRTL: 204.97±8.70; MIA: 134.13±12.37; p=0.0009). MIA+KET showed an increase in carbonyls (MIA+KET: 23.03±3.33; p=0.0040) and catalase activity (CRTL: 45.09±5.45; MIA+KET: 70.04±6.34; p=0.0420) and a decrease in SOD activity (MIA+KET: 138.39±7.95; p=0.0015) compared to CRTL. MIA+KET showed a reduction in MDA (MIA+KET: 2.29±0.16; MIA: 3.06±0.21; p=0.0392) and an increase in catalase activity (MIA: 40.80±7.69; p=0.0167) compared to MIA. MIA+KET showed an increase in carbonyls (KET: 11.82±2.25; p=0.0352) and catalase activity (KET: 43.30±1.76; p=0.0286) compared to KET. Regarding gene expression, there was a reduction in IL-1β in MIA (CRTL: 1.03±0.12 2ΔΔCt; MIA: 0.65±0.08 2ΔΔCt; p=0.0115) and MIA+KET (MIA+KET: 0.33±0.02 2ΔΔCt; p<0.0001) compared to CRTL and MIA+KET compared to MIA (p=0.0387). There was an increase in TNF-α gene expression in MIA compared to CRTL (CRTL: 1.08±0.21 (2ΔΔCt); MIA: 2.76±0.53 2ΔΔCt; p=0.0097) and MIA+KET (MIA+KET: 1.17±0.23 2ΔΔCt; p=0.0144).</p> <p>Conclusion: MIA induces anxiety-like behavior, reduced social interaction, modulation of cytokine gene expression and oxidative imbalance in the cerebellum. Treatment with ketamine is able to attenuate the behavioral and molecular alterations. Support: CAPES and FACEPE Protocol: 004/2021</p>



Title	Systemic and Local Effects of Low-Level Laser Therapy on an Experimental Mouse Model of Periodontitis
Authors	NICOLE LUANE GESSE DOS SANTOS, LARISSA TRARBACH FIGUEIREDO BRAGA, ISADORA MARTINS RIBEIRO, SARA CECÍLIA DE ANDRADE, GUILHERME HELEODORO BARBOSA, ELISARDO CORRAL VASQUEZ, MARCELLA LEITE PORTO, SILVANA DOS SANTOS MEYRELLES
Affiliations	Departamento de Ciências Fisiológicas, UFES, Departamento de Ciências Odontológicas, UFES, Departamento de Ciências Farmacêuticas, UVV, Departamento de Pesquisa, Pós Graduação e Extensão, IFES
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Periodontitis is a chronic oral disease initiated by a dysbiotic biofilm. It affects about 35% of the global population, is the major cause of adult tooth loss and has a very important systemic repercussions. Its development is marked by inflammation and alveolar bone loss and involves oxidative stress production. Low-level Laser Therapy (LLLT) has been investigated as an adjunct to periodontal treatments, but its systemic effectiveness is not well established. Objective: To investigate the impact of LLLT on Reactive Oxygen Species (ROS) and apoptosis production in gingival cells, as well as the systemic plasma levels of oxidative stress and inflammation in a mouse model of periodontitis. Methods: C57BL/6 mice (both sexes, 16 weeks old, weighting 25–30 g) were randomly divided into four groups: control (C), control plus LLLT (C+L), periodontitis (P), and periodontitis plus LLLT (P+L). A silk ligature was placed around each animal's right mandibular first molar. After 28 days of periodontitis induction, the ligature was removed. Scaling and root planing were performed using manual instruments, and LLLT was applied to the extraoral region of the mandible adjacent to the mandibular first molar. LLLT was administered using an 808 nm infrared diode at 133.3 J/cm² 40 seconds, for three days. On the day following the third laser application, the animals were euthanized, and plasma and gingival tissue were collected. ROS (superoxide and hydrogen peroxide) and apoptosis were measured in gingival cells using flow cytometry. Additionally, myeloperoxidase enzyme (MPO) and advanced oxidation protein products (AOPP) were evaluated in plasma by spectrophotometry. Results: In the gingival cells, superoxide and hydrogen peroxide production increased significantly ($p < 0.05$) in the P group (1338 ± 33.25 a.u.; 1340 ± 155.0 a.u., respectively) compared to C (958.2 ± 46.76 a.u.; 925.0 ± 30.23 a.u) and C+L (1040 ± 372.8 a.u.; 1003 ± 56.31 a.u) groups. LLLT significantly reduced superoxide and hydrogen peroxide levels in the P+L group (1087 ± 65.52 a.u.; 992.8 ± 10.43 a.u., $p < 0.05$, respectively). Apoptosis rates increased in the P group ($5.578 \pm 0.4431\%$, $p < 0.05$) compared to the C group ($3.345 \pm 0.2450\%$) and C+L group ($2.676 \pm 0.5875\%$). LLLT significantly reduced apoptosis in the P+L group ($3.782 \pm 0.3591\%$, $p < 0.05$). In the plasma, MPO activity was elevated in the P group (0.02623 ± 0.006534 mU/ml, $p < 0.05$) compared to the C (0.008850 ± 0.001308 mU/ml) and C+L (0.01509 ± 0.002361 mU/ml) groups. LLLT decreased MPO activity in the P+L group (0.01331 ± 0.002580 mU/ml, $p < 0.05$). AOPP levels were higher in the P group (184.8 ± 15.01 μmol/L, $p < 0.05$) compared to the C (125.2 ± 11.95 μmol/L) and C+L (79.40 ± 7.167 μmol/L) groups. LLLT significantly reduced AOPP levels in the P+L group (113.5 ± 10.29 μmol/L, $p < 0.05$). Conclusion: LLLT mitigates local tissue damage by reducing oxidative stress and apoptosis and exerts systemic benefits by lowering inflammation and oxidative stress markers. This study suggests LLLT is a promising adjunctive treatment for periodontitis, offering a non-invasive approach to managing both local and systemic pathological processes. Support: Brazilian National Research Council (CNPq, 311938/2021-3). Espírito Santo State Research Foundation (FAPES, 51028.788.21531.25082022). Protocol: Institutional Animal Care and</p>

Title	Genetic Profile of Lung Adenocarcinoma: A University Oncologic Center-based Survey in Rio de Janeiro
Authors	LUCAS PINTO DE AMORIM, TIAGO DE ABREU AMARAL SALGADO, PEDRO LEME SILVA, PATRICIA RIEKEN MACÊDO ROCCO, MARIA DE FÁTIMA DIAS GAUI, VERA LUIZA CAPELOZZI, CAMILA MACHADO BALDAVIRA, FERNANDA FERREIRA CRUZ
Affiliations	Laboratório de Investigação Pulmonar (LIP), UFRJ
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Lung cancer (LC) represents the leading cause of cancer-related death worldwide. There are high rates of somatic mutation and genomic rearrangement in lung adenocarcinoma (LUAD) and high risk for metastasis, even after surgery resection. Currently, public health management does not integrate large gene mutation evaluation. On the other hand, the application of next-generation sequencing (NGS) methodology can allow comprehensive profiling of genetic mutations in the Brazilian population to better guide diagnosis and personalize therapies for LUAD. Objective: To determine the mutational profile of patients with LUAD by NGS in a university oncologic center in Rio de Janeiro and associate the mutational profile with individual clinicopathological characteristics. Methods: The TCGA database (Lung Adenocarcinoma, PanCancer Atlas; n=585) was accessed as an exploratory cohort to determine the mutational frequency of 10 genes and the protein expression associated with these genes. Moreover, a cohort of 99 patients with LUAD was used to validate these genes by NGS and immunohistochemical analysis. These results will be associated with the clinical-pathological data and compared with the data obtained in the exploratory study. Results: The predominant population attending university oncologic centers included 53.1% white, 37.5% brown, and 8.3% black, and their descendants. However, several demographic factors (ethnicity, ancestral background, and exposure to smoking), and clinicopathologic features such as aggressive histologic subtypes, and advanced stages are different within the population. The in-silico analyses showed that among the 10 explored genes, TP53 was the most frequent (52%), followed by KRAS (32%) and KEAP1 (19%), ERBB2 and NRAS the ones with the lowest mutation frequency (only 4 % and 2.5%, respectively). The validated cohort counted more men (51.5%), with a mean age of 63 years, and 37.5% of mixed race. Among the LUAD histotypes, a reasonable frequency of micropapillary and solid aggressive subtypes was found, coinciding with the advanced pathological stage (IIIB/IV) in 70.1%, disease progression in 71%, and poor overall survival. Conclusion: The gene mutations in LC have different results among different countries. So, it is necessary to understand the comprehensive profiling of genetic mutations in the Brazilian population. Also, these preliminary findings highlighted that it is necessary to carry out targeted detection according to different clinical features for LUAD and emphasize why we should consider individual clinical performance, as this influences both the prognosis and the effectiveness of treatment. Support: This work was supported by the Sao Paulo Research Foundation (FAPESP; 2018/20403-6; 2023/02755-0), the National Council for Scientific and Technological Development (CNPq; 303735/2021-0). Protocol: 19052818.2.0000.5257</p>

Title	Gold nanoparticles impair the development of pathophysiology aspects associated with severe malaria
Authors	SARAH APARECIDA DOS SANTOS ALVES, DOUGLAS ESTEVES TEIXEIRA, RODRIGO PACHECO DA SILVA AGUIAR, MAYCK MEDEIROS, MONIQUE MARTINS MELO, SABRINA SODRÉ DE SOUZA SERRA, PATRICIA MACHADO RODRIGUES E SILVA MARTINS, MARCO AURÉLIO MARTINS, PATRICIA RIEKEN MACEDO ROCCO, PEDRO LEME SILVA, CELSO CARUSO NEVES, ANA ACACIA DE SÁ PINHEIRO
Affiliations	Carlos Chagas Filho Institute of Biophysics, UFRJ, Laboratory of Inflammation, FIOCRUZ
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Falciparum malaria is a life-threatening inflammatory disease. Severe form of disease progresses with cerebral malaria (CM) what could be associated with malaria-acute kidney injury (MAKI) and malaria-associated acute respiratory distress syndrome (MA-ARDS) worsening patients' outcome. Gold nanoparticles (AuNPs) appear as a potential therapeutic agent in different models of disease because of its anti-inflammatory effect. Objective: We aimed to verify the effect of AuNP treatment on the development of CM associated with MAKI and MA-ARDS. Methods: C57BL/6 male mice with 6-8 weeks were injected with 10⁶ erythrocytes infected with Plasmodium berghei ANKA. AuNPs (10µg/kg/day) were daily i.p. injected (CEUA UFRJ 032/23). The animals were kept in a metabolic cage for urine collection and evaluation of renal function. In addition, blood-brain barrier (BBB) and lung barrier stability and cognitive function were assessed. All analysis were performed at day 5 post infection (p.i.). Results: Body weight and, food and water intake were not changed in all groups. Infection induced spleen (2,4-fold), brain (1,26-fold), lung (1,18-fold) and kidney (1,12-fold) hypertrophy which was prevented by AuNPs administration. AuNP treatment increased survival of infected mice, reaching 26 days p.i., instead of day 10 p.i. for non-treated mice. The increase in survival was not associated with a decrease in parasitemia levels, since it courses linearly with time in all groups until 5 days p.i (Infected 13,97%, Infected+AuNP 12,59%). AuNP-treated group achieved 61,9% parasitemia at day 22 p.i. Infection induced a 1.54- and 1.66-fold increase in the population of CD4+ T cells producing INFγ and IL-17, respectively, which was prevented by AuNP treatment. Moreover, AuNP-treated mice had increased IL-4 producing CD4+ T cells frequency. PbA infection induced a 2-fold increase on BBB permeability, measured by Evans Blue dye extravasation assay, and cognitive damage quantified by SHIRPA score. Regarding MA-ARDS, infected group showed intense inflammatory cell recruitment, alveolar collapse, higher diffuse alveolar damage score and increase on protein concentration in bronchoalveolar lavage fluid. AuNP treatment prevented all brain and pulmonary injuries induced by malaria. In MAKI, infection induced a local 1,43- and 1,38-fold increase on CD4+ T cells producing INFγ and IL-17, respectively and reduced CD4+/CD25+/IL4+ T population. Treatment with AuNP changed the profile of the response by reducing the ratio Th1/Th2. Additionally, there was a decrease in the glomerular filtration rate and urinary flow of infected animals accompanied by an increase on plasma creatinine and urea. Bowman's capsule space was also decreased by infection. None of these parameters were avoided by AuNP treatment. On the other hand, AuNPs treatment prevented infection-induced decrease in protein uptake by the proximal tubule cells (2,6-fold n=6) as well as reduced urinary excretion of proteins. Moreover, treatment ameliorated urinary γGT enzyme activity (1,15-fold n=12), a tubular injury marker. In agreement, infected animals treated with AuNPs had smaller cortical interstitial space (9,91 times n= 3) and a reduced collagen deposition (7,34 times n=3), when compared to untreated infected mice. Conclusion: Together, our results bring AuNPs as a potential therapeutic target in malaria, reducing brain, lung and kidney damage, opening new perspectives for severe malaria treatment. Support: FAPERJ, CAPES, CNPq. Protocol: CEUA UFRJ 032/23</p>



Title	Parkinson`s Disease and Innovative Treatments: A Technological Patent Monitoring of Nanoproducts with Essential Oils
Authors	GIOVANNA LOPES FREITAS, PABYTON GONÇALVES CADENA
Affiliations	Departamento de Morfologia e Fisiologia Animal, UFRPE
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Parkinson`s Disease (PD) affects about 1% of the population over 60 years old and 4% of individuals over 85 years old (Ageing Res Rev. 42:72-85, 2017). The typical therapy is levodopa, which can cause side effects such as tardive dyskinesia and motor fluctuations (Cmaj. 188:1157-1165, 2016). Essential oils (EOs) have been proposed as preventive and therapeutic alternative therapies due to their biological properties, but their low aqueous solubility and bioavailability limit their effectiveness (Compr. Rev. Food Sci. Food Saf. 12:40–53, 2013). Nanotechnology can overcome these limitations by enhancing the efficacy of EOs. Consequently, new products are being developed to be tested as PD therapy. In light of this, there is a need to identify and analyze innovations in the use of nanoproducts with EOs in PD treatment. This study monitored patent databases for this purpose, as patents contains detailed information not found elsewhere.</p> <p>Objective: Our objective was to conduct technological patent monitoring to catalog, identify, and analyze documents related to the use of nanoproducts developed from EOs for PD treatment to identify innovations in the field. Methods: Collection and cataloging of documents was carried out in the international patent databases The Lens and European Patent Office (Espacenet – EPO). Searches used English keywords: `nano* AND “parkinson” AND “essential oil”. Patents related to EO nanoproducts targeting PD were included, while excluding duplicates and documents without mention of the keywords in claims. Data on inventors, depositing country, institution, patent classification codes, year of filing, and product type were tabulated and analyzed in Excel. Results: The monitoring resulted in 57 patents, with 18 from The Lens and 39 from Espacenet. After applying inclusion and exclusion criteria, 5 patents were selected, filed between 2002 and 2020, and no more than one patent was published per year. There was at least a two-year interval between each publication. The United States predominated in patent filings, being the only country with two patents in this technical field. The most represented IPC (International Patent Classification) codes were A61K9/00, A61P25/16, A61P25/28, A61K38/00, and A61Q19/00, while the most frequent CPC (Cooperative Patent Classification) codes included A61K9/0014, A61P25/00, A61P25/16, A61P25/28, A61K38/00, A61Q19/00, and A61K8/14. The most common types of nanoproducts found in three patents were: solid lipid nanoparticles, nanocapsules, and nanoemulsions. Various EOs were used, showing different therapeutic properties such as anesthetic activity (bergamot), promnesic, anti-amnesic, neuroprotective properties (marapuama), and anti-pruritic agents (lavender). Two patents did not highlight EO properties. Conclusion: Analysis of the selected patents revealed an emerging field focused on solid lipid nanoparticles, nanocapsules, and nanoemulsions. The EOs nanotechnology exhibited diverse therapeutic properties. The predominance of the United States in patent filings reflects its technological advancement. The limited number of patents suggests an opportunity for further research and investment to explore the full potential of EOs as nanotechnological products in PD treatment. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) Protocol: N.A.</p>



Title	Larvicidal potential of <i>Apuleia leiocarpa</i> seeds against the insect <i>Callosobruchus maculatus</i> : A physiological and biochemical assessment for management sustainable management of agricultural pests.
Authors	JOÃO VICTOR BARBOSA SANTANA
Affiliations	Laboratório Integrado de Biociências Translacionais, UFRJ
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Agriculture depends on pest control to maintain the quality and quantity of food produced. One of the most common ways to carry out this control is through chemical pesticide), which can cause harm to the health of people and animals. However, plants also have natural defense mechanisms against their predators, with seeds being one of the main sources of these defenses. Serving as shelter for the embryo, seeds present a huge variety of molecules that act in constitutive defense and therefore become potential sources in the search for molecules that have some toxic effect. The insect <i>C. maculatus</i> belongs to the order Coleoptera and subfamily Bruchinae, being popularly known as the bean weevil and one of the main pests that affect the production of legumes in Brazil, which can reduce the commercial value of crops by up to 95%. Because of this, it is essential to control or minimize the damage caused by this pest in agriculture.</p> <p>Objective: To evaluate the larvicidal action of <i>A. leiocarpa</i> seeds on the development of the insect <i>C. maculatus</i>. Methods: <i>A. leiocarpa</i> seeds were donated by the Banco Estadual de Sementes Florestais (BESEF), located in the municipality of Santa Maria Madalena, RJ. The insects are kept in the insectarium of the Institute of Biodiversity and Sustainability NUPEM/UFRJ in a BOD incubator with a controlled temperature of 28°C, and the matrix was donated by the Laboratory of Chemistry and Function of Proteins and Peptides – LQFPP – UENF. The tests to evaluate the toxicity of <i>A. Leiocarpa</i> seeds will be carried out using artificial seeds, from the flour of the seed coats and cotyledons. The artificial seeds will be exposed for 24 hours to two-day-old adult females of <i>C. maculatus</i>, so that they can lay their eggs in the seeds. After oviposition, the eggs will be counted and only 3 eggs will be left per seed. The toxic effects of fractions and proteins will be evaluated by insect development parameters, such as oviposition, hatching, larval development, larvae mass and adult emergence. The tests will last 20 or 40 days after oviposition (DAO).</p> <p>Results: The expected results are the toxic effect of the <i>A. leiocarpa</i> seed on the insect's development, where we assume significant changes in the parameters of the weevil's development, such as oviposition, hatching and larval development. We hope with this research to contribute to studies aimed at identifying toxic proteins and thus assisting in the effective control of this pest. Conclusion: Finally, we hope to contribute to knowledge about the biochemical properties of the <i>A. Leiocarpa</i> seed and its action on the physiology of the insect <i>C. maculatus</i>, and seeking to propose a more sustainable alternative in the control of agricultural pests, reducing dependence on and impacts of pesticides on agriculture. Support: FAPERJ Protocol: N.A.</p>

Title	INVESTIGATING THE IMPACT OF TGF-β INDUCED IN VITRO FIBROGENESIS ON GAP JUNCTIONS USING MULTICELLULAR LIVER SPHEROIDS
Authors	CIBELE FERREIRA PIMENTEL, JOÃO MOREIRA DUQUE MARQUES PORTO, LUCAS PIRES GUARNIER, GABRIELLA OLIVEIRA ALVES MOREIRA DE CARVALHO, JULIA HELENA OLIVEIRA DE BARROS, CHRISTINA MAEDA TAKIYA, MARLON LEMOS DIAS, FABIO DA SILVA DE AZEVEDO FORTES, REGINA COELI DOS SANTOS GOLDENBERG, REGINA COELI DOS SANTOS GOLDENBERG
Affiliations	Centro de Pesquisas Avançada em Medicina de Precisão, CPMP, UNIGRANRIO BIOTRANS/InMetro/UERJ ZO, Centro de Pesquisas Avançada em Medicina de Precisão, UFRJ, Departamento de Biologia (DEPBIO), UERJ ZO, Laboratório de Imunopatologia (LIPATO), UFRJ, Departamento de Genética, USP
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: In healthy livers, cells interact through gap junctions, formed by connexin proteins (Cx). Junction dysfunction affects many liver processes such as differentiation, cell death, inflammation, and hepatic fibrogenesis. Objective: To Investigate the impact of $\text{tgf-}\beta$ induced in vitro fibrogenesis on gap junctions. Methods: Multicellular spheroids were generated from HepG2, GRX and menstrual blood-derived mesenchymal cells (CeSaM) (n=10). Liver cell lines (HepG2/GRX) were acquired by Rio de Janeiro Cell Bank and stored in LN2. CeSaM obtainment was approved by the Clementino Fraga Filho University Hospital Ethics Committee, under registration number 056/09. To determine volumetric viability (mm^3) of the spheroids, 2 orthogonal diameters were measured using line morphometry with ImageJ and the formula $V=4/3\pi R^3$. A curve was made with the variables: number of cells and culture time (T) for HepG2/GRX/CeSaM spheroids in concentrations 1x, 2x, 3x and 4x10⁴, and T = 3, 7, 14, 21 days. Data were presented as mean \pm standard deviation, and comparisons between variables were made using Two-way ANOVA-Kruskal-Wallis. Volume of 3x10⁴ cells was chosen for HepG2+GRX+CeSaM multispheroid experiments at T:7, 14 days. To form spheroids, cells at 80% confluency were added to 96-well non-adherent culture plates coated with agarose. Cells were incubated at 37°C and morphofunctional and structural analyses were performed at T= 7, 14 days. Histological (H&E, Sirius red, Oil red and Tunnel) and immunofluorescence (IF) analyses (Cx26, Cx32, Cx43, albumin, αSMA, collagen I, III, Ki67), phase contrast, confocal and transmission electronic microscopy were performed. New spheroids were then made for fibrogenesis induction. 3 days after spheroid formation, 10 ng/mL of TGF-β were added to the culture medium. Multispheroids were grown for 7 and 14 days, and culture medium was changed every 3 days. Volumetric analysis was then performed, using One-way ANOVA followed by Tukey's post-hoc test. Results: HepG2/GRX/CeSaM cells maintained their morphological characteristics under culture. Volumetric analysis revealed significant changes in volume when comparing spheroids of 2x and 4x10⁴ cells ($P<0.01$). In H&E analysis was observed that the three cellular types seamlessly integrated, forming compact spheroids. The presence of CeSaM seemed to influence cell growth, creating more concise and uniform spheroids compared to HepG2. Fibrotic multispheroids were found to be smaller than control ones in the T:7,14 days ($P<0.05$). In addition, morphological changes were observed in the fibrotic multispheroids compared to the controls by MET. Cx26, Cx32, Cx43 and collagens I and III positive staining respectively suggest multispheroids produce extracellular matrices and establish gap junctions. Functional evaluation of the ultrastructure of spheroids by hepatic zones shows morphofunctional architecture of inherent liver organelles. Conclusion: Fibrotic spheroids induced by TGF-β were smaller than the controls, indicating an influence on cell proliferation; however, the cellular organization remained intact, as observed by H&E staining. Positive fluorescence for gap junction markers and extracellular matrix components confirmed their presence. These findings suggest that gap junctions are vital for maintaining liver cell communication and structural integrity during fibrogenesis. Support: CAPES,FAPERJ,CNPq,BIOTRANS,UERJ-ZO,IBCCF-UFRJ/CPMP, CENABIO-UFRJ Protocol: Clementino Fraga Filho Univers</p>

Title	DEVELOPMENT OF A CUSTOMIZED, LOW-COST SYSTEM FOR RECORDING ELECTROPHYSIOLOGICAL ACTIVITY USING THE ADS1298
Authors	LUIZ FELIPE NOGUEIRA VARANDAS, JOÃO PEDRO CARVALHO MOREIRA, MATHEUS COSTA PASSOS, MÁRCIO FLÁVIO DUTRA MORAES
Affiliations	DFIB, NNC, UFMG
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Oscillatory biological signals and the dynamics of their transitory coupling are fundamental to intra- and inter-system communication within complex organisms. Longitudinal studies that record system dynamics with high time resolution are promising approaches for understanding and potentially treating conditions such as epilepsy, movement disorders, and Alzheimer’s disease. The high costs associated with recording high-resolution bioelectric signals pose significant challenges for lower-budget laboratories, particularly in developing countries. While customized alternatives have been developed, issues such as weight, reproducibility, transmission rate and the need for expensive connectors hinder their widespread adoption. This work introduces a low-cost, custom-made, multi-channel electrophysiological recording device designed for longitudinal studies. The device leverages open-source embedded electronics — including amplification, conversion, digital signal processing, and storage — and software, making advanced research more accessible. Objective: The main goal of this study is to develop a low-cost system for longitudinal recordings of electrophysiological activities using both the Intan RHD2000 and the Texas Instruments ADS1298 chips, offering alternatives to existing solutions with improved affordability, functionality and portability. Methods: The chips Intan RHD2000 and ADS1298 were combined with the microcontroller Arduino DUE and a Python graphical user interface based on the PyQt5 library to develop MicroMAP (Multichannel Acquisition Pack). The system utilizes a Serial Peripheral Interface protocol to exchange data with the chips, then the acquired electrode data is sent in samples in a constant way to a personal computer or a Raspberry Pi and processed by the control routine of the interface, which plots the data of all channels. Results: Intan RHD2000 was validated in MicroMAP by comparing ten recordings of electrocardiographic (ECG) activity from a Male <i>Rattus norvegicus</i> (CEUA: 116/2021), with the industry gold-standard OpenEphys. This analysis presented successful results, with a mean and standard deviation of Pearson’s correlation coefficients of 0.9996 ± 0.0003. The innovation of this study consists in the ADS1298 chip integration into the acquisition system, which is no small feat (the ADS chip is 10-fold cheaper than its RHD2000 counterpart). Tests showed that recording short-period ECG signals with 24 bit resolution pass benchmarking tests when compared to commercially available solutions. Longitudinal 24-7 data recording experiments with 8 differential channels implanted into different brain areas are currently being conducted in order to further validate MicroMAP for spontaneous seizure recordings in animal models of Temporal Lobe Epilepsy. Conclusion: The development of a complete system for data capture and processing leads to a wide range of applications in both scientific research and healthcare. MicroMAP will enable hospitals to offer high-resolution clinical monitoring services at a reduced expense, which can significantly decrease the response time for urgent patient needs, including those in transit to medical facilities in ambulances. It may also enable individuals with diverse medical conditions to monitor their health data in real time and seek early treatment. In scientific research, this system can democratize long-term animal recordings, crucial for uncovering the origins of diseases and enhancing our understanding of their mechanisms. Support: This study was financed by the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: CEUA: 116/2021</p>



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Title	Effective Prevention of Chemotherapy-Induced Peripheral Neuropathy: Lithium Pretreatment Mitigates Nerve Damage
Authors	IZABELA BOUERI DA SILVEIRA, MATHEUS DE FREITAS ITABORAHY, URI FLEGLER VIEIRA-MACHADO, ISADORA ZHONG LIANG FERREIRA FENG, THALITA M. VALVERDE, GUILHERME M. J. COSTA, DANIELA DE LAET-SOUZA, JENNIFER D. S. GUIMARÃES, MARIA ALESSANDRA FERREIRA MARTINS, JULIA MELISSA MARQUES, ALFREDO M. DE GOES, BARBARA EHRlich, MARIA DE FÁTIMA LEITE
Affiliations	Departamento de Fisiologia e Biofísica, UFMG, Department of Pharmacology, Yale University, Departamento de Morfologia, UFMG, Departamento de Bioquímica e Imunologia, UFMG
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of cancer treatment, characterized by numbness, tingling and pain in the hands and feet. Monomethyl auristatin E (MMAE), a well established antimitotic agent, can be associated with CIPN in more than half of its patients. In this scenario, lithium, a mood stabilizer with known neuroprotective properties, emerges as a promising candidate for CIPN prevention. The ability of lithium in preventing peripheral neuropathy is well established for taxanes, as it acts as a stabilizer of calcium signaling, inhibiting loss of cell functions related to the progression of neuropathy. However, lithium protective properties are not yet described for MMAE-based chemotherapy. Objective: The aim of this study is to understand whether lithium is able to prevent CIPN in a mouse model treated with MMAE. Methods: Seven to eight-week-old female C57BL/6 mice assigned to 4 groups with 5 animals each: control (saline), lithium chloride (12.8 mg/kg), MMAE (0.12 mg/kg) and lithium chloride (12.8 mg/kg) administered 1 hour before MMAE (0.12 mg/kg). Drug injections were given every other day for 8 days. Common manifestations of CIPN were evaluated after treatment. To assess nociception, 1.54 µg of capsaicin was injected subcutaneously into the hind paws of mice, and the licking time was measured. Von Frey Hairs were used to check for the presence of allodynia. To investigate neuronal morphology, we loaded the fibers of the Dorsal Root Ganglia (DRG), which are responsible for sensory skills, with 4 µM FM 1-43 Dye and the width of the myelin was measured after visualization in a confocal microscope. Assessment of intracellular calcium signaling in DRG upon stimulation with carbachol was performed by using Fluo-4/AM fluorescent marker. Results: Mice treated with MMAE showed a lower licking time upon administration of capsaicin (73.59 ± 5.043) in comparison to the control group (104.7 ± 6.258) ($p < 0.001$), while lithium was able to maintain the response similar to the control group (102.8 ± 12.72) ($p > 0.05$). The MMAE treated group showed a reduced threshold (3.420 ± 0.4693) compared to saline group (4.183 ± 0.1666) ($p < 0.001$) when stimulated with Von Frey hairs, expliciting allodynia, which was not observed in the group treated with lithium and MMAE (4.259 ± 0.2177, $p > 0.05$ compared to saline). The measurements of DRG fibers stained with FM 1-43 showed a significant thinning of 25% of the myelin in the MMAE group compared to the control ($p < 0.0001$), which was not observed in mice treated with lithium and MMAE, that presented the same width compared to the control group ($p > 0.05$). Through calcium signaling assessment, it was observable that the amplitude of signal upon carbachol stimulation was significantly lower in the MMAE group (109.3 ± 5.231) in comparison to the control (119.2 ± 5.170) ($p < 0.01$), indicating that calcium plays a role in the mechanism of MMAE-induced CIPN. Lithium was able to prevent the reduction in calcium signal amplitude, with values comparable to the control group (121.2 ± 10.37) ($p > 0.05$). Conclusion: This study highlights the potential of lithium pretreatment as an preventive strategy for CIPN, offering a promising approach to mitigate the debilitating side effects of cancer treatment and improve patient quality of life. Support: CNPq, FAPEMIG, CAPES, INCT-NanoBioFar, Rede-FAPEMIG. Protocol: 201/2023</p>



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Title	Alzheimer Disease: Searching for an innovative Probiotic Resembling the classical kefir but replacing the hand-by-hand production by packaging capsules
Authors	MARY LEE DOS SANTOS, JOSIAS DOS SANTOS PAPA, GUILHERME GARCES ALMADA, SILVANA DOS SANTOS MEYRELLES, RADAEL REZENDE RODRIGUES JUNIOR, ELISARDO CORRAL VASQUEZ
Affiliations	Laboratory of Translational Physiology and Pharmacology, Pharmaceutical Sciences Graduate Program, UVV, Fisioterapia, Unileste, Programa de Pós Graduação em Ciências Fisiológicas, UFES
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Among chronic diseases, neurodegenerative disorders stand out as the most dramatic condition due to their incurable nature and the substantial suffering they inflict not only on patients but also on giving-care and their families. Alzheimer's Disease (AD) is delineated by a progressive decline in cognitive functions accompanied by functional impairments, accounting for a significant proportion of mortality and disability worldwide. Our research group has demonstrated over recent years an improvement in cognitive function, memory, oxidative stress, and cardiovascular system health through the administration of whole milk fermented with kefir grains. Recently, a technological innovation was approved and registered at Anvisa, Brazil, consisting of a supplement formulation that contains the two main components of kefir (Lactobacilli and Bifidobacterium) produced and sold on the pharmacy counters. The aim of the present study was to evaluate the effectiveness of this new formulation in patients with dementia. Objective: To evaluate the safety and preliminary effectiveness of a new encapsulated probiotic, Helveticus r0052 and Bifidobacterium longum r0175, on the cognition of patients diagnosed with AD in a Phase I Interventional Study Methods: This project was previously submitted to analysis and approved by the institutional ethics committee. This is a Phase I, cross-sectional, interventional study that included 16 patients with AD. The patients were administered the encapsulated supplement for 60 days to assess cognitive functions. We evaluated the score obtained in each classical cognitive dysfunction that characterize the AD and memories. We also measured the effects of the probiotic effects on oxidative stress and inflammatory cytokines. Results: This exploratory investigation assessed the ramifications of ingesting a probiotic blend comprising Lactobacillus helveticou R0052 and Bifidobacterium longum R0175 over a duration of 60 days on cognitive performance, inflammatory markers, and oxidative stress in subjects diagnosed with Alzheimer's disease (AD). The assessment employed validated instruments and serum biomarker analysis. Notably, a 27.8% enhancement in overall cognitive function as gauged by the Mini Mental State Examination, improvements of 25% in both immediate and delayed memory recall, a 22% progression in language competencies as measured by the Boston Naming Test, a 28% advancement in executive functional capabilities in the Verbal Fluency Test, a 38% elevation in visuospatial skills as assessed by the Cookie Theft Picture Description Task, a 33% leap in abstract reasoning with the Similarities Test, a 25% increment in attentional faculties with the Clock Drawing Test, and a 20% betterment in constructive abilities via the Trail Making Test Part A were documented. Analyzing the levels of advanced oxidative protein products underscored that the cognitive enhancement witnessed was accompanied by an over 90% decline in the systemic oxidative stress index ($p=0.0002$) and a statistically significant reduction in serum cortisol levels ($p=0.03$). Conclusion: The present study demonstrated a significant improvement in cognition deficits, as well as a reduction in the levels of inflammatory cytokines and a reduction in oxidative stress. The encapsulated probiotic allows researchers to use their data in a comparative way and reach conclusions without confounding factors due to the lack of standardization and quality control. Support: PROFIX 15/2022 FAPES Protocol: IRB University of Vila Velha,</p>

Title	O CARVACROL NÃO POSSUI EFEITO TÓXICO EM MODELO EXPERIMENTAL DE ZEBRAFISH (Danio rerio)
Authors	JOÃO MARCOS RODRIGUES DA SILVA, FRANCISCO ERNANI MAGALHÃES, ADRIANA ROLIM CAMPOS, GABRIELA ALVES DO NASCIMENTO, ARICLÉCIO CUNHA DE OLIVEIRA, KECIANY ALVES DE OLIVEIRA
Affiliations	Núcleo de Biologia Experimental, UNIFOR, Instituto Superior de Ciências Biomédicas, UECE
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O carvacrol (2-metil-5-(1-metiletil)-fenol) é um composto fenol monoterpênico líquido, encontrado principalmente no óleo de orégano (<i>Origanum vulgare</i>). Diversas propriedades ligadas ao carvacrol (CVC) foram investigadas, tais como ação antiinflamatória, antioxidante, anti-hiperglicemiante e antibacteriana. O modelo experimental zebrafish (<i>danio rerio</i>) vem sendo empregado como modelo experimental complementar ao uso de roedores em testes toxicológicos, genéticos e comportamentais.</p> <p>Objective: Avaliar o efeito toxicológico do CVC em modelo zebrafish (<i>Danio rerio</i>) adulto. Methods: Foram utilizados zebrafish (ZFa) adulto (n=50), selvagens, ambos os sexos, (60-90 dias) e mantidos em aquários de vidro (40 x 20 x 25 cm), contendo água desclorada e bombas de ar a 25 oC e pH 7.0, com ciclo cicardiano de 14:10 h e ração (Spirulina®) ad libitum. Os peixes (n = 8/grupo) foram tratados com 20 µL, via oral, de CVC (0,0001 ou 0,0005 ou 0,001 ou 0,005 ou 0,01 ou 0,05 ou 0,1 ou 0,5 ou 1,0 mg/mL) ou Veículo (DMSO 3%; 20 µL; v.o.). Foram realizados os testes de toxicidade aguda 96h e o teste de campo aberto. Todos os procedimentos experimentais foram aprovados pelo Comitê de Ética do Uso de Animais da Universidade Estadual do Ceará (CEUA-UECE), sob protocolo no 04009489/2023. Results: Sugere-se que a CL50 do CVC é de 0,04 mg/mL. O CVC mostrou-se tóxico frente ao ZFa até 96 h em concentrações acima de 0,01 mg/mL. As concentrações de CVC (0,0001 – 0,01 mg/mL) não alteraram a atividade locomotora dos ZFa, significativamente diferente (q = 6,302, p<0,001; q = 7,630, p<0,0001; q = 8,310, p<0,0001; q = 9,082, p<0,0001; q = 5,777, p<0,01) do diazepam (10 mg/mL; 20 µL; v.o.), usado como controle sedativo (q = 7,783, p<0,0001 vs. Naive; q = 5,653, p<0,0001 vs. Veículo). Conclusion: Os dados obtidos no presente trabalho revelaram que o carvacrol (CVC) é seguro frente ao ZFa (até 0,01 mg/mL) e não apresentou efeito sedativo frente ao zebrafish adulto. Support: UNIFOR (Edital FEQ 50/2021) e FUNCAP (PS1-00186-00240.01.00/21) cedidos à Profa. Dra. Adriana Rolim Campos da UNIFOR, bem como a FUNCAP (UNI-0210-00160.01.00/23 e FPD-0213-00140.01.00/23) cedidos ao Prof. Dr. Francisco Ernani Alves Magalhães (UECE-PPGNS). Protocol: 04009489/2023</p>

Title	SAFETY AND IMMUNOGENICITY OF THE ANTICOCAINE VACCINE UFMG-VAC-V4N2 IN WISTAR RAT
Authors	RAÍSSA LIMA GONÇALVES PEREIRA, SORDAINI MARIA CALIGIORNE, JULIANA SAD, BRIAN SABATO, IGOR ROCHA, FREDERICO DUARTE GARCIA
Affiliations	Saude mental, UFMG
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Introduction: In recent years, the most promising treatment for cocaine addiction is an immunological strategy called an anti-cocaine vaccine. A new molecule UFMG-V4N2, has been shown to be able to produce anti-cocaine antibodies in murine models, these antibodies reduce the passage of the drug to the brain. Developing a formulation with components approved for use in humans requires toxicity tests at repeat doses. Objective: This research is a pre-clinical, interventional, longitudinal study to assess the local and systemic toxicity and immunogenicity of the UFMG-V4N2 in rat model. Methods: Methodology: Forty adult animals, male (20) and female (20) of the specie Wistar were divided into two groups: Control has received adjuvant and treated group received 0,3mL of the vaccine UFMG-V4N2 through 4 intramuscular injections on days 0, 7, 21, 28, and 42. Food consumption and water intake were recorded daily, and the animal's weight was monitored. Tissue samples were immediately collected after the euthanasia for histopathologic analysis. Biochemical and hematological tests and ELISA were used to evaluate vaccine safety and immune response induction parameters. This study was submitted and approved by the Ethics Committee for the Use of Animals, CEUA, registered under protocol CEUA 37/2018. Results: In the first inoculation, no deaths occurred in any groups and none of the animals had lesions at the inoculation site. No significant differences were observed in the means of body weight, weekly food, and water intake. Both groups showed increased creatinine values, accompanied by statistically significant differences in urea values. No noteworthy changes were found in the systemic histopathological assessment. Evaluation of the injection site showed moderate focal panniculitis and myositis with mild fibrosis. Evaluation of the lymph nodes revealed mild lymphoid hyperplasia and evaluation of the spleen showed moderate lymphoid hyperplasia in all vaccinated animals. The mean levels of anti-cocaine IgG (OD) were significantly higher in the vaccinated rats when compared to the baseline. Conclusion: The anti-cocaine vaccine UFMG-V4N2 presented a favorable safety profile and induced immune response in a rat model. The results are in accordance with criteria required by the regulatory agencies to proceed with the vaccine for future clinical trials. Support: Fapemig, CNPq Protocol: CEUA 37/2018</p>



Title	O XAROPE DE YACON NÃO APRESENTA EFEITO SEDATIVO E TOXICIDADE AGUDA EM MODELO EXPERIMENTAL DE ZEBRAFISH (<i>Danio rerio</i>)
Authors	MARCOS FREITAS PEREIRA, DANILO SILVA ALVES, GABRIEL MARTINS DE ARAÚJO SOUSA, LIA GOMES CRISÓSTOMO SABÓIA, ARICLÉCIO CUNHA DE OLIVEIRA, KECIANY ALVES DE OLIVEIRA
Affiliations	Centro de Ciências da Saúde, UECE, Programa de Pós Graduação em Ciências Fisiológicas, UECE, Programa de Pós Graduação em Nutrição e Saúde, UECE
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: O yacon (<i>Smallanthus sonchifolius</i>) é uma raiz encontrada no Brasil, com baixo valor calórico e um elevado teor de frutooligossacarídeos (FOS). Investigações mostram que o xarope da batata yacon pode auxiliar na redução dos níveis séricos de glicose e lipídios, melhorar a absorção de minerais e saúde intestinal. O zebrafish (<i>Danio rerio</i>) vem sendo utilizado como um modelo experimental complementar aos roedores em estudos toxicológicos, genéticos e comportamentais. Objective: Avaliar o efeito toxicológico do xarope de yacon em modelo zebrafish (<i>Danio rerio</i>) adulto. Methods: Foram utilizados 50 zebrafish (ZFa) adultos, de ambos os sexos e com idade entre 60 e 90 dias. Esses peixes selvagens foram mantidos em aquários de vidro (40 x 20 x 25 cm) contendo água desclorada e com bombas de ar, a uma temperatura de 25 °C e pH de 7,0, sob um ciclo circadiano de 14:10 horas. Eles foram alimentados com ração Spirulina® ad libitum. Os peixes, divididos em grupos de 8, receberam por via oral 20 µL de xarope de yacon em concentrações de 0,01 mg/mL, 0,1 mg/mL ou 1 mg/mL, ou receberam apenas o veículo (DMSO 3%; 20 µL; v.o.). Foram realizados testes de toxicidade aguda de 96 horas e o teste de campo aberto. Todos os procedimentos experimentais foram aprovados pelo Comitê de Ética no Uso de Animais da Universidade Estadual do Ceará (CEUA-UECE), sob o protocolo número 04009489/2023. Results: Propõe-se que a CL50 do xarope de yacon pode exceder 1,0 mg/mL. As concentrações de xarope de yacon (0,01 – 1 mg/mL) não modificaram significativamente a atividade locomotora dos ZFa, mostrando diferenças não significativas ($q = 1,089$, $p < 0,05$; $q = 0,2178$, $p < 0,05$; $q = 4,065$, $p < 0,05$) em comparação com o diazepam (10 mg/mL; 20 µL; v.o.), utilizado como controle sedativo ($q = 14,44$, $p < 0,0001$ vs. ingênuos; $q = 14,63$, $p < 0,0001$ vs. veículo). Conclusion: Os resultados deste estudo indicam que o xarope de yacon é avaliado como seguro, uma vez que não demonstrou efeito sedativo em zebrafish adultos e não apresentou toxicidade aguda nas concentrações avaliadas. Support: Sem apoio Protocol: 04009489/2023</p>

Title	Acute App-Guided Slow Controlled Ventilation Reduces Salivary Cortisol Levels in High School Students
Authors	PALOMA GONÇALVES, BIANCA DA MOTTA SAMPAIO COELHO, ANA RAFAELY DA SILVA PEREIRA, LÍVIA BRUNI DE SOUZA, RENATA GIRARDI CASALI BRONZATTI, AMANDA SANT ANNA SCIAMMARELLA MONTECIN, PAULO EDUARDO DA COSTA FERREIRA, CAROLINA MARIA BRAGA DE OLIVEIRA, GABRIELLA MARIA DE FARIA, THAÍS CERQUEIRA REIS NAKAMURA, MAURO GUERRA TREXLER MOURÃO, FABIANA GOMES FERREIRA, KARINA RABELLO CASALI, TATIANA SOUSA CUNHA
Affiliations	Medicina, UNIFESP, Ciência e Tecnologia, UNIFESP, Instituto Embraer Colégios, IEC
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Studies investigating the implementation of relaxation practices, including controlled ventilation, within school settings show promising potential, with benefits observed in stress reduction due to vagal activation. Objective: To evaluate the effect of an acute session of slow controlled ventilation maneuver on cortisol concentration, and to correlate with stress, anxiety, and depression indices obtained through a self-reported questionnaire. Methods: High school students (n=39, 12 male / 27 female, 14-16 years old) were included in the protocol, completed an electronic survey Depression Anxiety Stress Scale-21 (DASS-21) and were submitted to a physical examination. Controlled ventilation (6 incursions per minute, 5 minutes duration) was performed with the support of a mobile application. Saliva samples were collected before (Baseline) and after slow ventilation (Intervention). Salivary cortisol levels were quantified using a commercially available high-sensitivity salivary cortisol ELISA kit (R&D, KGE008B R&D Systems kit), and data was analyzed by Student t paired test. The protocol was approved by the Institutional Research Ethics Committee. Results: According to the results of the DASS-21, the physiological symptoms of students were classified as “moderate” (anxiety: 15 ± 8.2, depression: 15 ± 8.3 and stress: 22 ± 8.0 points). The practice of 5 minutes of slow controlled ventilation induced a significant reduction of salivary cortisol concentration (B: 1.990 ± 0.0661 vs. I: 1.956 ± 0.0591 $\mu\text{g/dl}$, $p < 0.0001$), and there was a positive correlation between salivary cortisol at baseline (B) and stress, evaluated by DASS-21 ($r: 0.4304$, $p: 0.0062$). The correlation between stress levels and cortisol was not present when we performed the analysis using the concentration of the corticoid after the intervention ($r: 0.1804$, $p: 0.2717$). Conclusion: Our findings suggest that brief sessions of slow controlled ventilation can effectively reduce salivary cortisol levels and stress indicators. Future research should explore longer-term effects and consider integrating ventilation practices into educational settings to potentially enhance stress management strategies among students. Support: Coordination for the Improvement of Higher Education Personnel (CAPES-001), São Paulo Research Foundation (FAPESP 2023/09536-2). Protocol: CAAE 49629221.8.0000.5505</p>



Title	Development of a Spiking Vocabulary for Analyzing Circuit Interactions in Epileptic Seizures from Electrographic Patterns Using Hybrid Techniques of Dynamical Systems and Machine Learning
Authors	GIBRAM RAUL CAMPOS DE OLIVEIRA, JOÃO PEDRO CARVALHO MOREIRA, MÁRCIO FLÁVIO DUTRA MORAES
Affiliations	Departamento de Fisiologia e Biofísica, UFMG
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: Epilepsy consistently involves a specific circuit abnormally activated during ictogenesis in each patient. Understanding the dynamic relationships between small units of neural activities during seizure periods can provide unprecedented insights essential for accurate diagnosis, prediction, and precise treatments. However, comprehending the desired electrical brain activities during these periods and the interactions between circuits is extremely complex. Therefore, a technique has been developed that allows the conversion of brain activities into a spiking vocabulary. This transforms the problem from the electrical-physiological domain to the linguistic abstraction domain, allowing analyses and interpretations not previously experienced. Objective: This study aims to create a linguistic model to represent the electrographic patterns during epileptiform seizures using spiking and semi-spiking segments as unitary elements. Methods: Data from previous studies conducted by the “Núcleo de Neurociências, UFMG” were used. An 8-week-old Wistar rat (CEUA: 116/2021) was used to record bilateral activities in the amygdala complex and CA1 hippocampus, and kainic acid was administered to induce seizures. A supervised model was trained to detect seizure periods. After identifying seizures, spiking analysis and alphabet creation were performed. Each spike and sub-spike throughout the seizure was identified. Similar spikes were grouped as the same letter. Sequences of spikes that repeated more than once were considered words, forming sentences. A recurrence plot, a non-linear dynamical systems technique, was used for word creation and spike identification. Results: Seizure spike detection achieved an AUC of 0.98; spike identification had a similarity level greater than 80% (predominantly 90%); the constructed vocabulary validated the hypothesis that it is possible to form words (sequential segments of characters that repeat more than once) and consequently sentences. An example of a real sentence generated from the constructed vocabulary for a 3-second seizure segment: “YNE EMI NTE BWYCWYN RLW EFDHG TKEE HGWYN FEDH QNEDLYNEYQ NFED WYQ EDRML EPNEET RLW.” This segment represents a sentence whose words carry condensed and representative information of the analyzed segment. Conclusion: The results validate the hypothesis that it is possible to construct a representative vocabulary of electrographic patterns of epileptiform seizures. This approach enables the use of advanced NLP techniques, facilitating a deeper understanding of brain processes, now represented by textual data instead of temporal data, offering opportunities for advancements in the study and comprehension of cerebral processes. Support: This study was financed by the Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG), Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq). Protocol: CEUA: 116/2021</p>

Title	EFEITO DA FOTOBIMODULAÇÃO E DO CATABOLISMO DO TRIPTOFANO SOBRE ASPECTOS MORFOFUNCIONAIS DE CONDROCITOS E CÉLULAS MESENQUIMAIS HUMANOS EM CULTURA PRIMÁRIA
Authors	MARIA THERESA CALIL ANGELINI DE FREITAS, TAYANE CRISTINA SILVA VELASCO DE ALMEIDA, HUMBERTO DELLE
Affiliations	PÓS GRADUAÇÃO EM MEDICINA, UNIVERSIDADE NOVE DE JULHO
Session	9-Novas terapias, desenvolvimento tecnológico e Inovação
Abstract, Ethics Committee Number, and Financial Support	<p>Introduction: A cartilagem articular comprometida na osteoartrite tem baixo potencial de reparação. Sendo assim, o transplante autólogo de condrocitos surge como possibilidade de tratamento promissor. Na articulação artrossinovial, os condrocitos são nutridos e banhados pelo líquido sinovial composto também de células tronco mesenquimais pluripotentes (CTM) que possuem propriedades anti-inflamatórias e imunossupressoras aumentadas na OA. A indoleamina-2,3-dioxigenase (IDO) é uma enzima com capacidade de imunossupressão de CTMs que degrada o triptofano, induzindo anergia e apoptose em linfócitos T e células Natural Killers (NK). Seus catabólitos (reconhecidos como derivados da quinurenina) contribuem para a imunomodulação local, inibindo a proliferação e ativação de células T e Nk. A fotobimodulação (FBM) é uma opção não cirúrgica de tratamento da OA por promover a proliferação celular, migração e diferenciação de linhagens osteogênicas, miogênicas, angiogênicas e condrogênicas das células CTM. Objective: O presente projeto traz como proposta estudar a ação da IDO1 e a aplicação da FBM como alternativas que possam melhorar aspectos qualitativos e quantitativos da cultura primária de condrocitos e CTM adulto humanos, a fim de otimizarmos o transplante autólogo como tratamento de AO. Methods: Após a aprovação pelo Comitê de ética, o material cartilágneo foi obtido por uma punção padronizada de cartilagem da cabeça femoral do fragmento proximal das fraturas do quadril de 5 adultos idosos submetidos a artroplastia de substituição por trauma no Hospital Municipal Antônio Giglio, em Osasco. . O tecido cartilaginoso foi colocado em tubo estéril contendo tampão PBS e refrigerado em gelo até a chegada no laboratório. Foram colhidos 5 mL de medula óssea do próprio fêmur manipulado, a fim de isolamento de células tronco mesenquimal e colocados em tubos heparinizados (Roger et al., 2020). Foram incluídos pacientes acima de 45 anos, submetidos a artroplastia de substituição por fratura apenas. A cultura primária de condrocitos foi estabelecido segundo Isyar (Isyar et al., 2016). Para a caracterização dos condrocitos, foi feita a detecção de glicosaminoglicanas com coloração por Alcian Blue 1%. A cultura primária de CTM foi estabelecido segundo Baghaei. O protocolo descrito abaixo foi reproduzido com condrocitos em monocamada e CTM. As células da 3ª passagem foram semeadas em placas e incubadas segundo os grupos: • Controle: células incubadas com meio de cultura convencional; • FBM: irradiação com laser de Baixa intensidade (DMC®), luz vermelha • INCB: incubadas com o inibidor da IDO INCB024360; • KY: incubadas com o produto da IDO L-quinurenina; • FBM+INCB: Laser e incubadas com o inibidor da IDO • FBM+Ky: Laser e produto da IDO Foram realizadas as análise: de viabilidade celular pelo método redução do brometo de 3-(4,5-dimetiltiazol-2yl)-2,5-difenil tetrazolium (MTT) e Análise “live and dead”(Live/Dead® Viability/Cytotoxicity Kit, Lefe Technologies) Results: Foram isolados células mesenquimais e condrocitos de 5 pacientes idosos. Conclusion: Mostrou-se possível o isolamento de condrocitos e células mesenquimais de pacientes idosos, sem perda nem contaminação das culturas, com aproveitamento de cartilagem de fragmento ósseo que seria descartado em cirurgia do quadril. Alahdal M. Am J Transl Res. 2020 Jun 15;12(6):2322-2343 Isyar M. J Orthop. 2016 Apr 1;13(3):162-7 Baghaei. Gastroenterol Hepatol Bed Bench. 2017 Summer;10(3):208-213. Support: FAPESP Protocol: 68909823.0.0000.5511</p>