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Organização win EVENTOS

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# Simposio Luso-Brasileiro de Fisiologia

## Workshops

ID SBFSPFW1

### Physiological Computing

Physiological sensing is increasingly capacitated with specialised low-cost and open source tools, which are having a transformational role in the way people learn, experiment, and create imaginative solutions to outstanding problems that can benefit from embedded biomedical systems. The added value of such platforms is being recognised by policymakers and practitioners across different disciplines. As a result, new opportunities are generated for physiologists at different states of their careers, ranging from their first years of study to research and/or professional practice. During this workshop you will learn how to benefit from low-cost hardware and open source software to boost learning, research, and rapid prototyping in the field of physiological sensing. Particular emphasis will be given to BITalino, which is a prominent tool within the state-of-the-art. We will review the basic concepts, show multiple projects and applications involving physiological sensing, explore modular wireless biosignal acquisition systems for real time data acquisition, and become familiar with useful software resources.

*October 2rd*
Introduction to physiological computing. Review of the different types of biosignals and their meanings
Hugo Ferreira
Universidade de Lisboa, Faculty of Sciences - Institute of Biophysics and Biomedical Engineering, Lisboa, Portugal

*October 3th*
Techniques for acquiring biosignals. Analysis and processing of biosignals
Hugo Silva
Universidade de Lisboa, Instituto de Telecomunicações – Inst. Superior Técnico,Lisboa, Portugal

October 5th
Classification of biosignals. Introduction to machine learning techniques and to artificial intelligence in physiological signals
Patricia Bota, Mariana Abreu and Hugo Silva
Universidade de Lisboa, Instituto de Telecomunicações – Inst. Superior Técnico, Lisboa, Portugal

October 6th
Hands-on Bitalino
Hugo Silva
Universidade de Lisboa, Instituto de Telecomunicações – Inst. Superior Técnico, Lisboa, Portugal

ID SBFSPFW2

### Looking “to and through” the skin window – new insights into skin physiology

*A partnership between NEATEC - Faculdade de Ciências Farmacêuticas de Ribeirão Preto-USP and CBIOS, the Research unit in Biosciences and Health Technologies of the Universidade Lusofona - Lisboa*

Skin research has become a multidisciplinary area attracting many interests besides dermatology, and now encompasses the remarkable industrial development and innovation from cosmetics and toiletries, pharmaceuticals, medical devices, chemicals, and food supplements. New proposals on molecules, materials, views, and concepts targeting or involving human skin are now regularly produced with contributions from a wide range of diverse knowledge areas. Research in dermatology, cosmetic medicine and plastic surgery is now benefiting from increased interest in fields such as medicinal chemistry, molecular biology, pathophysiology, pharmacology and therapeutics, drug delivery, and food technology, resulting in new and exciting science.

The complexity of skin functions explains why many open questions still remain about its mechanisms. Therefore the present workshop introduces new exploratory insights into human skin applicable to basic or applied research but also to medical practice. Especially important is the non-invasive character of many of the approaches suggested here to keep us as near as possible to the normal physiological state.

*October 2nd*
Approaching the skin "barriers" - characterization and application
Luis Monteiro Rodrigues
CBIOS — Universidade Lusófona's Research Center for Biosciences and Health Technologies, Lisboa, Portugal

*October 3rd*
Epidermal hydration (superficial and deep; the epidermal map – relation to structure (applications of confocal microscopy and high resolution sonography)
Patricia Maia Campos
University of São Paulo, Faculty of Pharmaceutical Sciences of Ribeirão Preto, Brazil

*October 5th*
Approaching biomechanics and microcirculation – characterization and applications
Patricia Maia Campos and Luis Monteiro Rodrigues
University of São Paulo, Faculty of Pharmaceutical Sciences of Ribeirão Preto, Brazil; CBIOS — Universidade Lusófona's Research Center for Biosciences and Health Technologies, Lisboa, Portugal

*October 6th*
Skin biomechanics and Langer lines – assessment of skin perfusion as a model to study disease's mechanisms. Luis Monteiro Rodrigues , Liliana Tavares Marques e Clemente RochaCBIOS — Universidade Lusófona's Research Center for Biosciences and Health Technologies, Lisboa, Portugal

# Plenary Lectures

ID SBFSPFL1

**Mismatch novelty exploration training shaping of hippocampal synaptic plasticity and cognition and the role of disinhibition and VIP expressing interneurons**

Diana Cunha-Reis[1,2].

*[1]Departamento de Química e Bioquímica, and [2]Biosystems & Integrative Sciences Institute (BioISI), Faculdade de Ciências da Universidade de Lisboa, Lisboa, Portugal.*

Memory formation relies on experience-dependent changes in synaptic strength such as long-term potentiation (LTP) or long-term depression (LTD) of synaptic activity. The stability of the memories formed, and of the respective synaptic plasticity phenomena involved, is shaped by previously learning experiences (either recent or remote) through metaplasticity.

Acutely, spatial novelty enhances retrieval of a previously acquired memory through a mechanism that is dependent on NMDA receptor activation and LTD. Mismatch novelty exploration training enhances both LTP and depotentiation in the hippocampal CA1 area and influences hippocampal-dependent learning and memory processes[6], suggesting can be used to reshape brain circuits and promote cognitive recovery in physiological processes or pathologies where LTP/LTD imbalance occurs, such as aging, epilepsy or Down's syndrome.

VIP, expressed in hippocampal interneurons targeted by septal GABAergic and median raphe serotonergic afferents, has a restraining effect on hippocampal synaptic plasticity (LTP, LTD and depotentiation) essentially through VPAC1 receptor activation and modulation of disinhibition mechanisms.

We recently observed that novelty training decreased the influence of endogenous VIP on LTP expression but reinforced the influence of VIP on depotentiation expression thus shifting the paradigm of VIP modulation of hippocampal synaptic plasticity.

In this talk we will discuss how these recent findings might reflect an altered control of disinhibition mechanisms controlled by VIP expressing interneurons and their modulation by hippocampal serotonergic and other monoaminergic inputs.

Diana Cunha-Reis (dcreis@fc.ul.pt) is a Junior Researcher at the Department of Chemistry and Biochemistry (DQB) and BioSystems & Integrative Sciences Institute (BioISI) Faculty of Sciences University of Lisbon (FCUL) since July 2019 and course responsible for the Physiology course of the Biochemistry BSc degree at DQB, FCUL. She is secretary of the Portuguese Physiological Society (since October 2019).

She graduated with a degree in Biochemistry in 1999 from FCUL and completed her PhD in Biomedical Sciences, Neuroscience Specialty at the Faculty of Medicine University of Lisbon (FMUL), Portugal in 2007. As part of her PhD studies she was a visiting fellow at the Rudolph-Boehm Institute for Pharmacology and Toxicology, Faculty of Medicine, University of Leipzig, Germany and Swammerdam Institute for Neurobiology, Faculty of Biology, University of Amsterdam, The Netherlands.

From 2007 to 2010 she was a postdoctoral research fellow at the Neuroscience Unit, Instituto de Medicina Molecular, University of Lisbon, Portugal. From January 2012 to June 2019 she was a postdoctoral researcher fellow at Centro de Química e Bioquímica, DQB, FCUL, and Clínica Universitária de Neurologia and Instituto de Medicina Molecular, FMUL, Portugal. From September 2012 to September 2014 Dr. Cunha-Reis was assistant professor in Human Physiology (course responsible) at ECTS, Universidade Lusófona de Humanidades e Tecnologias, Lisbon, Portugal. She was PI of two FCT research projects and contributed as team member to 10 national (FCT) and European (COST) Research projects.

She is an invited Senior member of British Pharmacological Society (BPS) and International Society for Neurochemistry (ISN) since 2017. She is a member of Portuguese Physiological Society (SPFis). She is also member of Portuguese Neuroscience Society (SPN, which is a member of FENS and IBRO) and Portuguese Pharmacological Society (SPF, a member of EPHAR and IUPHAR).

Her research interests are focused on the development of alternative therapeutic strategies for mesial temporal lobe epilepsy (MTLE). In particular, she is committed to the elucidation of the therapeutic benefit of the ketogenic diet in MTLE, the development of neuropeptide therapeutic delivery strategies for MTLE prevention, and the development of cognitive training strategies to attenuate cognitive decline in MTLE.

ID SBFSPFL2

## Autism - a disorder of motor coordination and sensory integration

Carlos Nuno Filipe

*NOVA Medical School, Dept. of Physiology. Lisboa Portugal*

The criteria for the classification of autism and the clinical intervention in this developmental disorder goes on being guided by the interpretation that traditional psychology have made of it. Had the clinical orientation of the main researchers who described it been different - almost all psychologists or psychiatrists - and the criteria that define it would have been different. The exuberance of behavioural changes that people with autism exhibit was perhaps the main reason why this disorder fell into the preferred domain of psychology and led to, as a rule, less interest from neurology and neuroscience.

Pressure from parents' groups also contributed to this situation. In fact, in a few other clinical conditions, the weight of the influence of parents and family members was as important as in autism. Among all the characteristics and peculiarities that people with autism can present, one of the hardest and most difficult to accept by parents has always been the difficulty of communication and the little emotional reciprocity of children with autism: the apparent indifference, the difficulty in touching and be touched, the absence of manifestations of pleasure in sharing affection, the "inner isolation".

Considering Autism Spectrum Disorders (ASDs) to be "socialization disorders" seems, therefore, to be the shortest definition that comes closest to what was described by the first researchers. Considering them only (or mainly) as "socialization disorders" is, however, extremely reductive. ASDs are, neither in their origin nor in their implications, essentially disturbances of socialization. If not, it would imply that, in isolation, away from social

contact, the person with ASD would behave similarly to any other person under the same conditions, which is not the case at all. In ASD there are neurophysiological changes that affect socialization, among other neurocognitive functions. Furthermore, I do believe, the functions directly linked to socialization are not the primarily affected. The disturbance is upstream, in other functions without which socialization cannot be carried out competently.

People with autism have changes in movement coordination (sequence and timing), in the perception of the body, in emotional control, in selective attention and anticipation, in the perception and adequacy of social interaction and, consequently, in joint attention, grouping and conceptual generalization, which point to diffuse (or, at the very least, multifocal) changes of what we generally call Integrative Functions.

Changes in gait, such as the absence of alternating balance of the arms, rigid posture with little flexibility of the trunk or gait on toes, are very common in ASD. Changes in motor control (e.g. flapping, stereotypes, body balancing, vocal tics, and executive slowness with increased movement latency or difficulty in alternating movements) are common in ASDs and, as such, should be referred to and understood as characteristic of the disturbance.

Changes in sensitivities have also been well documented in the ASDs. Examples are hypersensitivity to noise, intolerance to certain smells or discomfort caused by the touch of certain textures. Habitual, too, is the special pleasure that some people with ASD seem to derive from particular forms of sensory stimulation, particularly in the tactile and luminous modalities (e.g. the touch of certain textures or the continued observation of certain shines or reflections).

Our work points to the existence of a disturbance in the mechanisms of integration of sensory information and motor coordination in people with ASD, namely in the mechanisms responsible for synchronizing and initiating the action. These mechanisms determine a different perception of the world and an altered interaction with the environment. For the same reasons, body perception may be changed and the awareness that people with ASD have about themselves will be different.

Carlos Nunes Filipe, MD. PhD (carlos.filipe@nms.unl.pt) is a psychiatrist, with a PhD in Neurophysiology and a sub-specialty Clinical Neurophysiology. He is an Associate Professor at the Nova Medical School / Faculty of Medical Sciences of the New University of Lisbon, and the Head of the Department of Medical Physiology

He has developed research in the areas of Physiology and Pathophysiology of the Nervous System in Portugal and The Netherlands. He was the Scientific Director of CADIn (Center for Support to Neurodevelopment and Inclusion), in Cascais between 2005 and 2015, and the Head of Department of Neurosciences at NOVA Medical School / Faculty of Medical Sciences of Universidade Nova de Lisboa between 2012 and 2016.

He has been the Head of Department of Medical Physiology at NOVA Medical School / Faculty of Medical Sciences of Universidade Nova de Lisboa since 2015. He is the Clinical Director of the Portuguese Association for Developmental Disorders and Autism (A.P.P.D.A.), Lisbon.

Over the past twenty years, his interest has been directed primarily at Neurophysiology, Psychopathology and Clinical Developmental Disorders and, in particular, at the manifestations of Developmental Disorders (e.g. Attention Deficit Disorders and Autism Spectrum Disorders) in adolescents and adults.

ID SBFSPFL3

## Invisibles – A New Frontier in Biomedical Sensing

Hugo Plácido da Silva

*IT – Telecommunications Institute IST – Universidade de Lisboa, Lisbon, Portugal, & School of Technology IPS, Setúbal, Portugal*

In the U.S. alone, there are almost twice more heart attacks than reported home structure fires every year. Nevertheless, a typical household has multiple fire detectors to help prevent the latter, and virtually no way of warning about the former. Biomedical sensing, analysis, and interpretation are basic elements of wellbeing assessment, preventive healthcare, and creation of better healing environments.

While wearables have contributed to make such elements a more pervasive and integral part of people's daily lives, biomedical sensing can take health monitoring one step further. By incorporating biomedical sensing in the surrounding environment in a more integrated way, biomedical sensing can become much more pervasive. Although this approach is not likely to "replace" regular methods, they may act as an invisible proxy or complement to regular care.

In this talk we will provide a brief introduction to the "invisibles" approach to biomedical sensing, describing some of the ways in which they can be incorporated in our everyday lives, and presenting practical examples of tools and conceptual installations that illustrate how the living space of the future may become an "invisible doctor."

Hugo Plácido da Silva (hsilva@lx.it.pt) holds PhD and MSc degrees in Electrical and Computers Engineering from the Instituto Superior Técnico (IST) - University of Lisbon (UL). He is a researcher at the IT - Instituto de Telecomunicações (http://www.it.pt/person_detail_p.asp?id=1293) since 2004, and a Professor at IST/UL (https://tecnico.ulisboa.pt/en/) since 2019. He is also one of the co-founders of PLUX – Wireless Biosignals, S.A. (http://www.plux.info), established in 2007 as an innovative technology-based company operating in the field of medical devices for healthcare and quality of life, where he is currently Chief Innovation Officer.

More recently, Hugo has been actively working towards making biomedical engineering more widespread through BITalino (https://www.bitalino.com), an open source software and low-cost hardware toolkit, which allows anyone from students to professional app developers, to create projects and applications with physiological sensors.

His main interest areas include biosignal research, system engineering, signal processing, and pattern recognition, and his work has been distinguished with several academic and technical awards such as the "alumniIPS" career award in 2019, the "Best Industrial and Enabling Technology" at the European Commission's DG-CONNECT Innovation Radar Prize in 2017, the 1st place at the Portuguese Young Engineer Innovation Awards in 2015, the "Most Innovative Technology" award at the MIT Portugal E3 Forum in 2013, just to name a few.

Both at a technical and scientific level, Hugo has actively contributed to and participated in more than 20 national and European projects, funded by grants from Horizon 2020 (H2020), the Seventh Framework Programme (EU-FP7), the National Strategic Reference Framework (QREN/NSRF), the FCT, and several other private and public institutions (e.g., Vodafone Foundation, Portugal Telecom Foundation, etc.). He has published 140+ papers in international refereed conferences, peer reviewed journals, and book chapters.

Hugo is an IEEE Senior Member since 2018 and IEEE Member since 2010, affiliated with the IEEE Engineering in Medicine and Biology Society. Furthermore, he is an active member of the IEEE EMBS Portugal Chapter, where he is currently one of the elected officers.

ID SBFSPFL4

## Physiological Computing - Using Biosignals in a Different Way

Hugo Alexandre Ferreira

*Faculty of Sciences, Institute of Biophysics and Biomedical Engineering, Universidade de Lisboa, Lisbon, Portugal*

In this lecture we will see how physiological signals can be used to investigate how people interact with computational systems and also provide the means to control them.

We'll start by addressing the various types of physiological signals and their meaning and then move on to how we can measure them using everyday devices and wearables. We'll then discuss in general terms how we can turn these signals into actionable data and finally we'll discuss a number of applications, both clinical, such as in writing, driving wheelchairs and treating phobias, and also non-clinical, such as in arts & design, consumer behavior, and sports.

Hugo Alexandre Ferreira (hugoferreira@campus.ul.pt) is a medical doctor and physics engineer, holding a PhD in Physics on the topics of nanotechnologies applied to biomedicine. He was founder and CEO of Haloris Nanotechnologies, a biosensor company for in vitro diagnostics, and worked for Siemens Healthcare as an in vivo imaging expert prior to returning to academia. Presently, he is a senior scientist at the Institute of Biophysics and Biomedical Engineering of the Faculty of Sciences of the University of Lisbon (FCUL). He researches in medical imaging, oncology, neurosciences, brain-computer interfaces and physiological computing. He is also a lecturer and coordinator of the Integrated Master's in Biomedical Engineering and Biophysics at FCUL. Additionally, he has recently founded and held C-level positions

at several digital health, med tech and sports tech companies, including: NeuroPsyAi, a company that improves diagnosis of neurological and psychiatric diseases using brain scans and A.I.; EmotAi, an IoT company that aims to improve sports athletes' performance using physiological data analytics and neurotechnology; Neroes, a company focused in using neurofeedback in sports; and Nevaro, a digital therapeutics company using VR/AR and biofeedback for treating psychiatric illnesses. Finally, he is also an evaluator and advisor for projects and companies in life sciences, nano tech, med tech, and other technology fields.

ID SBFSPFL5

## Neuromodulating metabolic diseases: the carotid body magic circuit!

Silvia V. Conde

*CEDOC, NOVA Medical School, Faculdade de Ciências Médicas, Universidade NOVA de Lisboa*

The carotid bodies (CBs), classically defined as O2 sensors, are involved in the development of peripheral insulin resistance and glucose intolerance. We recently described that CB activity is increased in animal models of metabolic disease and in prediabetes patients and showed that abolishment of CB activity, via resection of CB-sensitive nerve, the carotid sinus nerve (CSN), or via CSN electrical modulation, prevents and reverses diet-induced metabolic dysfunction and sympathoadrenal overactivity, meaning that the beneficial effects of decreasing CB activity on glucose homeostasis are modulated by target-related efferent sympathetic nerves, through a reflex initiated in the CBs. The present talk will provide a state-of-the-art update on the mechanisms of sensory transduction, neural circuitry, and reflex regulation of CBs chemoreceptor in metabolic diseases and will discuss the recent findings showing the efficacy of continuous kilohertz frequency alternative current device implanted on the CSN to reverse clinical features of metabolic diseases in rats.

Silvia Conde (silvia.conde@nms.unl.pt) is Professor of Pharmacology and Neuroscience at NOVA Medical School (NMS) and Principal Investigator at CEDOC (Chronic Disease Research Center) of NMS. She pursued her PhD in Pharmacology from the New University of Lisbon (Portugal) and in Biotechnology from the University of Valladolid (Spain) in 2007, on the role of purines in hypoxic signaling in the carotid body (CB). Afterwards, she dedicated to understanding the pathophysiological alterations in the CB and autonomic nervous system that are in the genesis of cardiometabolic and respiratory Human diseases. As a PI, she developed a new line of research on CB and dysmetabolism, based on the pioneering idea that CB controls glucose homeostasis. She is dedicated to characterization of pathophysiological biosignals, disease signatures and fingerprints that will allow the identification of targets for therapy, particularly bioelectronic targets, as her group described that high frequency electrical stimulation of carotid sinus nerve restores glucose homeostasis in type 2 diabetes models. Her research within this field originated two patents.

In 2009, she was awarded the L'Oreal Medals Honor for Women in Science Portugal and since then her group won several prizes from the Portuguese Society of Diabetes and from the Pulido Valente Foundation.

# PRÊMIO BRANCA DE ALMEIDA FIALHO

## Oral communications abstracts

ID: 3379

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Federal Rural do Rio de Janeiro - Seropédica - Rio de Janeiro - Brasil

Title: ANTIOXIDANT THERAPY WITH N-ACETYLCYSTEINE ATTENUATES THE PROGRESSION OF HEART FAILURE IN MYOCARDIAL-INFARCTED FEMALE RATS.

Introduction: Previous studies from our laboratory and others have shown that females subjected to myocardium infarction (MI) exhibited delayed progression of heart failure compared with males, including milder signs of autonomic and hydroelectrolytic imbalance, and cardiac dysfunction. The N-acetylcysteine treatment has been shown to be effective in reducing oxidative stress and damage to the myocardium. However, most studies use male animals and there is still a false perception that cardiovascular disease would not be particularly dangerous for women. Therefore, it is essential to stimulate the development of therapeutic procedures to improve the quality of treatment in women, since there is evidence that effective interventions are used unequally between the sexes.

Objective: To study the role of NAC treatment for 4 weeks on myocardial remodeling, cardiac function, autonomic modulation, and oxidative stress in infarcted female rats.

Methods: This study was approved by the Ethics Committee for Research of the Federal Rural University of Rio de Janeiro under the protocol number 015/2015. Female Wistar rats were infarcted by left coronary artery occlusion (MI) or sham-operated (SH) and treated with saline (SAL) or N-acetylcysteine (NAC, 250 mg/kg/day) by gavage 24h after surgeries for 28 days. Therefore, the animals were assigned into 4 groups (n=10/group) as following: SH-SAL, SH-NAC, MI-SAL, and MI-NAC. All groups underwent echocardiography (ECHO) and heart rate variability (HRV) study and then euthanasia for tissue collection, pathology, and biochemistry/molecular biology study. Two-way ANOVA with Tukey post-hoc was performed and significance set at $P<0.05$.

Results: The MI-NAC group showed decreased relative heart (4.2±0.3 vs. 5.1±0.9 mg/g body weight) and lung (6.6±0.4 vs. 8.2±0.4 mg/g body weight) weights compared to the MI-SAL group ($P<0.05$). The $H_2O_2$ generation was decreased (30.4±1.1 vs. 43.4±3.4 nmol.mg-1.h-1) while the activity of glutathione peroxidase (136.5±5.1 vs. 131.5±5.6 µmol.mg-1.h-1), and TIOL levels (84.6±5.6 vs. 60.9±7.0 nmol DTNB reduced/mg protein) were increased in MI-NAC compared to the MI-SAL group ($P<0.05$). ECHO recording showed an increased relative wall thickness of the posterior wall of the left ventricle (0.95±0.0 vs. 0.43±0.0 mm) and a decreased internal diameter of the left atrium and aorta ratio (1.0±0.0 vs. 1.35±0.0) in the MI-NAC group when compared to the MI-SAL group ($P<0.05$). The ejection fraction was increased (63.0±3.7 vs. 46.6±3.5%) in the MI-NAC group versus the MI-SAL group ($P<0.05$). The HRV analysis in the time domain showed decreased heart rate (157.0±6.8 vs. 225.4±6.8 bpm) and increased RMSSD (104.5±5.0 vs. 38.41±1.4 ms) in the MI-NAC group compared to the MI-SAL group ($P<0.01$). In the frequency domain, the MI-NAC group exhibited decreased low frequency (0.04±0.0 vs. 0.09±0.0 Hz) and increased high frequency component (0.33±0.0 vs. 0.17±0.0 Hz) compared to the MI-SAL group. As a result, LF/HF ratio was reduced (0.7±0.1 vs. 3.1±0.4) and NGF mRNA expression was decreased (1.8±0.6 vs. 3.7±0.3 x SH-SAL) in the MI-NAC group compared to the MI-SAL group ($P<0.05$).

Conclusions and Support: The NAC treatment delayed the progression of cardiac remodeling and cardiac dysfunction post-MI in female rats. These effects could be explained at least in part by improving the redox balance and the expression of NGF in the heart, as well as normalization of autonomic modulation of heart rhythm. Support: CNPq, CAPES.

ID: 3131

Área: FISIOLOGIA GERAL

Forma de Apresentação: TRABALHO ORAL

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Instituições: UNESP - FACULDADE DE ODONTOLOGIA DE ARARAQUARA - ARARAQUARA - Sao Paulo - Brasil

Title: Estradiol and central angiotensinergic mechanism on sodium intake and palatability in female spontaneously hypertensive rats

Introduction: Excessive salt intake has been associated with the development or worsening of chronic diseases such as hypertension. Spontaneously hypertensive rats (SHRs) have a typical increase in sodium preference. Our previous results showed that estrogens reduce sodium appetite by reducing the hedonic properties of sodium taste in female SHRs, but the mechanisms involved in these effects are still unknown.

Objective: Here we investigated the importance of central angiotensin II AT1 receptor (AT1r) activation for water deprivation-induced sodium intake and palatability in ovariectomized female SHRs treated or not with β estradiol.

Methods: Adult ovariectomized (OVX) female SHRs with a guide cannula implanted in the lateral ventricle (LV) and an intraoral (IO) cannula were used. Rats were treated with β estradiol (E2, 10 µg/kg of body weight – b.wt.; n = 8) or vehicle (VEH, sunflower oil, 0.1 ml; n = 6) subcutaneously (sc) during 8 days. Sodium intake was induced by 24 h of water deprivation followed immediately by partial rehydration with only water for 2 h (WD-PR protocol). At the end of WD-PR, the orofacial motor responses to intraoral infusion of 0.3 M NaCl (IO-NaCl) were recorded before and after the access to 0.3 M NaCl and water to ingest (sodium appetite test). Losartan (AT1r antagonist, 100 µg/1 µl) or saline was injected into the LV 15 min prior to start the IO infusions.

Results: In OVX rats treated with saline into the LV, the frequency of orofacial hedonic responses to IO-NaCl and WD-PR-induced 0.3 M NaCl intake were reduced with the treatment with E2 sc (E2 + saline: 60 ± 16/min and 1.1 ± 0.3, ml/100 g b.wt./h, respectively) compared to the treatment with VEH sc (VEH + saline: 177 ± 48/min and 3.5 ± 0.7 ml/100 g b.wt./h, respectively), with no change in aversive responses. Losartan into the LV decreased the frequency of orofacial hedonic responses and WD-PR-induced 0.3 M NaCl intake in OVX rats treated with VEH sc (VEH + losartan: 63 ± 10/min and 0.3 ± 0.2 100 g b.wt./h, respectively) compared to the treatment with VEH + saline (VEH + saline: 177 ± 48/min and 3.5 ± 0.7 ml/100 g b.wt./h, respectively), with no change on aversive responses. However, losartan into the LV did not significantly change the number of hedonic responses or WD-PR-induced 0.3 M NaCl intake in OVX rats treated with E2 sc (39 ± 10/min and 0.1 ± 0.01 ml/100 g b.wt./h, respectively) and also the aversive responses.

Conclusions and Support: The present results suggest that the effects of AT1r activation on WD-PR-induced sodium intake and palatability in female SHRs are reduced by estradiol.Financial support: CNPq, FAPESP.

ID: 3416

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Federal de Minas Gerais - Belo Horizonte - Minas Gerais - Brasil

Title: EFFECT OF RFAMIDE-RELATED PEPTIDE 3 AND NEUROPEPTIDE FF RECEPTOR ON NEUROENDOCRINE DOPAMINERGIC NEURONS AND PROLACTIN SECRETION

Introduction: The RF-amide peptide family comprises a group of neuropeptides implicated in reproductive function. The family includes kisspeptin (Kp), natural ligand of the kisspeptin receptor (Kiss1r), and the RFamide-related peptide 3 (RFRP3) that binds preferentially to the neuropeptide FF receptor 1 (NPFFR1). Kp is able to activate NPFFR and there is a remarkable cross talk between these peptides and their receptors. Kp stimulates prolactin (PRL) secretion, which is tonically inhibited by dopamine (DA) released in the median eminence (ME) by tuberoinfundibular dopaminergic (TIDA) neurons.

Objective: To investigate the effects of RFRP3 and NPFFR on the activity of TIDA neurons and PRL secretion in female rats.

Methods: To investigate whether Kp acts through NPFFR to stimulate PRL secretion, female rats were ovariectomized (OVX) and treated during 3 consecutive days with estradiol (OVX+E). On the fourth day, rats received intracerebroventricular (icv) injections of the antagonists of NPFFR, RF9 or GJ14, 60 and 15 min before icv Kp-10. Rats were decapitated 5 minutes after the last injection and trunk blood was collected for PRL and luteinizing hormone (LH) measurements. In other experiment, OVX+E rats were decapitated 5 minutes after the icv injection of RFRP3 for measurement of DA and 3,4-dihydroxyphenylacetic acid (DOPAC) levels in the ME. To investigate the role of NPFFR in the action of RFRP3, OVX and OVX+E rats had their jugular vein cannulated and received icv GJ14 60 and 15 min before RFRP3. Serial blood samples were collected for analyses of plasma PRL and LH. We then investigated the role of NPFFR in the estradiol-induced release of PRL and LH. For that, OVX+E rats were treated with icv GJ14 at 10:00 and 12:00 h and blood samples were collected hourly between 12:00 and 18:00 h through the jugular-vein catheter.

Results: Kp-10 injection increased PRL and LH secretion. The treatment with GJ14 did not block the rise in PRL release stimulated by Kp-10, which was changed by RF9. On the other hand, the response of LH to Kp was unchanged by GJ14, whereas it was disrupted by RF9. The icv injection of RFRP3 increased PRL secretion in a dose dependent manner, which was related to increased DOPAC levels and DOPAC/DA ratio in the ME. In OVX+E rats, PRL levels peaked 5 minutes after RFRP3 injection and remained elevated until 10 minutes. This response was blocked by GJ14 and was estradiol dependent, because it was absent in OVX rats. Finally, the peak phase of the estradiol-induced PRL surge was blunted by GJ-14. In contrast, the LH secretion induced by estradiol was increased by GJ14.

Conclusions and Support: We provide evidence that Kp does not bind to NPFFR to increase PRL. On the other hand, RFRP3 increases PRL secretion through the activation of NPFFR. This effect does not seem to be mediated by the reduction in DA inhibitory tone, which is increased by RFRP3. Moreover, RFRP3 seems to play a role in the genesis of the E2-induced PRL surge probably through the release of a PRL releasing-factor. This work was supported by CNPq and CAPES.

ID: 3731

Área: FISIOLOGIA GERAL

Forma de Apresentação: TRABALHO ORAL

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Title: EXERCISE DURING PREGNANCY PREVENTS MEMORY DEFICITS CAUSED BY MATERNAL SEPARATION IN PRE-PUBERTAL FEMALES

Introduction: Maternal separation (MS) causes harm changes linked to stress and is a lead risk factor to mental disorders such as depression, anxiety, and Alzheimer's disease (AD). Its effects include learning and memory deficits related to oxidative stress increase and alterations in neurotransmitters systems. Physical exercise reverses memory deficits caused by MS through the restoration of neurotransmitters levels and redox balance. In addition, maternal exercise prevents AD-related memory deficits. However, the effects of maternal exercise on offspring female rats submitted to MS have not been elucidated.

Objective: To investigate the effects of physical exercise (PE) performed before and/or during pregnancy on the memory of maternal separated prepubertal female offspring.

Methods: This study was approved by the Institutional Committee of Animals Use (protocol 042/2018). 24 adult female rats were divided into 3 groups: I. Pre-gestational and Maternal exercise (PGE); II. Maternal Exercise (ME) and; III. Control (CT). The group I underwent to a 60-70% VO2max treadmill running PE for 4 weeks. After, this group continued the PE during all pregnancy (3 weeks; 8m/min until pregnancy day 14; 6m/min until delivery). The group II only performed the PE during the pregnancy. The group III did not perform PE. After birth, the offspring of each group were separated into two subgroups of 8 rats per dam: no intervention (NI) or MS. MS offspring were separated from their mothers 3h per day during the first 10 days of life. Only female offspring were evaluated in this study. In the postnatal day 22, the females were submitted to recognition and spatial memory tests: object recognition (OR), social recognition (SR) and Barnes Maze (BM). Data from OR and SR was converted in percentage of time and analyzed by one-sample t-test (theoretical mean = 50%). Data from BM by repeated measures ANOVA and two-way ANOVA followed by Fisher's LSD post-hoc.

Results: In the OR test, CT+NI group explored for more time the novel object ($P = 0.02$), as well PGE and ME non-submitted to MS groups (PGE+NI: $P = 0.02$; ME+NI: $P = 0.01$), demonstrating memory consolidation. MS caused memory deficit since exploration time was about 50% in both objects (CT+MS: $P = 0.06$). ME was able to prevent this deficit (ME+MS: $P = 0.01$). Surprisingly, PGE did not prevent the memory deficit caused by MS (PGE+MS: $P = 0.28$). In the SR test, CT and non-MS groups explored for more time the non-familiar animal (CT: $P = 0.01$; CE: $P = 0.04$; ME: $P = 0.04$), demonstrating memory consolidation. MS caused memory deficit ($P = 0.051$) and only ME was able to prevent MS effect (ME+MS: $P = 0.04$; CE+MS: $P = 0.99$). During the BM training, ME was the only group that learned and was able to find the escape on the first day of training (Trial 1 vs Trial 3 $P = 0.02$). In the BM test, ME+NI needed less errors compared to PGE+NI offspring to find the escape ($P = 0.024$). Additionally, the PGE+MS group spent a lower time than CT+NI group on the target quadrant of BM, which means memory deficit ($P = 0.038$). Still, ME+MS group performed better than the PGE+MS group ($P = .01$), spending more time in the target quadrant.

Conclusions and Support: The practice of physical exercise initiated during pregnancy avoids deficits in spatial and recognition memory caused by maternal separation. Support: CNPq.

ID: 2728

Área: FISIOLOGIA GERAL

Forma de Apresentação: TRABALHO ORAL

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Title: THE ANTIDEPRESSANT EFFECT OF RAPANEA FERRUGINEA AND ITS MAJORITARY COMPOUND MYRSINOIC ACID B IN FEMALE DIABETIC RATS IS ASSOCIATED WITH REDUCED OXIDATIVE STRESS IN THE PREFRONTAL AND HIPPOCAMPAL CORTICES.

Introduction: Major depressive disorder (MDD) is one of the most prevalent mental disorders today and affects approximately 322 million people worldwide, in which about 5.1% are women, and 3.6% are men. MDD is a common comorbidity in patients with diabetes mellitus (DM), and a possible pathophysiological mechanism that correlates the two diseases is the increase in oxidative stress due to hyperglycemia. Rapanea ferruginea Mez. (Primulaceae) is popularly known as "capororoca". Studies indicate that the plant exhibits several pharmacological properties, which can be attributed to myrsinoic acid A (MAA) and B (MAB). Previous results demonstrated plant effects on the central nervous system, leading us to explore possible psychotropic effects.

Objective: To evaluate the antidepressive properties of the prolonged treatment of hydroalcoholic extract of the bark of R. ferruginea (HEBRF) and the isolated compounds MAA and MAB on behavioral responses related to depression and on oxidative damage parameters evaluated in the hippocampus (HIP) and prefrontal cortex (PFC) of diabetic female rats.

Methods: We investigated the action of HEBRF (150 mg/kg, o.g.), MAA (5 mg/kg, o.g.) or MAB (3 mg/kg, o.g.) on the depressive behavior

of streptozotocin-induced diabetic female rats (STZ, 75 mg/kg, i.p.). We use female rats because MDD is a disease that affects more women than men, and even a lot of studies are conducted in males, and the results are considered for the entire population. So, the female rats were treated for 28 days after the STZ injection and submitted to the forced swimming test (FST) and open field test (OFT). The levels of lipid peroxidation (LOOH), reduced levels of reduced glutathione (GSH), and activities of the catalase (CAT) and superoxide dismutase (SOD) enzymes in the HIP and PFC were measured for analysis of the action on oxidative stress parameters. The experimental protocol was approved by the local Ethical Committee (CEUA/UNIVALI 002/17).

Results: About the depressive behavior of STZ-induced diabetic rats submitted to FST, HEBRF and MAA showed no changes in behavior, but MAB reduced immobility time when compared to vehicle-treated diabetic rats, although none of the three treatments prevented the increase in plasma glucose levels or weight loss caused by DM. Treatment with HEBRF, MAA and MAB were able to reduce the increased activity of CAT and SOD due to hyperglycemia and were also able to decrease the levels of LOOH in the HIP and PFC. MAB was also able to prevent the reduction of GSH levels in the HIP.

Conclusions and Support: The results indicated that MAB is a compound with a potential antidepressant activity that also acts to combat oxidative damage in diabetic female rats. Support: UNIVALI, CAPES, CNPq

ID: 2729

Forma de Apresentação: TRABALHO ORAL

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Title: MOMETASONE FUROATE ADMINISTERED ORALLY PRESENT ANTI-INFLAMMATORY ACTIVITY WITH MINOR ADVERSE EFFECTS ON FEMALE RAT GLUCOSE AND LIPID METABOLISM

Introduction: Glucocorticoids (GCs) are drugs widely used based on their immunosuppressive and anti-inflammatory (AI) actions. Sex-based biology has identified physiological and pharmacological differences between women and men at the cellular and systemic levels, as well as differences in the development of specific diseases. Autoimmune diseases (rheumatoid arthritis, lupus erythematosus) treated with GCs are three times more prevalent in women. However, most murine studies are carried out on males and scientific findings are often extended to the population, often generating other health problems and inadequate treatments. So, this question merits investigation because sex may lead to different GC effectiveness, which is important for clinical applications. Despite the beneficial effects of GCs, when in excess GCs cause metabolic disturbances in humans and rodents such as glucose intolerance, insulin resistance, and dyslipidemias. Thus, new GC ligands with the potential therapeutic application and minor adverse effects are welcome. Mometasone furoate (MF) is a GC used for the topic and inhaled purposes and based in vitro evidence it potentially exhibits lower side effects.

Objective: To evaluate the sexual dimorphism of the treatment with MF on inflammatory, glycemic, and lipidic parameters in rats

Methods: Female and male Wistar rats (3-months-old) were used. We performed the carrageenan (Cg)-induced peritonitis test (500 µ/cavity, intraperitoneally (ip)) to evaluate the acute anti-inflammatory effect of MF and dexamethasone in rats that were previously treated with different GC doses and routes of administration. In another set of experiments, rats were daily treated for 7 consecutive days, either by oral gavage (og) or ip route, with MF (1 mg/kg, body mass (bm)) for analysis of metabolic parameters. The experimental protocols were approved by the Institutional Ethical Committee (CEUA Nº 5012250518).

Results: MF administered by og and ip routes prevented the inflammatory process induced by Cg in both sexes. Independent of the route of administration, MF treatment reduced the bm gain and food intake in both sexes. Also, all female and male groups presented a decrease of insulin sensitivity on ip insulin tolerance test (ipITT) but just the MF ip male and MF ip and og female groups presented compensatory hyperinsulinemia. Just the MF ip male group presented a glucose intolerance on ip glucose tolerance test (ipGTT). Lipid metabolism was affected only in the ip treatment in both sexes, with hypercholesterolemia and hypertriglyceridemia.

Conclusions and Support: MF possess anti-inflammatory activity when administered through systemic routes in both sexes and exhibit minor metabolic adverse effects when it is orally delivered in the female. Support: CAPES, CNPq Conflict: MF was kindly donated by Aché Pharmaceuticals

ID: 3061

Área: FISIOLOGIA COMPARADA

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Title: THE EFFECT OF ACUTE EXPOSURE TO ATMOSPHERIC PARTICULATE MATTER EMITTED BY THE STEEL INDUSTRY ON HEMATOLOGY AND IMMUNITY IN NILE TILAPIA (Oreochromis niloticus)

Introduction: Steel industry emissions of atmospheric particulate matter (PM) is responsible for cross air-water contamination, depositing metals/metalloids contaminants in aquatic ecosystems. That source of contamination is not observed in environmental monitoring protocols and it has been left outside the scope of ecotoxicological studies.

Objective: We analyzed the effects of acute exposure (96 h) to sublethal PM contamination emitted by steel-industry in hematological and immunological variables in a teleost fish, Nile tilapia, Oreochromis niloticus.

Methods: We analyzed blood samples to access functional indexes related to oxygen transport capacity, immune activity and stress, after acute exposure (96h; n=20, 132.65 ± 26.33g; Ctrl and PM groups) to sublethal contamination with raw PM (1 g×L-1) (CEUA-UFSCar protocol#8105110718).

Results: Acute PM contamination affected the support for oxygen-carrying capacity, reducing hematocrit, hemoglobin, erythrocyte and mean corpuscular hemoglobin concentration. We also observed compensatory increments in the mean corpuscular volume and mean corpuscular hemoglobin. PM exposition also decreased immune activity, observed as a reduction in: leukocytes, thrombocytes and monocytes counting; total plasma protein; leukocyte respiratory activity; and also, as an increase in lysozyme. Furthermore, PM increased glucose and cortisol.

Conclusions and Support: The acute exposure to raw PM caused relevant alterations in the capacity to manage aerobic metabolism and to respond to pathogens. Besides, this acute contamination was also associated with stress response deviating energy from homeostasis maintenance. These problems relate to the capacity for homeostasis maintenance, environmental use and ecological interactions. Hence the aquatic sublethal contamination caused by PM trigger physiological alterations that potentially reduces species fitness leading to serious ecological consequences. These results raise attention to the necessity of both proper protocols for monitoring air-water cross-contamination; and also, for better protocols to address sublethal damage. Keywords: Metals/Metalloids, Environmental risks, Physiological responses, Immune responses, Health status Financial support: This study was financially supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior/CAPES, Brazil.; FAPESP (2019/08491-0).

ID: 3453

Área: NEUROFISIOLOGIA

Forma de Apresentação: TRABALHO ORAL

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Title: DERMATAN SULFATE OBTAINED FROM THE ASCIDIAN IS RESPONSIBLE FOR ANTIOXIDANT ACTIVITY AND NEUROPROTECTION

Introduction: Neurodegenerative diseases are characterized by progressive loss of neurons in the central nervous system (CNS). Several molecules play a role in mammalian CNS regeneration, including glycosaminoglycans (GAGs). GAGs are found in abundance in many marine invertebrates, such as ascidians that belong to the phylum Chordata, which show a high CNS regeneration capacity even in adulthood. Here, we investigated the roles of dermatan sulfate, a type of GAG that was obtained from the ascidian Phallusia nigra.

Objective: We investigated the neuroprotective and antioxidant properties of Phallusia nigra dermatan sulfate (PnDS) after neurotoxic damage induced by the pesticide rotenone using the Neuro-2A cell lineage.

Methods: To evaluate the action of PnDS in the neuroprotection, the Neuro-2A cells were incubated with rotenone and/or PnDS was observed through a mitochondrial activity analysis and morphometric analysis. To evaluate the action of PnDS in the antioxidant system, the Neuro-2A cells were incubated with rotenone and/or PnDS were quantified for total antioxidant capacity against peroxyl radicals and activity of the enzymes superoxide dismutase and catalase.

Results: PnDS in an MTT assay revealed limited growth, as observed in mitochondrial activity. The number of cells after using PnDS alone or in co-incubation with rotenone stopped this growth. This could be attributed to cell death, induced by PnDS. However, morphometric analysis showed that more cells were viable after PnDS incubation in comparison with rotenone. We suggest that PnDS does not induce cell death and it may act in reducing cell proliferation and inducing cell differentiation, as observed by the neuronal appearance, with long neurites emerging from the soma, observed by ultrastructural analysis and acquired after the addition of PnDS. PnDS showed antioxidant activity that reduced reactive oxygen species (ROS) even in co-incubation with rotenone. The reduced ROS probably occurred because PnDS increased the activity of the antioxidant enzymes superoxide dismutase and catalase and improved total antioxidant capacity, which protected cells from damage, as observed through decreased levels of lipid peroxidation.

Conclusions and Support: In conclusion, ours results demonstrated that PnDS showed a notable neuroprotective and antioxidant role after rotenone Neuro-2A exposure. The cell morphology changed, presenting long unbranched neurites, cell viability was improved, ROS production decreased, and CAT activity was enhanced after the addition of PnDS. Together, the results showed a new function of the DS molecule obtained from ascidian marine invertebrates. The special structure of this molecule associated with effective neuroprotective and antioxidant characteristics elucidated a new function of PnDS, which could be useful in the future for pharmacological treatments or in regenerative medicine strategies applied to delay the progression of neurodegenerative diseases or to promote tissue regeneration. Support: This work was supported by the Coordination for the Improvement of Higher Education Personnel (CAPES), the Institute of Biodiversity and Sustainability (NUPEM), and through Young Scientists of the New State grant number E-26/203.021/2018, of the Research Support Foundation of the State of Rio de Janeiro (FAPERJ).

ID: 3458

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: TRABALHO ORAL

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Title: IMPACT OF TEN WEEKS OF EXERCISE TRAINING AND DETRAINING IN OLDER WOMEN ON POSTURAL CONTROL AND BLOOD PRESSURE REGULATION

Introduction: Postural instability during the initial orthostasis seems to be related to the drop in blood pressure in response to active standing in older women and physically active elderly showed have better postural control. Physiological adaptations from exercise training are not permanent, when training is discontinued physical capacity is gradually decreased over subsequent weeks losing the gains obtained with the exercise training.

Objective: The purpose of the current study was to investigate blood pressure and postural balance responses during initial orthostasis in older women after ten weeks of whole-body exercise training and ten weeks of detraining.

Methods: Fifteen healthy older women (64±7 yrs.) underwent a maximal exercise test with a ramp protocol on a cycle ergometer to obtain peak oxygen consumption (VO2peak). Orthostatic test (ORT) consisted in subjects in a supine position (REST) for 10 minutes followed by upstanding to orthostatic position (ORT) for more 7 minutes. The movement of the center of pressure (COP) was recorded with a force platform, stroke volume (SV), cardiac output (CO), heart rate (HR) were recorded by transthoracic electrical bioimpedance and systolic blood pressure by infrared finger plethysmography. The analysis was performed during the first 15seconds of the active standing (onset). For hemodynamic analysis, the NADIR was considered the lowest value for SBP (mmHg) upon onset and recovery point was the first value equal to or higher than the baseline values after onset. Both changes are evaluated COP speed (mm/s) and distance (mm) and changes in SAP from REST to NADIR (ΔNadir) and RECOVERY (ΔRecovery). The time of ΔNadir (NADIRtime) and ΔRecovery (RECOVERYtime) were also calculated. The whole body exercise training protocol (rowing ergometer) consisted of three weekly sessions (30 minutes) at 60-80% of maximal heart rate, acquired by a previous maximal exercise test. Exercise training protocol lasted for 10 weeks and detraining period consisted in 10weeks of no exercise, evaluating volunteers in pre, post-training (+10w) and detraining (-10w). One-way ANOVA for repeated measurement and post hoc of Tukey were employed ($\alpha \leq 0.05$).

Results: As an expected VO2peak increased after +10w and decreased -10w ($p < 0.000$). During ORT test, COP was reduced in +10w and increased after -10w in distance (Pre: 697.6± 101.1; +10w: 580.0± 86.9; -10w: 725.0± 170.0. $p < 0.01$) and speed (Pre: 46.5± 6.7; +10w: 38.7± 5.8; +10w: 48.3± 11.3. $p < 0.01$). At the onset of SBP oscillation was founded lowest values after +10w and highest values after -10w in ΔNadir (Pre:-29.4±15.0; +10w: -19.1±12.3; +10w: -29.7±12.6 $p < 0.01$) and ΔRecovery (Pre: 3.4± 4.6; +10w: -0.5± 2.1; +10w: 0.9± 2.3 $p < 0.01$). The time of oscillation was reduced after +10W and increase after -10W in NADIRtime (Pre: 8.3±5.5; +10w: 5.9±1.8; +10w: 8.3±2.7 $p < 0.05$) and RECOVERYtime (Pre: 13.9±6.5; +10w: 10.3±3.15; +10w: 15.6±4.3 $p < 0.01$).

Conclusions and Support: Whole body exercise training enhances systolic arterial pressure and postural control during orthostatic stress onset in older women, and these improvements were abolished after ten weeks of detraining. Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro (E-6/110.079/2013) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior. Ethics' Comittee Approval (CEP-851.371/14).

ID: 3718

Forma de Apresentação: TRABALHO ORAL

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Title: ACTION OF OXYTOCIN AND STRENGTH TRAINING, ASSOCIATED OR NOT, ON THE BONE TISSUE OF RATS IN THE PERIESTROPAUSE

Introduction: The increase in the number of elderly individuals, focusing on the female population, has drawn attention to studies that investigate preventive measures for diseases. Osteoporosis is a very common disease for the period whose consequences are alarming. Positive effects of oxytocin and strength training have been described in the bone tissue of female organisms.

Objective: Therefore the objective from this study was to analyze the effects of OT associated or not with ST on the femur of rats during the periestropause period.

Methods: Forty seventeen-month-old healthy female rats were subjected in four groups: 1- vehicle (Veh group), 2- OT (Ot group), 3- Strenght training (St) and 4- Ot+St (n = 10/group). OT was administered intraperitoneally in a 12-h interval, every 30 days for 120 days, totaling 8 injections, whereas the vehicle groups received a saline solution. The animals in the St and Ot+St groups performed ST on a ladder three times per week, for 120 days. After experimental period the blood was collected to proceed with live damage and bone biomarkers analyses. Right femurs were collected for microtomography (micro-CT), DXA and biomechanical test (Protocol number: 2018 1636 001566 2/2).

Results: In Ot group there was increase in the average cortical thickness (Ct.Th) and elasticity. In St group there was decrease in the asparate amniotransferase (AST), increase in the bone mineral density (BMD) from total femur, increase in the elasticity from compression test, stiffness and elasticity from three point bending test. In Ot+St group there are more differences. There was decrease in the alkaline phosphatase (ALP) and tartrate-resistant acid phosphatase (TRAP). Improvement was detected in the cortical bone microtomography with increase in the Ct.Th and polar moment of inertia (J) and decrease in the pore number (Po.N); and in the trabecular bone with increase in the bone volume fraction (BV/TV) and trabecular thickness (Tb.Th). There was differences in bone densitometry with increase in the bone mineral density (BMD) from femoral neck bone and total femur. In compression test: increase in the maximum load and decrease in the elasticity; and three-point bending test: increase in the stiffness in relation to Veh and Ot group and decrease in relation to St group, as well as decrease in the elasticity.

Conclusions and Support: We conclude that the isolated therapies have discreet effects on the bone tissue of these animals, while in the combination of the therapies the improvements were much more evident, highlighting the combination of therapies as a promising anabolic strategy for the prevention of osteoporosis in the period of the periestropause. Support: Capes.

ID: 3516

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Title: SELECTIVE LOSS OF KNDY NEURONS IN FEMALE RATS REVEALS MULTIPLE ROLES IN GONADAL AND PROLACTIN AXES

Introduction: Hyperprolactinemia, a highly prevalent dysfunction of the hypothalamus-pituitary axis, is frequently associated with reproductive disorders in women. An important stimulator of the hypothalamus-pituitary-gonadal axis is kisspeptin, a key neuropeptide for fertility. Hypothalamic arcuate nucleus (ARC) neurons that coexpress kisspeptin, neurokinin B and dynorphin A (KNDy) play an important role in the control of luteinizing hormone (LH) and prolactin (PRL) secretions, but the neuroendocrine mechanisms involved are to be elucidated.

Objective: To determine the effects of selective neurochemical ablation of KNDy neurons on the estrogenic regulation of LH and PRL secretion in female rats.

Methods: Adult female Wistar rats received intra-ARC stereotaxic injections of neurokinin B receptor 3 agonist conjugated with saporin (NK3-SAP; n = 5) or vehicle (Veh; n = 6). Estrous cyclicity was monitored over 21 days followed by ovariectomy. Ovaries were processed for histological analysis. Rats were treated with estradiol (E2) cypionate (OVX+E2; 10 µg/rat, s.c.) daily for 3 days. On the fourth day, blood samples were withdrawn from the tail tip at 30-min intervals from 13:00 h to 19:00 h. After 6 days, the rats received oil treatment for additional 3 days (OVX). and blood samples were collected using the same protocol. Whole blood LH and PRL levels were measured by ELISA and brains were immunohistochemically labeled for kisspeptin, tyrosine hydroxylase (TH) and phosphorylated TH (pTH).

Results: NK3-SAP animals displayed an average loss of 66% in the number of kisspeptin-immunoreactive (ir) neurons in the ARC ($P < 0.001$). This lesion decreased body weight gain ($P < 0.001$) and caused irregular estrous cycles ($P < 0.05$). Ovarian analysis revealed increased follicular atresia ($P < 0.05$) and a reduced number of small healthy follicles ($P < 0.05$) in NK3-SAP rats. However, ovulation was not affected, as revealed by the unchanged number of corpora lutea. In the OVX+E2 model, E2-induced LH surge was amplified ($P < 0.01$) and advanced by 1 hour ($P < 0.05$). The PRL surge, in turn, was attenuated in NK3-SAP rats ($P < 0.01$). In the OVX model, basal LH secretion was unaffected by the NK3-SAP lesion, and PRL levels were undetectable in both groups. NK3-SAP and Veh rats presented similar number of TH-ir neurons in the ARC but the pTH-ir and pTH/TH ratio were increased in the median eminence of NK3-SAP rats ($P < 0.05$).

Conclusions and Support: Selective loss of KNDy neurons differently affects E2 regulation of LH and PRL secretion in female rats. Our results support a inhibitory role of KNDy neurons in the generation of the LH surge. The partial loss of KNDy neurons seems to facilitate the LH surge and ovulation even in a condition of irregular estrous cyclicity. The reduction of PRL surge, associated with the increased activity of tuberoinfundibular dopaminergic neurons, reveals that KNDy neurons inhibit neuroendocrine dopamine and this effect is implicated in the E2-induced increase in PRL secretion. This suggests a new pathway for the neuroendocrine control of PRL secretion, in which KNDy peptides orchestrate changes in the PRL release through dopaminergic neurons. Thus, KNDy neurons seem to exert multiple hypothalamic effects impacting the female reproductive function. Support: CNPq, CAPES and FAPEMIG.

ID: 3527

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Federal de Minas Gerais - Belo Horizonte - Minas Gerais - Brasil

Title: Noradrenergic projections to the median preoptic nucleus and KNDy neurons are related to changes in vasomotor control in ovariectomized rats

Introduction: The hot flushes are characterized by excessive peripheral vasodilatation and heat dissipation caused by the post-menopause reduction in estradiol (E2) levels. Recent studies validated the use of ovariectomized (OVX) rats as an animal model of the vasomotor effects induced by the lack of E2. Noradrenaline (NA) projections to the preoptic area are recognized for their role in thermoregulation. Neurons in the arcuate nucleus (ARC) coexpressing kisspeptin, neurokinin B, and dynorphin A (KNDy) have been demonstrated to be involved in the genesis of hot flushes in women and animal models. However, the interaction between NA and KNDy neurons and its role in vasomotor control remains poorly understood.

Objective: Investigate changes in the density of hypothalamic NA terminals in the hot flush model of OVX rats and whether KNDy neurons receive contacts from noradrenergic terminals.

Methods: Wistar rats (CEUA Nº43-2016) were familiarized to the container daily, for 4 weeks. Afterwards, the rats were ovariectomized and implanted with subcutaneous capsules containing corn oil (OVX) or E2 (OVX+E2), and intraperitoneal datallogers. Measurements of tail skin temperature (Ts), body temperature (Tc), and oxygen consumption (VO2) were performed on day 14th after ovariectomy. At the end of the experiment, rats were perfused and the brains were immunohistochemically processed for dopamine-beta-hydroxylase (DBH) single labeling in the median preoptic nucleus (MnPO), medial preoptic nucleus (MPO), anteroventral periventricular nucleus (AVPV), paraventricular nucleus (PVN), and ARC. Dual label immunofluorescence for kisspeptin and DβH in the ARC was evaluated by confocal microscopy.

Results: OVX+E2 rats displayed increased uterus weight and plasma E2 levels compared with OVX rats. Ts was increased in OVX rats and this was prevented by E2 treatment (28 .09 ± 0.53 vs 25.39 ± 0,65 ºC; $P < 0.05$). Nevertheless, there was no difference in Tc and VO2 between OVX and OVX+E2 rats. The integrated optical density (IOD) of DBH-immunoreactive (ir) fibers in the MnPO was 2 times as high in OVX than in OVX+E2 rats (100.0 ± 1180 vs 43.77 ± 9.38 % control; $P < 0.01$). On the other hand, there was no difference between groups in DBH immunoreactivity in the MPO, PVN, or ARC. Interestingly, in the ARC of OVX rats, 74% of kisspeptin-ir neurons were found to be in close apposition and contacted by DBH-ir fibers.

Conclusions and Support: Our data confirmed the phenomenon of increased Ts caused by the lack of E2 in OVX rats, resembling the vasomotor effects of postmenopausal hot flush, and suggest that this effect is not due to metabolic changes. Our findings demonstrate an increase in the density of noradrenergic fibers in the MnPO of OVX rats, which may be involved in the mechanism of increased Ts. Moreover, we show that KNDy neurons receive direct NA inputs, providing a new pathway for the noradrenergic modulation of thermoregulatory and hormonal control. CNPq

# PRÊMIO ÁLVARO OZÓRIO DE ALMEIDA

## Oral communications abstracts

ID: 2831

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Federal de Sergipe - São Cristóvão - Sergipe - Brasil

Title: OXYTOCIN INDUCES ANTI-CATABOLIC AND ANABOLIC EFFECTS ON PROTEIN METABOLISM IN RAT OXIDATIVE SKELETAL MUSCLE

Introduction: Although it is well established that skeletal muscle contains oxytocin (OT) receptors and OT-knockout mice show premature development of sarcopenia, the role of OT in controlling skeletal muscle mass is still unknown.

Objective: The present work aimed to determine OT's effects on skeletal muscle protein metabolism.

Methods: For that, total proteolysis, proteolytic system activities and protein synthesis were assessed in isolated soleus muscle from prepubertal female rats incubated with 10-4 M WAY-267,464 (WAY), a selective non-peptide OT receptor (OTR) agonist. In in vivo experiments, rats received 3-day OT treatment (3UI.kg-1.day-1, i.p.) or saline, and muscles were harvested for mass-gain assessment. All procedures were approved by the Animal Research Ethics Committee (CEPA) of Sergipe Federal University, Brazil, under protocol number 62/2017. The results are expressed as means ± SEM. Normality of the data was assessed with the Shapiro–Wilk test and statistical significance was assessed with the Student t-test, Mann-Whitney test or one-way analysis of variance (ANOVA) followed by Bonferroni's test. $p \leq 0.05$ was taken as the criterion for significance.

Results: In vitro OT receptor stimulation reduced total proteolysis (24% vs. control group), specifically through attenuation of the lysosomal and proteasomal proteolytic systems (38% and 46% vs. control group, respectively), and in parallel increased the Akt/FoxO phosphorylation levels by 60% and 110%, respectively as measured by western blotting. To substantiate these results, the rats were submitted to a three-day motor denervation (DEN)-induced atrophy model and the soleus were incubated with WAY. As expected, DEN resulted in protein upregulation expression of atrophy markers (MuRF-1and atrogin-1) and this effect was attenuated by WAY (76% and 106%, respectively), in comparison with DEN free-WAY muscles. While the protein synthesis was not altered by in vitro treatment with the OT receptor selective agonist, in vivo short-term OT treatment enhanced this process (~65% vs. saline-treated rats), resulting in soleus mass gain (~9%), probably through an indirect effect. The soleus hypertrophy was confirmed by a ~12% increase in its fiber cross-section area. Interestingly, mRNA expression of atrophy markers was not altered in soleus obtained from OT-treated rats compared to controls.

Conclusions and Support: Taken together, these data show for the first time that OTR activation promotes anti-catabolic and anabolic effects on rat oxidative skeletal muscle protein metabolism, probably through crosstalk with the Akt/FoxO signaling pathway. Although the results obtained in OT-treated animals appeared to be indirect, the stimulating effect of protein synthesis indicates that this neuropeptide is a physiological regulator of skeletal muscle mass. Support- CNPq, no. 423854/2018-6; FAPITEC/SE, no. 12/2016 and CAPES, no. 88887.497740/2020-00.

ID: 3098

Área: FISIOLOGIA CELULAR

Forma de Apresentação: TRABALHO ORAL

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Instituições: Centro Universitário da Fundação Herminio Ometto - Araras - Sao Paulo - Brasil

Title: ANTI-INFLAMMATORY RESPONSE OF BACTERIAL BIOCELLULOSE AND ALGINATE GEL IN SKIN BURN

Introduction: Engineering of new materials having therapeutic applications is a major issue in biomedicine. The biotechnology research field aims at the use of natural and synthetic polymers, emerging materials with various properties. Among natural polymers, polysaccharides such as cellulose and alginate have been considered for biomedical application because of their high availability and biocompatibility. Bacterial cellulose has been shown to be promising for wounds and burns healing, standing out for its appropriate physicochemical properties, nanotechnology facet and nanofibres organized in a threedimensional network, which provides mechanical properties, high crystallinity, malleability, porosity and hydrophilicity. Alginate is a malleable structure and easily associated with bivalent ions, such as calcium to form hydrogel that resembles the extracellular matrix and wound moisture preservation. Ion exchange between calcium from the biomaterial and sodium from the wound leads to the formation of a stable gel.

Objective: Evaluate neutrophils and macrophages activity, IL-10 and TGF-β1 antiinflammatory response by treating skin burns with cellulose and alginate gel.

Methods: The Animal Ethics Committee of the Hermínio Ometto Foundation (CEUA_053/2018) previously approved the use of animals. Male Wistar rats were anaesthetised with ketamine (75mg/kg) and xylazine hydrochloride (25mg/kg). An aluminium metal plate (2.0cm diameter) was kept in contact with the animals back for 20 seconds at 120ºC constant temperature. Oral analgesic dipyrone sodium (50mg/kg) and tramadol injection (5mg/kg) was considered during 72 hours of the burning procedure. Four experimental groups: untreated, CMC (Carboxymethylcellulose), Cellulose (CMC with bacterial cellulose) and Cellulose/alginate (CMC with bacterial cellulose and alginate). The animals were followed by 7/14/21/28/35 days. Myeloperoxidase (MPO) and nacetylglycosaminidase (NAG) enzymes levels were evaluated to determine neutrophil and macrophage activation, respectively, by biochemical assay. Moreover, IL-10 and TGF-β1 levels were assessed by immunohistochemistry.

Results: Cellulose/Alginate group presented lower level of MPO on the 14th, 21st and 28th days compared to other groups. On the 21st experimental period, cellulose groups also presented lower level compared to untreated and CMC groups. NAG evaluation also showed lower levels for cellulose and cellulose/alginate groups compared to untreated and CMC groups, especially for cellulose/alginate on the 21st day. The other experimental periods all groups presented similar levels of MPO and NAG. Cellulose/Alginate group presented higher level of TGF-β1 on the 21st day compared to the untreated group, and both of them, IL-10 TGF-β1 were also higher in Cellulose/Alginate and Cellulose groups in the 28th day. The use of cellulose seems to reduce neutrophils activation; however, the association of cellulose with alginate faster mediated the effect. Such association also contributed to reduce the macrophage activation, an anti-inflammatory effect, without impairing the transition to tissue formation phase, since the association of cellulose and alginate enhanced IL-10 and TGF-β1 stimulation.

Conclusions and Support: The use of cellulose/alginate gel reduced the neutrophil and macrophageactivation, and enhanced IL-10 and TGF-β1 levels, which could contribute to regulate the inflammatory response, a positive impact to treat chronic wounds and burn injuries. SUPPORT: FAPESP 2019/14977-2

ID: 2843

Área: FISIOLOGIA GERAL

Forma de Apresentação: TRABALHO ORAL

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Instituições: Instituto de Ciências Biomédicas - Universidade de São Paulo - São Paulo - Sao Paulo - Brasil

Title: HYPERCAPNIA INDUCES SELECTIVE ACTIVATION OF MICROGLIA AT THE LEVEL OF RETROTRAPEZOID NUCLEUS

Introduction: Microglia are resident immune cells in the brain considered constitutively active because of their continuous surveillance function. They survey the activity of neuronal circuits via fine processes and respond to a broad range of brain insults which can disrupt brain homeostasis.

Objective: The current study examines the hypothesis that microglia cells can exhibit changes in their morphological characteristics elicited by high levels of CO2 (hypercapnia) in the ventral medullary surface in a region called retrotrapezoid nucleus (RTN).

Methods: C57Bl/6 mice (CEUA: 8256040619) were subjected to hypercapnia (7% CO2, 21% O2, bal N2) or normocapnia (N: 21% O2, bal N2) for 1 hour. The microglia branches and number of endpoints/cell were quantified from immunohistochemistry images of RTN region using skeleton and fractal analysis. The expression of P2Y12 receptors (selective marker for microglia in the central nervous systems) was also analyzed using optical density (OD) method.

Results: Quantitative analysis reveals that exposure to hypercapnia decreased the number of branches of microglia cells in the RTN region:

(branch number/cell: 1437 ± 87, vs. N: 1623 ± 29, p = 0.034) and (end points/cell: 54 ± 3, vs. N: 63 ± 2, p = 0.024). However, after fractal analysis, no differences were observed in the circularity of microglia in the group exposed to hypercapnia (0.847 ± 0.006, vs. N: 0.850 ± 0.007, p = 0.6). According to our data, hypercapnia decreased P2Y12r expression (0.6580 ± 0.010 vs. N: 0.5520 ± 0.038, p = 0.026) indicating an activation state of microglia cells.

Conclusions and Support: Our partial findings illustrate that microglia activation after hypercapnia includes both decreased cell ramification and decreased expression of P2Y12 receptors within RTN region. Importantly, the quantitative analyses of microglial morphology and phenotype are feasible and would assist in the comprehensive identification of neuroinflammatory condition caused by increased CO2 levels. Financial support: FAPESP, CAPES/PROEX and CNPq

ID: 3108

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: TRABALHO ORAL

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Title: SUBLETHAL CONTAMINATION WITH ATMOSPHERIC PARTICULATE MATERIAL IMPAIRS RESPIRATORY RESPONSE TO HYPOXIA IN FRESHWATER SHRIMP, MACHROBACHIUM AMAZONICUM,

Introduction: Introduction: In Brazil, recent studies demonstrated that water beds and aquatic environments could be cross-contaminated by atmospheric particulate matter (PM) with adverse effects in aquatic fauna and human population. PM is a complex mixture of solid and/or liquids particles of organic and inorganic substances. PM mass is partially composed of a wide range of metals/metalloids particles.

Objective: Objective: We have evaluated how sublethal contamination by rough PM (96h) affects the capacity to respond to environmental hypoxia of the freshwater shrimp, Machrobacium amazonicum.

Methods: Methods: For the experimental trials, shrimps (n = 24, 9.39 ± 2,19g) were exposed to acute PM contamination (1 g.L-1, for 96h, PM group, n = 12; Ctrl group, n = 12), at 25 ± 2°C. After contamination protocol, shrimps underwent progressive hypoxia protocol, in which oxygen availability was depleted by animal aerobic metabolism in a closed experimental chamber. Oxygen signal (MO2 - mMolO2. kg−1. h−1) was continuously recorded thorough the process (optode system - OXY-4 mini PreSens). Based on O2 decline curve, MO2 was calculated for each 3min interval. We analyzed routine metabolic rate (RMR); the critical oxygen tension (Pcrit); and the capacity of aerobic regulation (Regulation value - R) for each animal

Results: Results: PM exposure increased RMR (7.46 ± 0.07 mMolO2.kg−1.h−1) and impaired the capacity to deal with hypoxia, denoted by the R reduction (44,46 ± 1,50 %, PM; 83,85 ± 0,71 %, Crtl). The respiratory impairment was strong enough to alter hypoxia strategy from oxy-regulatory to oxy-conformist-like profile; which revealed a possible compromise in energy allocation and environmental use. Therefore, PM contamination induced physiological limitations to couple with critical environmental challenges.

Conclusions and Support: Conclusion: Despite sublethal, the PM contamination protocol altered the capacity for survival in the natural environment leading to potential ecological consequences. PM cross-contamination needs to be properly considered by the regulatory agencies. Keywords: metals/metalloids, metabolic rate, respiratory strategy, physiological responses Area: Comparative Physiology Financial support: CAPES; FAPESP (2019/08491-0).

ID: 3383

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: TRABALHO ORAL

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Instituições: UFC - Fortaleza - Ceara - Brasil

Title: ACUTE EXERCISE PROMOTES GASTRIC EMPTY RETARDATION WITH PARTICIPATION OF RENIN-ANGIOTENSIN SYSTEM AND DIMINICTION OF GASTRIC MUSCULATURE CONTRATILITY AND INCREASE IN NEURONAL DENSITY IN ENTERERIC NERVOUS SYSTEM

Introduction: It is documented that acute exercise reduces gastric emptying in rats, a phenomenon abolished by pre-treatment with sodium bicarbonate. However, little is known about what pathways are involved.

Objective: To assess the participation of the renin-angiotensin pathway in delaying gastric emptying due to acute exercise and whether exercise changes the contractility in the stomach muscles and the neural density of the enteric nervous system.

Methods: Male Wistar rats (230-280g) were kept under stable temperature conditions (22 ± 2 ° C) and 12h-12h light and dark cycle, with access to food and water. The animals were divided into two groups: acute exercise (AE) and sedentary (SED). The animals underwent a

process of adaptation to the liquid medium (collective swimming, 5 consecutive days, lasting 10-40min) and were submitted to the exercise that consisted of swimming with an overload of 5% of body weight. The sedentary group was in contact only with shallow water. The animals were pretreated with (Captopril 5mg/kg, Losartan 10mg/kg, Spironolactolone 50mg/kg, Aliskiren 50mg/kg) 30min before the experiment, afterwards a gastric retention evaluation was performed by dilution of dye and in vitro contractility. To evaluate the in vitro contractility, the isometric recordings were obtained from bands of stomach segments. The fabrics were tied with one end attached to a fixed pin in the bath chamber and the other end attached to a force transducer coupled to a data acquisition system. The histochemical technique of NADH-diaphorase was used to perform the labeling of neurons. The analysis of the neuronal number density was performed to obtain the number of neurons per field and to verify if the performance of the acute exercise changes the values of the neurons of the myenteric plexus. Data are expressed as mean ± SEM, and analyzed by ANOVA. CEUA-UFC Protocol-115/2016.

Results: Results: Pretreatment with Captopril, Losartan and Spironolactolone reversed gastric emptying delay due to acute physical exercise (SED:48,24 vs AE:69,5±3,4 vs AE+CAP:40,88 ±4,2 vs AE+LOS:55,6±4,7 vs AE+SPL: 50,77±3,7). AE reduced contractility at the fundus of the stomach (SED:0,66 vs AE:0,47±0,18g/mg), when pretreated with captopril and losartan, the reversal of the decrease in contractility (AE:0,47±0,18 vs AE+CAP:0,68; AE+LOS:0,69±0,6g/mg) and AE promove increased the neuronal number density per field obtained by the reaction to NADH with a 100x increase in the Optical Microscope at Stomach (SED:9,13±0,80 vs AE: 16,63±0,76); Ileus (SED:8,82±0,78 vs AE:15,02±1,95) and Colon (SED:12,61±1,17 vs 19,46 ± 0,89). The values of $p < 0.05$.

Conclusions and Support: The delayed emptying due to acute physical exercise has a participation of the renin-angiotensin pathway and the acute exercise promotes a decrease in the in vitro contractility of the stomach fundus and an increase in neuronal density in the myenteric plexus of the enteric nervous system. Support: CAPES; CNPq.

ID: 3385

Área: FISIOLOGIA CELULAR

Forma de Apresentação: TRABALHO ORAL

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Instituições: Faculdade de Medicina de Ribeirão Preto/USP - Ribeirão Preto - Sao Paulo - Brasil

Title: GENE EXPRESSION CHANGES OF THE SEROTONERGIC SYSTEM ON DORSAL RAPHE NUCLEUS AND ITS RECEPTORS ON BASOLATERAL AND CENTRAL AMYGDALA OF WISTAR AUDIOGENIC RATS SUBMITTED TO AUDIOGENIC KINDLING

Introduction: The Wistar Audiogenic Rat (WAR) is an animal model of epilepsy that, when submitted to chronic acoustic stimuli (audiogenic kindling), may present recruitment of mesencephalic and/or limbic structures. The serotonergic system is implicated with behavioral responses by acting on its receptors in the central nervous system.

Objective: Thus, the aim of this work was to analyze the impact of audiogenic kindling and consequent mesencephalic or limbic recruitment on the dorsal raphe nucleus serotonergic system and its receptors in amygdala of WARs

Methods: Our work was approved by the Comitê de Ética para Uso de Animais da FMRP-USP by the protocol number 242/2018. Wistar and WARs were divided into control or submitted to audiogenic kindling groups (2 daily sessions for 10 days). At the end of this protocol, the WARs were subdivided into limbic recruited group, if they had three or more limbic seizures or with mesencephalic recruited group, if they had two or less limbic seizures and presented constants mesencephalic seizures throughout the audiogenic kindling protocol. Nearly twelve hours after the last audiogenic kindling session, the animals were euthanized, with the brains collected for subsequent qPCR. The expressions of the mRNA for Tph1, Tph2, Slc6a4 (SERT) and autoreceptor Htr1a in the dorsal raphe nucleus, as well as the expression of the Htr1a and Htr2c receptors in basolateral and central amygdala were analyzed in Wistar and WARs.

Results: At the end of the audiogenic kindling protocol, nine out of 18 WARs presented limbic recruitment. In the dorsal raphe nucleus, the expression of Tph1 increased in both Wistar and WARs after audiogenic kindling. The Slc6a4 expression also increased after audiogenic kindling in Wistar and WARs, especially those with mesencephalic recruitment. However, this increase was smaller in WARs, when compared with Wistar rats. The expression of Htr1a in dorsal raphe nucleus were increased both by the strain and the audiogenic kindling, with a slight increase in WARs in comparison with Wistar rats, both after the audiogenic kindling. In addition, there was a reduction in the expression of Htr1a in the central amygdala after the audiogenic kindling. Our data indicate that the WAR strain and the audiogenic kindling lead to important changes in the gene expression of the serotonergic system components in the dorsal raphe, as well as the expression of Htr1a receptor in amygdala.

Conclusions and Support: These findings indicate the possible involvement of this system on the pathophysiology of epilepsy and/or its comorbidities. Finantial support: CAPES and CNPq

ID: 3150

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Estadual de Londrina - Londrina - Parana - Brasil

Title: EFFECTS OF PROLONGED TREATMENT WITH GLUCOCORTICOID ON ENERGY HOMEOSTASIS AND ADRENAL GLANDS IN NEONATAL OVERFED MALE RATS

Introduction: One of the neonatal programming models that has been widely used is the manipulation of the litter size in the first days of life, which results in higher body weight gain and adiposity of small litter animals, accompanied by higher concentration of circulating glucocorticoids. It is known that obese rodents are more sensitive to the anabolic effects of glucocorticoids and less responsive do glucocorticoids feedback on hypothalamic-pituitary-adrenal (HPA) axis than lean animals.

Objective: Thus, the objective of the present work was to evaluate the effects of glucocorticoids on litter size reduction-induced responses on energy homeostasis and adrenal glands.

Methods: For this purpose, male Wistar rats (n=65) were obtained by mating of females and males from Central Facility of the State University of Londrina (UEL). On postnatal day 3 (DPN), 3 pups (small litter - SL) or 10 pups (normal litter - NL) were kept with each female. From PND 60 to 88, animals received Water or Corticosterone (CORT-15mg/L) as the only liquid. Body weight and food intake were evaluated during these 28 days of treatment. On 27th day of treatment, animals were subjected to glucose tolerance test, and on the following day, animals were euthanized by decapitation for trunk blood collection and visceral adipose tissues and adrenal glands removal. The experimental procedures were approved by the Ethics Committee on the Use of Animals undergoing experimentation for approval (CEUA: 3457.2109.11).

Results: After 28 days of treatment with corticosterone in NL animals, there was increase in body weight gain, food intake, LEE index, glucose intolerance, total and LDL cholesterol, and adrenal medulla, in addition to decrease in plasma concentration of corticosterone, weight and cortex of adrenal glands. For SL animals, corticosterone induced increase in body weight gain, food intake and LEE index, in addition to reduction in weight and medulla of adrenal glands. In Water-treated animals, litter size reduction caused glucose intolerance, increased weight of epididymal adipose tissue, plasma concentrations of total and LDL cholesterol, triglycerides, free fatty acids and corticosterone, as well as in adrenal medulla. For animals treated with corticosterone, reduction of litter size promoted greater weight of epididymal adipose tissue and plasma concentrations of triglycerides, free fatty acids and corticosterone.

Conclusions and Support: In summary, treatment with glucocorticoid promoted anabolic responses and litter size reduction induced obesity-related metabolic changes; however, the anabolic effects of glucocorticoids were not potentiated in neonatal overfed animals. On the other hand, glucocorticoid treatment reduced corticosterone plasma levels and adrenal cortex only in NL group, without effects on SL animals. Thus, different from other experimental models of obesity, neonatal overfeeding does not change the responsiveness to the anabolic effects of glucocorticoids, but it seems to reduce the feedback responses of glucocorticoids on HPA axis. Financial Support: PROAP CAPES, CNPq.

ID: 3177

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: TRABALHO ORAL

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Title: DIFFERENCES IN KNEE EXTENSORS AND FLEXORS MUSCLE DAMAGE FOLLOWING PLYOMETRIC EXERCISE IN HEALTHY ADULTS

Introduction: Plyometric exercises involve rapid movements and force production using the stretch-shortening cycle. In the transition from eccentric to concentric phases, high mechanical demand is placed on the knee flexors and extensors which may contribute to exercise-induced muscle damage. As knee flexor and extensor muscle function differ during plyometric exercises, muscle damage may also differ due to differences in muscle architecture, joint function and mechanical demands.

Objective: To determine the acute effect of plyometric exercises on muscle damage of the vastus lateralis (VL) and biceps femoris (BF).

Methods: We conducted a clinical trial (NCT04273971) with young physically active men (Ethical approval-CAAE: 96793518.3.0000.5323) who visited the laboratory on two days, 48 h apart. On day one, they completed a 40-min plyometric exercise session including the following exercises: vertical, box, half-squat, high (straight up), bounding, and drop jumps (3 series/15 rep) and a 10-m sprint battery (3 series/8 rep). Rate of perceived exertion (RPE, 0-10 points Borg scale) was assessed immediately post-exercise. Muscle damage was evaluated before,

immediately after, and 48 h after exercise using longitudinal and transverse ultrasound images (40mm probe, 7,5 MHz) in the VL proximal, medium, and distal muscle regions and in the medium region of BF from the preferred leg. The mean grayscale value (increase indicating muscle damage) was measured using Image-J software. At 48 h post-exercise, pain was assessed using a 10-cm visual-analog scale while participants walked down a step. Generalized estimating equations were performed to verify VL time and region interaction, and BF time effect, followed by Bonferroni pairwise comparisons ($p<0.05$).

Results: Data were collected from 21 men (age: 25±3 years old, body mass: 77±9 kg, and height: 174±5 cm; mean±SD). Average RPE was 9±1 points, while mean pain 48 h post-exercise was 4±3/10 points. A time-by-muscle region interaction effect was found for VL ($p<0.001$) with muscle damage in distal and medium regions increasing immediately after exercise ($p<0.001$) for both longitudinal and transverse images and returning to baseline values 48 h after exercise ($p<0.001$). Proximal VL showed similar results for transverse images ($p<0.001$), but longitudinal images revealed increased damage only immediately after exercise compared to 48 h ($p<0.001$). Higher damage was found for the VL distal compared to medium and proximal regions ($p<0.001$, mean difference from 8 to 13 a.u.). The medium region also showed increased damage compared to the proximal region ($p\leq0.023$, mean difference from 6 to 8 a.u.). Despite the echointensity recovery 48 h post-exercise, VL medium and distal values were higher compared to proximal values ($p\leq0.004$), and VL distal higher than medium region ($p<0.001$). Muscle damage in BF showed a time effect for transverse images ($p=0.023$) with increased damage 48 h after exercise compared to baseline ($p=0.021$).

Conclusions and Support: Plyometric exercises induced muscle damage in VL and BF muscles. A distinct difference damage behavior was identified between VL and BF. While VL largely demonstrated immediate post-exercise damage with return to baseline values within 48h, BF demonstrated a more delayed effect with damage only at 48h after exercise. The reasons for the different acute muscle damage behavior require further investigation, but specific responses may depend on their different structural characteristics and exercise demands. Support: CNPq

ID: 3694

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Instituições: UFMG - Belo Horizonte - Minas Gerais - Brasil

Title: REDOX SIGNALING VIA GP91phox(NOX-2) MEDIATES THE RAPID EFFECTS OF ALDOSTERONE IN HEART

Introduction: Aldosterone has a large range of actions on the cardiovascular system, including changing its redox balance. It is already well described that aldosterone activates gp91phox, leading to the production of ROS (reactive oxygen species); and this increase in ROS contributes to the fibrosis caused by chronic treatment with aldosterone for 4 weeks. However, the mechanisms involved in these effects are poorly understood.

Objective: To evaluate the contribution of redox signaling via gp91phox to the rapid cardiac effects of aldosterone.

Methods: Male C57BL/6J and gp91phox-/- mice aged 10-12 weeks were used in this study. Mice were injected with a single dose of aldosterone (60ug/kg) intraperitoneally. Cardiac tissue was removed one hour after the injection. For the experiments with isolated cardiomyocytes, the hearts were collected and transferred to a perfusion system with collagenase and nutrient solution. After isolation, the cardiomyocytes were treated with aldosterone (1µmol/L) or AS605240, a pharmacological inhibitor of PI3Kγ. All experiments performed in this study were conducted in agreement to the ethical norms for research with animals and were approved by CEUA/UFMG (Protocol number: 117/2020).

Results: Aldosterone treatment induced increases in ROS, and total protein carbonylation in cardiac tissue. Additionally, we observed an increase in CaMKII oxidation in response to aldosterone. These effects were suppressed in gp91phox knockout mice, confirming the role of gp91phox in aldosterone induced ROS generation. In ventricular myocytes, aldosterone increased ERK1/2 phosphorylation and calcium transient amplitude. Once again these effects were abolished in cardiomyocytes from mice with deletion of gp91phox. Overall these findings indicated that redox signaling via gp91phox is a necessary downstream signal for aldosterone effects on ERK and calcium in the cardiac cells. Cardiac samples from mice treated with aldosterone presented upregulation of gene transcription related to inflammation (TNF-α, IL-6, SGK-1 and IL-10). Moreover, aldosterone treatment promoted the nuclear translocation of NF-KB in cardiac myocytes. Strikingly, aldosterone induced transcription of inflammatory genes and NF-KB translocation to the nucleus were abolished in cells from gp91phox-/- mice. Moreover, the increase in ROS induced by aldosterone in cardiomyocytes was blocked by the selective inhibitor of PI3Kγ, indicating the upstream participation of this enzyme in the aldosterone signaling pathway.

Conclusions and Support: These findings demonstrate that redox signaling via PI3Kγ/gp91phox/ROS is necessary for aldosterone to exert its rapid effects in the heart, highlighting its potential as a therapeutic target during cardiac disease development. Support: CNPq, CAPES, FAPEMIG.

ID: 3715

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

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Instituições: Laboratório de Investigação Pulmonar, Instituto de Biofísica Carlos Chagas Filho da Universidade Federal do Rio de Janeiro (IBCCF/UFRJ) - Rio de Janeiro - Rio de Janeiro - Brasil

Title: PROTEOMIC PROFILE OF MESENCHYMAL STEM CELL AND EXTRACELLULAR VESICLE IN A HYPOXIA CONDITION

Introduction: Mesenchymal stromal cells (MSCs) are known to be a candidate in the treatment of diverse respiratory disease mainly due to its immunomodulation, angiogenic, and tissue repair capability. However, MSC therapy presents limitations on account of the number of cells that need to be administrated and risk of thromboembolic event. On this basis, extracellular vesicles (EVs) presents as an alternative to a non-cellular treatment, since MSCs effects are mainly attributed to its paracrine secretion of EVs. Pre-conditioning of MSC in hypoxia conditions has been shown to increase the therapeutic effects of MSCs in several diseases. Here we hypothesized that EVs from MSCs conditioned to hypoxia may show a different proteomic profile compared to normoxia.

Objective: To compare the protein profile of MSC conditioned to normoxia (MSC-norm) and their EVs (EVs-norm) to MSC conditioned hypoxia (MSC-hyp) and their EVs (EVs-hyp) by proteomic analysis.

Methods: MSC cells were isolated from the bone marrow of 6 male Wistar rats. After achieving 80 to 90% of confluence, cells were then incubated in normoxia (21%O2, 5%CO2, 74%N2) or hypoxia (1%O2, 5%CO2, 94%N2) conditions during 48 hours. The MTT assay was performed to verify cell viability. Oxygen consummation rate (OCR) of MSC was measured using a high-resolution respirometer (Oroboros®), in which we used the following drugs: pyruvate, malate, succinate (PMS), adenosine diphosphate (ADP), oligomycin, carbonyl cyanide 4-(trifluoromethoxy) phenylhydrazone (FCCP) and potassium cyanide. Total proteins from MSCs and EVs were isolated to mass-spectrometry analysis. Proteomic profile data were analyzed by STRING, PANTHER, and Reactome softwares.

Results: MTT assay indicated that cell viability was higher in MSC-hyp than MSC-norm ($p<0.001$). Basal respiration ($p=0.002$), ATP uncoupled respiration ($p=0.005$), maximal respiration ($p<0.001$) were lower in MSC-hyp than MSC-norm, while ATP coupled respiration ($p=0.847$), and non-mitochondrial respiration rate ($p=0.847$) did not differ. An overall of 3049 proteins were detected from MSC-norm and MSC-hyp, of which 635 proteins were identified only in MSC-norm and 250 only in MSC-hyp. Additionally, 1019 proteins were identified in EVs-norm and EVs-hyp, of which 89 were found only in EVs-norm and 316 only in EVs-hyp. Proteins found in MSC-norm and EVs-norm were mainly involved in immune system activation and angiogenesis process while proteins found in MSC-hyp and EVs-hyp were mainly involved in glycolysis and gluconeogenesis but also in immune system activation and angiogenesis process.

Conclusions and Support: Prior incubation of MSC to hypoxia conditions changed the protein profile of cells and their EVs to a more glycolytic profile, which has been shown to enhance cells' immunomodulatory and angiogenic capacity. This change in proteomic profile may provide a better therapeutic effect in respiratory diseases with an inflammatory profile and tissue damage. CEUA: 024/17 Financial Support: CNPq, CAPES, INCT-Regenera, FAPERJ

ID: 3206

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Instituições: FMRP-USP - Ribeirão Preto - Sao Paulo - Brasil

Title: MATERNAL VITAMIN D DEFICIENCY SELECTIVELY INDUCES HYPERTROPHY AND STRENGTH GAIN IN GLYCOLYTIC MUSCLES IN MALE ADULT OFFSPRING RATS

Introduction: Fetal stage is a developmental critical window for the skeletal muscle, but little information is available about the impact of maternal vitamin D deficiency (VDD) during pregnancy on offspring skeletal muscle development.

Objective: To analyze the effects of maternal VDD in utero and early postnatal life on muscle development in adulthood of male and female rats.

Methods: Twelve 5-week-old female Wistar Hannover rats were fed either a control diet (Vit. D3+ diet; AIN93G with 1000 IU vitamin D3/kg diet) or Vit. D3- diet (AIN93G without vitamin D3) for six weeks and then bred to male rats. Females were maintained on the diets throughout gestation and lactation. At weaning, male and female offspring were separated into four groups: male and female offspring control (M-CTRL and F-CTRL, respectively) from dams with Vit. D3+ diet and male and female offspring VDD (M-VDD and F-VDD, respectively) from dams with Vit. D3- diet. Offspring received a standard diet (Nuvilab) until 180 days of age, at which point tissues were harvested for analysis. *P≤0.05. (CEUA 052/2018).

Results: Both male and female VDD groups showed a reduction in the calcidiol serum concentration (23±1 vs 40±2 ng/ml in M-CTRL and 23±2.2 ng/ml vs 36.6±0.9 ng/ml in F-CTRL) without affecting Ca+2 serum. In the first month, male and female VDD weighed less than their respective controls (69±2 vs 78±2 g in M-CTRL and 66±2 vs 76±1 g in F-CTRL) showing a delay in the development, but they recovered weight in the 60 days post-weaning. At 180 days, Extensor digitorum longus (EDL) muscle from the M-VDD showed a decrease (20 %; $p<0.05$) in the number of total fibers but an increase in the cross-sectional area of IIB (17 %; $p<0.05$), IIA (19 %; $p<0.05$) and IIAX (21%; $p<0.05$) fibers. The fiber hypertrophy was accompanied by the activation of the myogenic program as indicated by the higher protein levels of MyoD (43%; $p<0.05$) and Myogenin (160%; $p<0.05$) and in the number of satellite cells (128.8±14 vs 91±7.6 nuclei Pax7+ in the M-CTRL ). Moreover, M-VDD showed an increase in the levels of serum insulin (INS), mRNA IGF-I, and Glut4 protein, as well as in the phosphorylation levels of IGF-1/INS receptor and different INS downstream targets related to protein synthesis including Ser 473 Akt and Ser 21/9 GSK-3β. These changes were not found in Soleus from the M-VDD group and in both EDL and Soleus from the female offspring. Consistently with muscle hypertrophy, EDL from M-VDD showed attenuation in the decline of post-fatigue specific force (FSF) (78%) and specific tetanic force during the fatigue protocol (66% ) indicating fatigue resistance. On the other hand, Soleus showed lower FSF in the pre and post-fatigue conditions (39% and 62% respectively) as well as a decrease in force production (~45%) during fatigue induction indicating a functional impairment.

Conclusions and Support: Maternal VDD differentially affects the development and function of male offspring rat skeletal muscles. While EDL develops type-II muscle fiber hypertrophy, activation of myogenesis, and attenuation in the decrease of FSF and fatigue resistance, Soleus shows impairment in these functional parameters. The muscle protein accretion and myogenesis are probably due to the activation of the INS/PI3K/Akt signaling pathway, which leads to the inactivation of GSK-3β. Muscles from female offspring seem to be protected from this metabolic disturbance showing a clear sex-specific effect induced by maternal VDD. Support: FAPESP (19/06517-1; 18/10089-2).

ID: 2725

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Federal de São Paulo - Diadema - Sao Paulo - Brasil

Title: DEVELOPMENT AND IMPACT OF A TEACHING-LEARNING SEQUENCE ON THE HUMAN MUSCULAR SYSTEM FOR SCIENCE TEACHER TRAINING IN DEAF EDUCATION

Introduction: Inclusive education is a mandatory requisite in science teacher training programs, which must include Brazilian Sign Language (LIBRAS) education. The universalization of higher education in Brazil increased the demand for faculty professional development to teach deaf students. However, instructional material for physiology education using LIBRAS is scarce.

Objective: The present study aimed to develop a teaching-learning sequence (TLS) on the human muscular system for deaf education, and evaluate the impact of the TLS on pre-service science teacher training.

Methods: A hands-on TLS covering skeletal muscle anatomy (bench 1), skeletal muscle histology (bench 2), patellar reflex (bench 3) and electromyography (bench 4) was created as part of the educational program "Deaf people meet sciences", in which primary and secondary deaf students learn scientific concepts. Pre-service science teachers (PST) created the TLS, facilitated the activity, answered a survey on their opinion, and monitored their emotions according to the self-assessment manikin scale.

Results: Among the vocabulary required to teach the TLS, fifteen scientific words were already existent, four words were adapted (e.g. patellar reflex), and one word was created (PowerLab – physiograph). The interaction student-PST within all study benches elicited high pleasure, arousal, and dominance of PSTs, but bench 4 was more effective to provoke these emotional reactions. The majority of PSTs considered the TLS as an excellent (100%) contributor for science teacher training, excellent (57.1%) for engaging students, and excellent (71.4%) activity for learning the human muscular system. However, the majority of the PSTs were neutral regarding their prior preparedness to apply the TLS using LIBRAS.

Conclusions and Support: Although the TLS was developed based on well-known hands-on activities, its application using LIBRAS was challenging to adapt. The development of the TLS was effective to elicit emotional engagement of PSTs, and to train them to teach deaf students. PROEC-UNIFESP

ID: 2766

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: TRABALHO ORAL

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Title: MODULATION OF EXTRA-PINEAL MELATONIN SECRETION IN RESPONSE TO AN IMMUNE CHALLENGE WITH LPS IN TOADS (Rhinella icterica). Cyrino, J.C.1 Figueiredo, A.C.1 Gomes, F.R.1 Titon, S.C.M.1 / 1. Departamento de Fisiologia, Instituto de Biociências/Universidade de

Introduction: Melatonin is a hormone well-known for its circadian production by the pineal gland. However, the melatonin production in extra-pineal sites shows other regulatory functions, such as immune regulation. Pineal and extra-pineal production of melatonin is modulated through pathogens associated molecular patterns. While central production of melatonin is lowered, its production in other tissues, specially by immune cells enhances in response to an immune challenge in mammals. The occurrence of the extra-pineal melatonin production in different tissues and periods, and its modulation by an immune stimulus, would represent an important contribution to understanding the melatonin role in anuran's physiology.

Objective: The goal of this project is to investigate melatonin production in different organs of (pineal vs. extra-pineal) of cururu toads (Rhinella icterica). We predicted that plasma melatonin would be higher at night when compared with the day; and that an immune challenge with lipopolysaccharide (LPS) would decrease the central production of melatonin (showed through the plasma concentration) and increase the production in extra-pineal sites (lungs, liver, bone marrow and intestine).

Methods: The animals were held in a 12:12 L/D cycle and received an LPS (2mg/kg) or saline injection at 10 a.m. and 10 p.m. and were sampled 2 hours after the injection (noon and midnight). Blood samples were collected by cardiac puncture for plasma melatonin quantification followed by decapitation. Then, the following tissues were collected: bone marrow, lungs, liver, and intestine. The tissues were weighed (60mg), homogenized in TRIS-HCl (400ul), and then assayed for melatonin quantification. Plasma and tissue homogenates melatonin were determined by ELISA kits (IBL).

Results: Melatonin concentration in bone marrow and liver were affected by the body mass, in which larger animals displayed lower and higher melatonin concentration in bone marrow and liver, respectively. Melatonin concentration in the bone marrow was affected by the interaction treatment*period, being higher in the LPS group when compared with the saline group, during the day. Also, the melatonin in the bone marrow in the LPS group is higher during the day, when compared with LPS in the night. Otherwise, melatonin showed a tendency for higher concentration in the LPS than in the saline-injected toads, during the night. The melatonin concentration in the intestine was affected only by the period, with the higher melatonin during the night. Plasma melatonin levels and lung melatonin concentration were not affected either by the treatment or the period.

Conclusions and Support: Our results showed that melatonin is present in extra-pineal tissues in R. icterica toads, and its concentration is modulated in different tissues by an immune challenge. Moreover, the melatonin in extra-pineal sites seems to be locally produced, since melatonin concentration in the organs is much higher values than those levels measured in plasma. Interestingly, the period of increased response of melatonin production in response to LPS differ between tissues, evidencing the complexity of individual defense against pathogens.

ID: 3287

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade de São Paulo - USP - Ribeirão Preto - Sao Paulo - Brasil

Title: AUTONOMIC AND RESPIRATORY PROFILES OF MICE SUBMITTED TO SHORT-TERM SUSTAINED HYPOXIA

Introduction: Previous studies from our laboratory described changes in the coupling between sympathetic and respiratory activities in rats submitted to sustained hypoxia (SH), resulting in increased sympathetic activity and hypertension. Current studies in our laboratory are showing that the same protocol of hypoxia in mice does not induce hypertension. However, studies about possible changes in the sympathetic and respiratory coupling in mice submitted to SH are lacking in the literature.

Objective: To characterize the sympathetic and respiratory activities of mice submitted to SH using the in situ working heart-brainstem preparation (WHBP).

Methods: C57BL/6J mice (7-8 weeks old, ~25g) were submitted to normoxic or SH protocol (24h, FiO2 0.1). At the end of SH or normoxic protocol, mice were deeply anesthetized with Isoflurane, sectioned sub-diaphragmatically, exsanguinated, eviscerated and decerebrated precollicularly. Mice were then placed into a recording chamber for the WHBP, the descending aorta was catheterized and perfused with ACSF. This catheter was also used to record the perfusion pressure. In addition, phrenic (PN), abdominal, (AbN), cervical vagus (cVN) and

thoracic sympathetic (tSN) nerves were dissected and their activities were recorded using bipolar glass electrode. All experimental protocols were approved by the institutional Ethics Committee on Animal Use (CEUA #163/2019).

Results: The frequency of the baseline PN discharge (PND) was significantly reduced in the SH (n=11) in relation to control (n=26) group (0.69 ± 0.06 vs 1.13 ± 0.10 Hz, P=0,0154). The incidence of Late-E bursts in the abdominal nerve AbN activity (AbN) in the SH group (n=10) was significantly increased in relation to control (n=20) group (83.3 ± 7.7 vs 24.3 ± 8.0%, P<0,0001). The duration of the total expiratory phase in SH (n=11) was longer than in control (n=22) group (1.13 ± 0.16 vs 0.67 ± 0.07s, P= 0,0002) as well as the duration of post-inspiration (0.78 ± 0.12 vs 0.35 ± 0.04s, P= 0,0032). The tSNA in the SH group (n=10) presented a significant reduction in comparison to the control group (n=16) in the final expiration phase (E2, 19.0 ± 4.3 vs 39.7 ± 4.2%, P= 0,0203).

Conclusions and Support: The data are showing that SH mice presented active expiration and longer expiratory phase in the WHBP. The changes in the respiratory pattern were associated with reduction in the sympathetic activity in the E2 phase of the respiratory cycle. We conclude that changes in SH mice's respiratory pattern reduce the baseline sympathetic activity, which may explain why these animals are not hypertensive after SH. Support: FAPESP, FAEPA, CAPES, CNPq

ID: 3289

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Title: CARDIOVASCULAR PROFILE OF CONSCIOUS FREELY MOVING MICE AFTER SHORT-TERM SUSTAINED HYPOXIA

Introduction: Short-term sustained hypoxia (SH) induces hypertension in rats as a result of sympathetic overactivity, which is linked to changes in sympathetic-respiratory coupling. However, there is no consistent data about the effect of SH on mice due to the different protocols of hypoxia and difficulties associated with the handling of these animals under freely moving conditions.

Objective: To evaluate the effects of SH exposure on the baseline mean arterial pressure (MAP), heart rate (HR), and cardiovascular responses to chemoreflex activation of conscious freely moving mice.

Methods: C57BL/6 mice (7-8 weeks old) under anesthesia with Isoflurane had a catheter inserted into the femoral artery for recording pulsatile arterial pressure (PAP). Another catheter was inserted into the jugular vein for drug administration. Four days after the surgery, mice were submitted to normoxia or SH protocol (24h, FiO2 0.1). At the end of the protocol, cardiovascular parameters were recorded. Peripheral chemoreflex was activated by intravenous administration of KCN (0,16 mg/Kg, i.v.). Statistical analysis was performed by non-paired Student's t test. All experimental protocols were approved by institutional ethical committee (CEUA # 140/2019).

Results: SH mice (n=13) presented no significant changes in baseline MAP compared with the control (n=17) group (109 ± 2 vs 106 ± 2 mmHg). However, SH mice presented a significant decrease in baseline HR (510 ± 22 vs 633 ± 16 bpm; P = 0.002) in comparison with the control group. Mice from control (n=11) and SH groups (n=8) presented similar pressor responses to chemoreflex activation with KCN (27 ± 3 vs 22 ± 3 mmHg), but the magnitudes of bradycardic responses were greater in SH mice than in controls (-329 ± 36 vs -210 ± 30 bpm, P=0.02).

Conclusions and Support: The data are showing that the 24-h SH protocol produces no major changes in the baseline MAP of mice, which may be linked to increased parasympathetic tone to the heart, as revealed by a reduction in baseline HR and a large increase in the bradycardic component of the chemoreflex response. We suggest that the observed autonomic imbalance favoring the parasympathetic component to the heart may prevent the development of hypertension in mice submitted to SH. FAPESP, CAPES, CNPq.

ID: 3046

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Title: HEPATIC NORADRENERGIC FIBERS ACTIVATE GLUCONEOGENESIS THROUGH CREB/CRTC2 RECRUITMENT DURING THE COLD STATE

Introduction: The physiologic role of sympathetic innervation in the regulation of hepatic gluconeogenesis remains elusive. Understanding the mechanisms capable of regulating the hepatic glucose production is of great importance for new approaches in the treatment of diseases such as diabetes and obesity.

Objective: We aimed to investigate the role of sympathetic noradrenergic fibers in the activation of hepatic gluconeogenesis and the involvement of CREB and its coactivator CRTC2 in such effect.

Methods: Neonate male C57BL/6 mice (ethical committee nº183/2015) were submitted to pharmacological sympathectomy (6-OH-Dopamine). In adulthood, animals were exposed to cold stimulus (4ºC) for 3 and 6 h and blood glucose was measured each hour. Liver was harvested for enzymatic activity, western blot, and Rt-PCR analysis. The transcriptional activity of CREB in vivo was evaluated by an imaging system (IVIS) using mice reporter for CRE-luciferase. Catecholamines were estimate by HPLC and hormones by ELISA. The results were expressed as means ± SEM and were submitted to appropriate statistical analysis ($p<0.05$).

Results: Cold exposure (6h) of innervated mice increased plasma levels of glucose (1332±34 vs 899±26 in controls; AUC), glucagon (65.5±9.9 vs 10.5±1.3 in control; pg/dl) and corticosterone (13.5±3.5 vs 5.1±2.2 in control; µg/dl) but suppressed insulinemia, and did not affect plasma epinephrine. Cold also increased activity and mRNA levels of PEPCK and G6Pase, two key-enzymes of gluconeogenesis, the hepatic content of norepinephrine (185.4±13 vs 135.8±11 in control; ng/g) as well as the phosphorylation levels (1.45±0.03 vs 1±0.07 in control; AU) and in vivo transcriptional activity (3.1e9±1.5e9 vs 5.2e6±6.9e6 in controls; p/s) of CREB. All these effects were abolished or attenuated by sympathectomy. Moreover, cold stress increased dephosphorylation of the CREB co-activator CRTC2 at Ser171/275 in innervated mice, a covalent modification that activates CRTC2. The phosphorylation status of PKA and PKC substrates and their downstream targets were modulated by either cold and/or sympathectomy suggesting the involvement of both signalling in the activation of CREB and gluconeogenesis by noradrenergic fibers in response to cold stress.

Conclusions and Support: The data suggest that the hepatic sympathetic nerves acutely stimulate the gluconeogenesis in response to cold with the participation of CREB/CRTC-2 pathway. Support: FAPESP (2018/10089-2; 2019/05900-6; 2019/26583-9).

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Área: FISIOLOGIA GERAL

Forma de Apresentação: TRABALHO ORAL

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Title: EFFECTS OF Artemisia annua ALCOHOL EXTRACT ON PHYSIOLOGICAL AND INNATE IMMUNITY OF NILE TILAPIA (Oreochromis niloticus) TO IMPROVE HEALTH STATUS

Introduction: Herbal immunostimulants have recently emerged for complementary and alternative use in aquaculture. Plants are a potential source of active molecules and are environmentally safer and cheaper than synthetic antibiotics. Bioactive compounds of Artemisia annua have shown pharmacological activities and are used globally as a supplement.

Objective: The present study tested whether dietary supplementation with alcohol extract of the plant A. annua (ae-Aa; patent BR10201902707) improves the health status of juvenile Nile tilapia and increases resistance to diseases when fish are challenged with the bacteria Aeromonas hydrophila.

Methods: The experimental design was completely randomized with four experimental groups (0.0, 0.1, 0.25, and 0.5% ae-Aa in the diets) with five repetitions (12 fish per repetition/experimental unit). We assessed serum glucose and cortisol levels in plasma, leukocyte respiratory activity, total plasma protein, serum lysozyme levels, as well as the number of circulating red blood cells and fish leukocytes at the end of the 30 days of feeding (phase I) and 24h after exposure to bacteria (phase II). All procedures were conducted after approval of the Committee of Ethics in Animal Experimentation (CEUA-UFSCar) protocol n° 1518230217.

Results: The supplementation of 0.5% of ae-Aa was sufficient to increase the respiratory burst of leukocyte and lysozyme activity, total plasma protein, blood thrombocytes, neutrophils and monocytes after bacterial challenge ($P <0.05$), and minimized stress response with decreases in plasmatic glucose and cortisol ($P <0.05$).

Conclusions and Support: Results of the present study demonstrate the benefits of supplementing the Nile tilapia with ae-Aa as a strategy to mitigate effects of stress conditions in aquaculture. Nile tilapia fed with 0.5% ae-Aa for 30 days before exposure to A. hydrophila showed efficiency in modulating innate immunity system, protecting against stress, and increase in disease resistance. Thus, results of this study provide practical strategies to improve health, bacterial resistance, and in turn the productivity of Nile tilapia in fish farming through the dietary supplementation of ae-Aa. Keywords: Artemisia annua L, Artemisinin, Bacterial challenge, Fish farming, Herbal immunostimulants, Stress, Immune system Financial support: This study was financially supported by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior/CAPES, Brazil. The activities of the present study were developed in partnership with the project "BRS Aqua" a partnership between the Brazilian Development Bank, Embrapa, and Ministry of Agriculture, Livestock and Food Supply, and support from National Council for Scientific and Technologicalcom and Eliseu Alves Foundation.

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Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Title: BROWN ADIPOSE TISSUE AND THERMOGENESIS ABNORMALITIES AFTER OBESOGEN TRIBUTYLTIN EXPOSURE IN MALE RATS

Introduction: Obesity is a pandemic that affects almost 2 billion people in the world. Obesity is an endocrine-metabolic disease that can be developed for different factors, such as high caloric intake, sedentary lifestyle, genetic and environmental factors. Among the environmental factors, there are xenobiotics called obesogens, that disrupt body energy balance and adipogenesis. Tributyltin (TBT) is an obesogen that binds to nuclear receptors impairing proper metabolic control. Brown adipose tissue (BAT) plays an important role in energy management by the thermogenesis process, which expends energy for heat production. Notably, BAT assessment of obese individuals has demonstrated a loss of its regular phenotype and function, a process called whitening. However, a possible influence of an obesogen, as the TBT, in this process is not yet evaluated.

Objective: To evaluate the whitening process in BAT after exposure to TBT.

Methods: To evaluate the effects of TBT on BAT, we administered vehicle (CON, ethanol 0.4%. n = 22) and TBT (TBT, 100 ng/kg/day, n = 24) in Wistar male rats (300-320 g) for 15 days by gavage. All the protocols were approved by the Comissão de Ética no Uso de Animais – UFES (60/2017). The rectal temperature was assessed during the exposure and after a cold challenge protocol by a rectal probe. The body weight, adiposity (the total amount of white adipose depots weight collected), and BAT weight were assessed. Further, the serum and organs were collected for other analyses. The serum lipid profile was evaluated. BAT histological analysis was performed by H&E staining. All data are reported as the mean ± SEM. Comparisons between groups were performed using the t Student test or two-way ANOVA (Bonferroni's multiple comparisons test). A value of $p < 0.05$ was regarded as statistically significant.

Results: TBT rats showed a reduction in the body temperature compared to CON rats (CON: 34.0 ± 0.1 vs TBT: 33.8 ± 0.1 °C; $p < 0.01$; n = 12-15). Furthermore, during the cold challenge protocol the TBT rats showed reduced body temperature compared to CON rats (CON: 33.1 ± 0.1 vs TBT: 32.6 ± 0.1 °C; $p < 0.01$; n = 12). Nevertheless, the weight gain, body weight, adiposity, and BAT weight showed no significant difference between groups ($p > 0.05$). In the morphological evaluation, TBT rats showed a higher lipid accumulation in BAT compared to the CON rats (CON: 70.6 ± 0.7 vs TBT: 76.4 ± 0.4 %; $p < 0.0001$; n = 4). The TBT exposure increased serum LDL levels (CON: 10.01 ± 1.6 vs TBT: 15.1 ± 1.2 mg/dL; $p < 0.05$; n = 5). However, the triglycerides, cholesterol total, and HDL levels, as LDL levels in rats exposed to cold, showed no significant difference between groups, either cold exposed or not ($p>0.05$).

Conclusions and Support: Although the TBT exposure did not change the body or BAT weight, it induced an increase in the BAT lipid accumulation, as well as an increase of serum LDL levels. Moreover, TBT exposure caused a reduction in body temperature, both at room temperature and during a cold challenge protocol. Therefore, the TBT impairs the thermogenesis by an apparently BAT whitening process that may be associated with obesity and other metabolic complications. FAPES, CAPES, CNPq.

ID: 3066

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

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Title: TEMPORAL EFFECTS OF MATERNAL VITAMIN D DEFICIENCY ON BROWN ADIPOSE TISSUE DEVELOPMENT IN RATS OFFSPRING

Introduction: Maternal vitamin D deficiency (VDD) has been linked to impaired development of different tissues in offspring, leading to adverse metabolic outcomes. However, much little is known about the implications of this condition on brown adipose tissue (BAT) physiology along the time.

Objective: To investigate the role of vitamin D on brown adipose tissue development in male rats offspring.

Methods: Twelve 5-week-old female Wistar Hannover rats were fed either a standard diet (AIN93G) or modified diet (AIN93G without vitamin D) for six weeks. At the end of this period, they mated and both diets were maintained throughout gestation and lactation. At weaning, the male offspring was separated in four groups: 21-days and 180-days male offspring born and breastfed from mothers fed with

standard (SD21; n=6 and SD180; n=15) or modified diet (VDD21; n=6 and VDD180; n=16). After weaning, the 180-days male offspring was fed with standard until the day of the eutanasya, when BAT and white adipose tissue (WAT) were harvested for analysis *P≤0,05 (CEUA 52/2018).

Results: VDD groups showed a reduction in the calcidiol serum concentration at both ages (5.3±0.3 vs 29±0.9 in SD21 group and 23±1.1 vs 40±2 in SD180 group). At 21 days of age, VDD group weighed less (32±1 vs 42±2 g in SD21 group) and showed a great loss of white adipose tissue (WAT) mass (epididymal: 88±12 vs 184±27 mg in SD21 group; retroperitoneal: 120±15 vs 263±30 mg in SD21 group), without changes in BAT mass. However, BAT showed a decreased content of lipid droplets, with no alterations on the content of BAT noradrenaline as well as on thermogenic and mitochondrial proteins as estimated by Western blot. This was accompanied by lower serum insulin (0.8±0.1 vs 2.3±0.3 ng/ml in SD21 group) and calcium concentrations (7±0.1 vs 8.7±0.1 mg/dL in SD21 group). Most of these effects were reverted in the VDD180 group, which showed no differences in total body weight, but an increase in WAT (epididymal: 11.58±0.78 vs 7.98±0.53 mg in SD180 group, retroperitoneal: 9.73±0.68vs 6.92±0.62 mg in SD180 group), and BAT mass (382±34 vs 302±30 mg in SD180 group) as well as in serum insulin levels (6,7±0,6 vs 3,5±0,5 ng/ml in SD180 group), without differences in plasma calcium levels.

Conclusions and Support: The data suggest that vitamin D deficiency during pregnancy and lactation results in a biphasic effect on BAT development, with lower lipids droplets associated with reduced insulin levels at weaning, followed by an increased BAT mass and a metabolic syndrome phenotype in adult life. Suport: FAPESP (2019/19993-6).

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Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

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Title: RECRUITMENT OF STRESS INDUCIBLE PROTEIN (STI1) PLAYS A PROTECTIVE ROLE IN THE HEART AGAINST CARDIAC STRESS

Introduction: Previous data suggest that chaperones can play an important role during cardiac disease development. Among the chaperone members, Stress inducible protein (STI1) is a key co-chaperone of Hsp70/Hsp90 machinery that has been studied in neurons, where it plays a role in protein maturation and cytoprotection. In the heart, the role of STI1 is unknown. Importantly, we found that STI1 is present and human hearts and its expression levels are reduced in heart failure patients.

Objective: The aim of this work is to investigate the role of STI1 in response to cardiac stress.

Methods: We used a genetically engineered haploinsufficient mice with global reduction of STI1 (STI1+/-) and littermate wild-type mice (WT, C57/BL6). We subjected mice to cardiac stress by treating them with isoproterenol (ISO). Two distinct doses of ISO were used in this study: 20mg/kg/day (i.p.) for 7 days or a single dose of high ISO 300mg/Kg (i.p.). Hearts were collected and subjected to immunofluorescence, western-blot and proteomic analyses at 3 and 8 days after the injection. Experiments were performed according to protocols approved by the Institutional Animal Care and Use Committee at UFMG (CEUA: 57 / 2013).

Results: Hearts from STI1+/- mice presented a 50% reduction in STI1 expression, compared to wild-type (WT). Moreover, western blot assay revealed an increase in STI-1 expression after ISO treatment in WT mice, suggesting that this machinery is recruited under this condition. Regardless the ISO dose used, both WT and STI-1KO+/- mice showed an increase in heart weight by tibia length ratio, when compared to their saline-treated controls. Strikingly, only ISO-stimulated WT cardiomyocytes presented cardiomyocyte hypertrophy. Conversely, STI-1KO+/- mice stimulated with ISO showed a significant increase in stromal tissue, inflammatory cells and collagen deposition. Proteomic analyses indicated an inhibition of elf2α signaling, and NRF2-mediated oxidative stress response in STI-1KO+/- mice treated with isoproterenol, compared to ISO/WT mice. Bioinformatics predictions also revealed an increase in proapoptotic response in hearts from ISO-treated STI-1KO+/- mice. We validated these findings by showing a decrease in cardiomyocyte number with concomitant increase in activated caspase in the cardiac tissue of ISO/STI-1KO+/- mice.

Conclusions and Support: Our findings show STI1+/- mice are more susceptible to cardiac injury caused by adrenergic stress induced by ISO, as demonstrated by the more aggravated cardiac phenotype seen in this model. These data uncover a novel protective role of STI1 in the heart, and highlights its potential as a therapeutic target during cardiac disease development. Support: CNPq, CAPES, FAPEMIG, PRPq and INCT NanoBioFar.

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Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

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Title: THE ROLE OF NITRIC OXIDE/GMPc PATHWAY ON VASCULAR RESPONSE TO MENTAL STRESS IN POSTMENOPAUSAL WOMEN WITH TREATMENT-RESISTANT HYPERTENSION

Introduction: Approximately 21% of patients with hypertension fulfill the criteria of treatment-resistant hypertension (TRH). Those patients usually present increased susceptibility to the development of mental stress (MS)-related cardiovascular events. This risk is even greater in postmenopausal women, due to the diminished of estrogen-mediated cardioprotection. We suggest that the MS-induced decrease in nitric oxide (NO) bioavailability may aggravate vascular function in those patients.

Objective: To determine the effects of increasing NO bioavailability during MS through inhibition of phosphodiesterase-5 (PDE-5) on vascular response in postmenopausal women with TRH.

Methods: This is a cross-sectional, randomized, crossover, double-blind and placebo-controlled protocol. In two experimental sessions, postmenopausal women with TRH [age: 61 ± 4; systolic blood pressure (BP): 138 ± 14; diastolic BP: 91 ± 9; n=5] underwent a randomized oral administration of PDE-5 inhibitor (iPDE5; sildenafil 50 mg) or placebo (PL). After 30 minutes, the patients were submitted to MS (modified Stroop Color Word Test) for five minutes. Flow-mediated dilatation (FMD; vascular ultrasound) and pulse wave analyses (applanation tonometry) were measured at baseline, immediately after (MS) and 30 minutes after MS (MS30). During all experimental protocol, heart rate (HR) was measured by a lead II electrocardiogram and non-invasive beat-by-beat BP was continuously monitored by finger photoplethysmography. Data are presented as mean ± standard deviation. Two-way repeated measures ANOVA were used to compare baseline, MS and MS30 measurements between PL and iPDE5 sessions. Paired Student's T test was performed to compare the delta values between baseline and MS30 of each session, followed by Cohen's D test to demonstrate the effect size. This study protocol was approved by the institution's ethics committee (CAAE:79958017.3.0000.5243).

Results: Preliminary results showed that MS increased the HR (PL, baseline: 61 ± 4 vs. MS: 69 ± 4 bpm; iPDE5, baseline: 62 ± 2 vs. MS: 72 ± 3 bpm, $p<0.01$) and mean BP (PL, baseline: 115 ± 14 vs. MS: 123 ± 18 mmHg; iPDE5, baseline: 111 ± 18 vs. MS: 116 ± 24 mmHg, $p<0.05$) in both sessions. Baseline differences was observed in FMD between sessions (PL: 14,46 ± 2,60 vs. iPDE5: 5,81 ± 1,34 %, $p=0.02$). However, there was a reduction in FMD immediately and 30 minutes after MS in the PL session (PL, MS: 3.42 ± 3.57, MS30: 0.92 ±4.44 %; $p<0.01$ vs. baseline), while FMD was higher 30 minutes after MS in the iPDE5 session compared to both baseline and PL session (iPDE5, MS30: 11.36 ± 3.37 %; $p=0.05$ vs. baseline; $p<0.01$ vs. PL). Additionally, the FMD response 30 minutes after MS was higher in iPDE5 compared to PL session with a medium effect size (ΔPL: -13.54 ± 9.91 vs. ΔiPDE5: 5.55 ± 7.71, $p=0.02$; Cohen's D: 0.64). Regarding aortic increment index (AIx-75%), no differences was observed throughout the protocol (PL, baseline: 39 ± 3 vs. MS: 42 ± 2 vs. MS30: 41 ± 3 %, $p>0.05$; iPDE5, baseline: 41 ± 4 vs. MS: 42 ± 2 vs. MS30: 39 ± 3 %, $p>0.05$) or in the response 30 minutes after MS. Nevertheless, a large effect size of iPDE5 on AIx-75% 30 minutes after MS has been demonstrated (ΔPL: 1.50 ± 2.43 vs. ΔiPDE5: 0.33 ± 4.93, $p=0.68$; Cohen's D: 1.33).

Conclusions and Support: Present data suggest that the PDE-5 inhibition attenuates the deleterious effects of MS on endothelial function in postmenopausal women with TRH. SUPPORT: FAPERJ, CNPq, CAPES, PROPPI/UFF.

ID: 3707

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Instituições: UFG - Goiânia - Goias - Brasil

Title: Glutamatergic neurotransmission in RVLM is required for cardiovascular and sympathetic responses induced by PVN TNFα

Introduction: Studies demonstrate the involvement of the central nervous system (CNS) in the development and maintenance of hypertension. In the hypothalamic paraventricular nucleus (PVN) and rostral ventrolateral medulla (RVLM) pro-inflammatory cytokines (PIC) have been associated in driving sympathetic nerve activity (SNA) in support of neurogenic hypertension. However, the central pathways involved in this process remain to be clarified.

Objective: Investigate the role of the RVLM glutamatergic neurotransmission in cardiovascular and autonomic responses induced by tumor necrosis factor alpha (TNFα) in PVN in spontaneously hypertensive (SH) rats.

Methods: SH rats (250-300g; ethics committee: nº 061/17-UFG) were anesthetized with a mixture of α-chloralose (40 mgžmL-1) and urethane (400 mgžmL-1) and instrumented to record blood pressure (BP), heart rate (HR) and splanchnic SNA. Nanoinjections (50 nL) of kynurenic acid (Exp group; n=7; glutamate receptor antagonist; 50mM) or vehicle (Sham group; n=5; ringers solution) were performed in the RVLM prior to TNF± (12 µM) nanoinjections in the PVN.

Results: Vehicle nanoinjections did not change the baseline BP (Δ: +0.2 ± 1.5 %, 10 min after vehicle, from baseline), HR (Δ: -3.7 ± 2.4 %, 10 min after vehicle, from baseline) or SNA (Δ: +7.2 ± 1.6 %, 10 min after vehicle, from baseline) values. However, PVN TNFα nanoinjections promoted progressive ramp-like increase in SNA (Δ: +82.8 ± 9.9 %, $p < 0.05$, 60 min after TNFα, from baseline) and did not alter BP (Δ: +7.9 ± 3.2 %, 60 min after TNFα, from baseline) and HR (Δ: +6.3 ± 3.0 %, 60 min after TNFα, from baseline). Kynurenic injections in RVLM did not change BP, HR and SSNA baseline values in Exp group (BP: Δ -3.8 ± 3.2 %; HR: Δ -5.3 ± 0.7 %; SNA: Δ -2.5 ± 3.8 %; 10 min after kynurenic, from baseline). In addition, the previous glutamatergic blockade of RVLM abolished the splanchnic sympathoexcitation induced by nanoinjections of TNFα into PVN (Sham: Δ +82.8 ± 9.9 % vs. Exp: Δ +2.3 ± 6.7 %, $p < 0.05$, 60 min after TNFα), without affect BP (Sham: Δ +7.9 ± 3.2 % vs. Exp: Δ +16.3 ± 2.0 %, 60 min after TNFα) and HR (Sham: Δ +6.3 ± 3.0 % vs. Exp: Δ +5.2 ± 4.1 %, 60 min after TNFα) responses.

Conclusions and Support: These results indicate that the sympathoexcitation promoted by TNFα into the PVN is dependent on glutamatergic neurotransmission in RVLM. Support: CNPq, CAPES, FAPEG and FUNTEC.

ID: 3454

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Title: ANGIOTENSIN-(1-7) MODULATES CARDIOVASCULAR EFFECTS OF ENDOTHELIN-1 IN NORMOTENSIVE AND HYPERTENSIVE RATS.

Introduction: Angiotensin-(1-7) [(Ang- (1-7)] has broad protective effects in the cardiovascular system. Preliminary studies have shown that Ang-(1-7) attenuated the pro-inflammatory effects of ET-1 in human microvascular endothelial cells. However, it is unknown whether Ang-(1-7) can modulate other cardiovascular effects induced by ET-1.

Objective: To evaluate the influence of Ang-(1-7) on the cardiovascular effects of ET-1.

Methods: Male normotensive (Wistar, WT) and spontaneously hypertensive (SHR) rats were used. Blood pressure was assessed in awake rats 24 hours after cannulation of the femoral artery and vein. ET-1 (0.3 nmol) was administered before and during infusion of Ang-(1-7) (7 pmol/min). Coronary vasomotricity was assessed in isolated hearts using the Langendorff technique with constant flow. The hearts were infused with either: ET-1 (0.1 nmol/L), Ang-(1-7) (1 nmol/L), ET-1 + Ang-(1-7) or A-779 (2 nmol/L) + Ang-(1-7) + ET-1. Vascular effects were evaluated in isolated thoracic aortic rings with (E+) and without (E-) endothelium. ET-1 (10 pmol/L) was administered in the presence or absence of Ang-(1-7) (100 nmol/L). All protocols were approved by the Animal Use Ethics Committee of the Federal University of Goiás (#039-17).

Results: Ang-(1-7) attenuated the increase of systolic and diastolic blood pressure induced by ET-1 in WT rats, but did not change the effect of ET-1 in reducing the heart rate. ET-1 promoted a biphasic effect on the perfusion pressure (PP) of hearts isolated from WT, with an initial coronary vasodilation followed by vasoconstriction. Ang-(1-7) reduced the vasodilation and potentiated the ET-1-induced vasoconstriction. The A-779, a Mas receptor antagonist, blocked the vasodilation and reduced the potentiation of vasoconstriction promoted by Ang-(1-7). In SHR hearts, the ET-1 promoted only coronary vasoconstriction, which was attenuated by Ang-(1-7). The A-779 blocked the attenuating effect of Ang-(1-7) on ET-1-induced vasoconstriction. The aortic vasoconstriction elicited by ET-1 was greater in E- aorta from WT and SHR. Ang-(1-7) potentiated the constrictor effect of ET-1 in E+ aorta from normotensive rats and the A-779 further potentiated this effect. On the other hand, Ang-(1-7) attenuated the constrictor effect of ET-1 in E+ aortic rings from SHR and the A-779 blocked the Ang-(1-7) effect.

Conclusions and Support: These results show that Ang-(1-7) is able to attenuate the pressor effect of ET-1 in normotensive rats. Furthermore, Ang-(1-7) differently modulates the coronary and aortic effects of ET-1 in normotensive and hypertensive animals. Support: CAPES, CNPq e FAPEG.

ID: 3710

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Title: HIGH SALT AND SUCROSE INTAKE INCREASES BROWN ADIPOCYTE SIZE AND INDUCES UPREGULATION OF PPAR-α OF YOUNG WISTAR RATS

Introduction: The development of obesity, nowadays, is related to the consumption of ultra-processed foods that are rich in carbohydrates and sodium. There are some factors that promote the regulation of triglyceride metabolism and energy homeostasis. PPAR-α is activated by increased circulating fatty acids. However, little is known about the relationship between high salt and sucrose diet and how it affects PPAR signaling.

Objective: To evaluate the effects of a high salt/sucrose intake in the brown adipose tissue (BAT) morphology, in the lipid profile and the expression of PPARα, PPARγ, AKT and β3-AR in the BAT.

Methods: Male Wistar rats, 21 days old, were divided into two groups: control (CO), for which was offered tap water; and experimental (SS), for which was offered a solution containing 1.8% NaCl and 20% Sucrose for 60 days. Both groups had ad libitum access to standard chow. The animals were kept under controlled temperature (22 °C ± 2 °C) and light/dark cycle (12/12). On the last day of experimental period, after a 12-hour fast, euthanasia was performed to collect blood, white adipose tissue (WAT) and brown adipose tissue (BAT). Then, biochemical measurements were performed to analyze the lipid profile, and histological analysis of BAT. Finally, BAT samples were subjected to the quantification of PPARα, PPARγ, AKT and β3-AR by western blot. The protocols were approved by the ethics committee of the UFG (process no. 023/2015).

Results: At the end of the experimental period SS group showed reduced body weight (CO 315.3 ± 11.3 g, N = 9, vs. SS 196.4 ± 8.9 g, N = 8) and as a consequence they were smaller when compared to the CO group (CO 20.38 ± 0.27 cm, N = 5, vs. SS 17.48 ± 0.39 cm, N = 4). SS group showed an increase in retroperitoneal adipose tissue (CO 466.3 ± 60.5 g/bw., N = 9, vs. SS 1125 ± 87.0 g/bw., N = 8), periedidymal (CO 547.8 ± 62.32 g/bw. vs. SS 932.8 ± 103.7 g/bw, N = 8), inguinal (CO 282.7 ± 38.32 g/bw, N = 9, vs. SS 583.0 ± 63.11 g/bw, N = 8) and brown adipose tissue (CO 203.9 ± 33.26 g/bw, N = 9, vs. SS 375.8 ± 38.70 g/bw, N = 8). Adipocyte areas were increased in the SS group (CO 381.9 ± 17.97 μm², N = 4, vs. SS 500.3 ± 41.11 μm², N = 5). We observed an increase in PPARα expression, in the SS group, (51 ± 12 % N = 4/group) however, PPARγ expression, UCP-1, β3-AR, AKT and pAKT did not show significant differences between groups. Also, plasma levels of total cholesterol, triglycerides and HDL did not show significant differences between groups.

Conclusions and Support: In summary, our results show that high salt and sucrose diet, in youth, promotes loss in body mass gain and rats development. In addition, the rats showed an increase in WAT and BAT, but without changes in the lipid profile. With the increase in PPAR-α in BAT and adipocyte hypertrophy. Taken together our results suggest a compensatory effect on plasma lipid levels induced by high salt and sucrose diet. Support: CAPES, CNPq, FAPEG, FUNTEC.

ID: 3725

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Instituições: Universidade Estadua Paulista "Júlio de Mesquita Filho" - FOAr-UNESP - Araraquara - Sao Paulo - Brasil

Title: PARTICIPATION OF CATECHOLAMINERGIC A2 NEURONS IN RENOVASCULAR HYPERTENSION AND PULMONARY VENTILATION IN THIS HYPERTENSION MODEL

Introduction: Recently, it was demonstrated that renovascular hypertension dependents on the carotid body integrity. Moreover, carotids afferent modulated the ventilation in the two kidneys one clip model (2K1C). The A2 noradrenergic neurons receives information from carotid body afferents, and mediates the ventilatory response to hypoxia in normotensive animals. However, the involvement of these neurons in the cardiovascular and respiratory modulations in rats with renovascular hypertension remain unknown.

Objective: The present study examines the effects of A2 noradrenergic neurons lesions on the baseline of cardiovascular and respiratory parameters in unanesthetized 2K1C rats. In addition, we sought to determine the involvement of A2 neurons on the ventilatory response during hypoxia in these rats with renovascular hypertension.

Methods: All experimental and surgical procedures were approved by the Ethics Committee of the Universidade Estadual Paulista "Júlio de Mesquita Filho" - FOAr-UNESP (CEUA: 08/2018). Holtzman rats (150-180 g) were anesthetized (ketamine 10%; 1 mL/ kg and xylazine 2%; 0.7 mL/kg), received a silver clip around the left renal artery to induce hypertension (n = 16). In the same surgery, a telemetry transmitter (TA11PAC-40) was placed in the abdominal aorta so that it was possible to record the mean arterial pressure (MAP) and heart rate (HR) for 24 h, once a week. After three weeks, the animals were anesthetized to perform nanoinjections (100 nL) of anti-DβH saporin

(0.105 ng · nl -1) in group 2K1C-LA2 (n = 7) or saline in group 2K1C (n = 8). After 6 weeks of placement of the silver clip, the 2K-1C rats were submitted to full body plethysmography to obtain baseline respiratory frequency (fR), tidal volume (VT) and minute volume (VE) and after hypoxia stimulation (7% O2).

Results: The histological analysis showed that nanoinjeções saporin anti-D βH reduced on average 67% of the neurons in 2K1C group A2 -LA2. We observed a decrease in MAP in animals 2K1C-LA2 (149.6 ± 5 mmHg vs. 2K1C: 171.4 ± 4 mmHg). Regarding pulmonary ventilation, animals 2K1C-LA2 showed a reduction in baseline values VT (4.39 ± 0.22 mL/Kg vs. 2K1C: 6.50 ± 0.49 mL/Kg) and VE (539.2 ± 47.7 mL/Kg/min vs. 2K1C: 851.5 ± 52.8 mL/Kg/min), no change in fR was observed. The ventilatory response of animals 2K1C-LA2 to hypoxia not different from baseline, but reduced when compared to group 2K1C: VT (2K1C-LA2: 5.59 ± 0.48 mL/Kg vs. 2K1C: 7.81 ± 0.4 0 mL/Kg) and VE (743.0 ± 76.9 mL/Kg/min vs. 2K1C: 1251.0 ± 49.6 mL/Kg/min).

Conclusions and Support: These findings suggest that A2 noradrenergic neurons integrate the central pathways involved in raising arterial blood pressure in 2K-1C rats.. In addition, these neurons play an important role in central control of ventilation in baseline and during hypoxia conditions in renovascular hypertensive rats. FUNTEC, FAPEG, CAPES, CNPq and FAPESP

ID: 3479

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: TRABALHO ORAL

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Title: EFFECTS OF SHORT-TERM SUSTAINED HYPOXIA ON THE ELECTROPHYSIOLOGICAL PROPERTIES OF CAROTID BODY GLOMUS CELLS FROM RATS

Introduction: The carotid bodies peripheral chemoreceptors, besides their role as sensors for acute changes in PaO2, contribute to the ventilatory acclimation in response to sustained hypoxia (SH). The sustained activation of the carotid bodies produces active inspiratory and expiratory responses, generating a persistent pulmonary hyperventilation. Herein, we hypothesized that short-term SH increases the excitability of the carotid body glomus cells from rats.

Objective: To evaluate the effects of short-term SH on the electrophysiological properties of the carotid body glomus cells from rats.

Methods: Rats were submitted to short-term SH (FiO2 = 0.1) or normoxic (FiO2 = 0.21) conditions during 24 hours. The carotid bodies glomus cells were then isolated and plated on glass coverslips. The electrophysiological properties were recorded using whole cell patch clamp, in the voltage-clamp configuration for membrane conductance analysis, and in the current-clamp configuration for membrane potential and input resistance analyses (CEUA #195/2019).

Results: Short-term SH did not affect cell capacitance (2.63 ± 1.27 vs 2.57 ± 1.07 pF; p=0.95; n=18), membrane conductance (0.85 ± 0.58 vs 0.56 ± 0.49 nS; p=0.12; n=18), input resistance (2.11 ± 2.12 vs 3.03 ± 2.45 GΩ; p=0.22; n=18 and n=17, respectively) or membrane potential (-25.31 ± 16.03 vs -33.12 ± 15.04 mV; p=0.07; n=18 and n=17, respectively). On the other side, holding current (-50 mV; -30.51 ± 26.43 vs -14.87 ± 13.53 pA; p=0.03; n=18) significantly increased after short-term SH.

Conclusions and Support: We conclude that short-term SH does not increase the excitability of carotid body isolated glomus cells from rats. Financial support: CAPES and FAPESP.

ID: 3735

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Title: CARDIOVASCULAR OUTCOMES RELATED TO EXCESSIVE ALCOHOL USE BY VULNERABLE HOMELESS POPULATION IN DOWNTOWN SÃO PAULO

Introduction: Cardiovascular diseases (CVD) emerge first among the causes of death in Brazil, representing 30% of the cases reported in the country in 2019. The WHO in the recent survey conducted in 2015 about 17.7 million people died representing 31% of the global population. In the case of people in a situation of street vulnerability, a greater problem in this context of risk factors (RF) for cardiovascular diseases is observed. Among them, excessive alcohol use is an important RF for cardiovascular involvement in adding the curve for coronary heart disease, heart failure, transient ischemic attack, and peripheral arterial disease including cardiac arrest.

Objective: To relate alcohol consumption and its cardiovascular effects in the vulnerable homeless population in downtown São Paulo.

Methods: We used the quantitative method, being an exploratory and cross-sectional field research, approved by the Institutional Ethics Committee under protocol 036417,CAAE:21519413.40000.5511. Conducted in downtown São Paulo, the survey included 200 volunteers in vulnerable homeless situations between November 2019 and March 2020, between 18 and 60 years old, submitted to a questionnaire previously selected for convenience. We applied an instrument with socio-demographic characterization, indexing THE, for cardiovascular diseases, with measurement of blood pressure and heart rate and anthropometric data

Results: After data analysis and statistical treatment, we observed that the population studied has gender characteristics: 64% male, 7% female 3% Transsexuals from 100% of the interviewees 74% reported using alcoholic beverages, those who claim not to use alcoholic beverages stands out 18% of the population studied, 84% of the interviewees in general did not know how to characterize alcohol consumption as an RF. Against hand to another identified result regarding the use of health services, as a form of self-care and control, we observed as a response, a low demand for them associated with broad disinformation.

Conclusions and Support: We conclude that alcohol use is related to frequent lifestyle and substitute for other fluids such as water, and for psychoemotional and active purposes, of the population studied. It is possible to observe that it contains several reasons for alcohol consumption, misinformation observed in the population, the lack of demand for health units for treatment is a great challenge for the SUS, educating and raising awareness of the population and the health team about the harms of alcohol abuse. Nursing plays a fundamental role in promoting lifestyle changes based on public health practices, interventional proposals and reducing the incidence of alcoholism, in order to improve quality of life. Keywords: Heart disease; Risk Factors; Alcoholism; Cardiovascular diseases, Nursing interventions.

ID: 3490

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Title: Hypothyroidism impairs fasting-induced autophagy and metabolic adaptaion in the heart of rats

Introduction: Hypothyroidism is a risk factor for heart failure and is associated with increased mortality by cardiovascular diseases. Thyroid hormones (THs) are well known for playing a crucial role in heart homeostasis and function. However, THs regulation of heart metabolism remains poorly understood, especially in a hypothyroid state. Additionally, hypothyroidism effects on autophagy, a physiological process by which cellular constituents are degraded for recycling and use as an energy source, are unknown in the heart. Autophagy plays an essential role in providing cellular adaptation and protection in environmental stress conditions, such as fasting.

Objective: Investigate the influence of the hypothyroid state in autophagy, energy metabolism, and mitochondrial function-related genes in the heart at fed and fasting conditions.

Methods: Male Wistar rats were divided into four groups: euthyroid (Eu; n=8), euthyroid + fasting (Eu+Fas; n=8), hypothyroid (Hypo; n=8) and hypothyroid + fasting (Hypo+Fas; n=8). Hypothyroidism was induced with methimazole (0.03%) diluted in drinking water, provided for 3 weeks (Ethics Committee #757). Twenty-four hours before the end of the treatment, food was withdrawal from Eu+Fas and Hypo+Fas groups. On the day after, animals were euthanized and the left cardiac ventricles were weighed and frozen for analysis. mRNA expression was analyzed by qPCR. Statistical analysis was performed using One-way ANOVA test followed by Tukey post-test.

Results: Consistent with the literature, fasting increased mRNA expression of autophagy markers (Becn1, Atg5, Map1lc3b), fatty acid-responsive genes (Pdk4, Ppara, Dgat2, Lpl, Acadm) and mitochondrial-related genes (Ppargc1a, Uqcrc2, Atp5fb1, Opa1). Interestingly, despite not affecting the expression of most of the genes analyzed in the fed state, hypothyroidism impaired fasting effects on autophagy, lipid metabolism, and mitochondrial function. This compromised response in the hypothyroid-fasted animals was not compensated by changes in the heart glucose metabolism-related genes (Glut1, Glut4, Hk). These results suggest THs are critical for autophagic and metabolic response to fasting in the heart. Thus, the adaptive cellular response upon fasting might be deficient in this tissue in the hypothyroid condition. Sirt1 expression, a master metabolic regulator, was also increased by fasting in euthyroid animals, and an upward profile of Sirt1 levels was also found in hypothyroid groups, regardless of nutrition status. However, SIRT1 established effects stimulating autophagy, metabolism and mitochondrial function were not identified in those animals, suggesting the presence of adequate levels of THs are necessary to elicit the effects of SIRT1 in the heart.

Conclusions and Support: The present findings suggest that THs are critical for autophagic and metabolic response to fasting, and are also important for evoking SIRT1 effects in the heart. Support: FAPERJ, CAPES, CNPq, Proppi-UFF.

ID: 3493

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: TRABALHO ORAL

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Title: SHORT, MEDIUM AND LONG-TERM CONSEQUENCES OF PRENATAL CHRONIC STIMULATION OF THE ENDOCANNABINOID SYSTEM ON CARDIORESPIRATORY CONTROL OF MALE AND FEMALE RATS

Introduction: The prenatal period is highly sensitive to pharmacological interventions; thus, the cardiorespiratory network development can be affected by the use of drugs of abuse during pregnancy, leading to short, medium or long-term consequences of the offspring. Cannabis use in pregnancy has increased, specially with the legalization for recreational use in many countries. Exposure to cannabinoids in utero can disturb the fetal endogenous cannabinoid system, since the psychoactive compounds of Cannabis acts directly on this system. The effects of external cannabinoids on the central cardiorespiratory network development, as well as in the chemosensitivity and the future consequences in postnatal life is still unclear.

Objective: Therefore, the present study aimed to evaluate the effects of prenatal exposure to cannabinoid on the cardiorespiratory control system, metabolic rate and mitochondrial respiration of neonatal (P0, P12-13), juvenile (P27-28) and adult (P80) male and female rats.

Methods: Osmotic pumps were implanted subcutaneously in pregnant rats at embryonic day 0 and delivered vehicle or CB1 receptor agonist (WIN 55212-2, 0.5 mg/Kg/day) for 21 days. Ventilation (VE) of neonatal animals was recorded by pressure plethysmography and whole-body plethysmography for juvenile and adult rats during normoxia normocapnia, hypercapnia (7% CO2) and hypoxia (10% O2). The O2 consumption (VO2) was measured by indirect calorimetry method. The mean arterial pressure (MAP) and heart rate (HR) of juvenile and adult rats also were monitored under these conditions. For adult rats, EEG and EMG electrodes were implanted to record sleep and wakefulness state. Mitochondrial respiration of brainstem was determined by oxygen consumption monitored by Oxygraph-2k respirometer in neonatal and juvenile rats.

Results: Cannabinoid use during pregnancy resulted in a higher basal VE of P0 and P27-28 treated male rats compared to control groups. The hypercapnic ventilatory response (HCVR) was higher for treated males at P0, P12-13 and P27-28. In addition, P80 treated males had an increased HCVR during sleep. For females, P12-13 and P27-28 treated rats showed an increased HCVR, but P80 treated rats showed an attenuated HCVR during sleep. The hypoxic ventilatory response was higher only in treated males at P0 and P80 during sleep. The ventilatory changes were not correlated with metabolic rate alterations. With regard to the cardiovascular parameters, only a small decrease in the HR was observed in the P27-28 treated male group during CO2 challenge. For adults, treated females showed a hypertensive response during 7% CO2 and 10% O2, and an increased HR during hypoxia, whether in sleep or wakefulness state. The mitochondrial respiration analysis showed a higher endogenous uncoupling, and increased uncoupling percentage with lower liquid phosphorylation for P0 treated males. At P12-13 ages, male treated rats showed a lower O2 consumption during uncoupling stimulation, and an increase in the percentage of phosphorylation.

Conclusions and Support: The results suggest that prenatal chronic stimulation of endocannabinoid system promotes alteration in the respiratory system development affecting mainly males and the chemosensitivity to CO2. Brainstem mitochondrial function seems to be affected for the males in the early ages. Additionally, prenatal WIN-treatment mainly affects cardiovascular control of females in a long-term resulting in hypertension. Financial support: FAPESP and CNPq.

ID: 3505

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: TRABALHO ORAL

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Title: THE EFFECT OF ACUTE AEROBIC EXERCISE ON REDOX HOMEOSTASIS AND MITOCHONDRIAL FUNCTION OF RAT WHITE ADIPOSE TISSUE

Introduction: Physical exercise is characterized by an increase in physical and metabolic demand in face of physical stress. It is reported that a single exercise session induces physiological responses through redox signaling to increase cellular function and energy support in diverse organs. However, little is known about the effect of a single bout of exercise on the redox homeostasis of white adipose tissue (WAT).

Objective: We aimed at evaluating the effects of acute aerobic exercise on WAT redox homeostasis and mitochondrial metabolism.

Methods: Adult male Wistar rats weighing 400–450 g with 18 weeks age were maintained in an animal room with controlled lighting (12-h light-dark cycle) and temperature (23–24°C). The Institutional Committee for Use of Animals in Research approved the study (Protocol No. 132/18 and Process No. 01200.001568/2013-87). Animals were submitted to a single aerobic exercise session and were divided into five groups: control (CTRL, without exercise), and euthanized immediately (0h), 0.5, 1, or 2 hours after the end of the exercise session. According to the respective time, they were euthanized and NADPH oxidase and antioxidants enzymatic activity, mitochondrial function and ROS production, oxidative damage markers, and cytoprotective mRNA levels were analyzed.

Results: NADPH oxidase activity was higher in 0h and 0.5h group when compared to CTRL group ($p<0.0001$). Extramitochondrial ROS production was higher in 0h group in comparison to CTRL and 2h groups ($p<0.0001$). Mitochondrial respiration in phosphorylative state increased in 0 h group when compared to CTRL, 0.5, 1, and 2h groups. On the other hand, mitochondrial ATP production was lower in 0h in comparison to 0.5h group, increasing in 1 and 2h groups when compared to CTRL and 0h groups ($p<0.05$). CAT activity was lower in all exercised groups when compared to CTRL ($p<0.05$). Regarding oxidative stress biomarkers, we observed a decrease in reduced thiol content in 0h group compared to CTRL and 2h group ($p<0.05$), and higher levels of protein carbonylation in 0 and 0.5h groups in comparison to the other groups($p<0.001$). The levels returned to basal condition in 2h group. Furthermore, aerobic exercise increased NRF2, GPX2, HMOX1, SOD1, and CAT mRNA levels ($p<0.05$).

Conclusions and Support: Taken together, our results suggest that one session of aerobic exercise can induce a transient pro-oxidative state in WAT, followed by an increase in antioxidant and cytoprotective gene expression. This research was funded by National Council for Scientific and Technological Development (CNPq), Coordination for the Improvement of Higher Education Personnel (CAPES), and Research Support Foundation of the State of Rio de Janeiro (FAPERJ).

ID: 3525

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: TRABALHO ORAL

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Title: SELECTIVE LOSS OF KNDY NEURONS IN FEMALE RATS REVEALS MULTIPLE ROLES IN GONADAL AND PROLACTIN AXES

Introduction: Hyperprolactinemia, a highly prevalent dysfunction of the hypothalamus-pituitary axis, is frequently associated with reproductive disorders in women. An important stimulator of the hypothalamus-pituitary-gonadal axis is kisspeptin, a key neuropeptide for fertility. Hypothalamic arcuate nucleus (ARC) neurons that coexpress kisspeptin, neurokinin B and dynorphin A (KNDy) play an important role in the control of luteinizing hormone (LH) and prolactin (PRL) secretions, but the neuroendocrine mechanisms involved are to be elucidated.

Objective: To determine the effects of selective neurochemical ablation of KNDy neurons on the estrogenic regulation of LH and PRL secretion in female rats.

Methods: Adult female Wistar rats received intra-ARC stereotaxic injections of neurokinin B receptor 3 agonist conjugated with saporin (NK3-SAP; n = 5) or vehicle (Veh; n = 6). Estrous cyclicity was monitored over 21 days followed by ovariectomy. Ovaries were processed for histological analysis. Rats were treated with estradiol (E2) cypionate (OVX+E2; 10 µg/rat, s.c.) daily for 3 days. On the fourth day, blood samples were withdrawn from the tail tip at 30-min intervals from 13:00 h to 19:00 h. After 6 days, the rats received oil treatment for additional 3 days (OVX). and blood samples were collected using the same protocol. Whole blood LH and PRL levels were measured by ELISA and brains were immunohistochemically labeled for kisspeptin, tyrosine hydroxylase (TH) and phosphorylated TH (pTH).

Results: NK3-SAP animals displayed an average loss of 66% in the number of kisspeptin-immunoreactive (ir) neurons in the ARC ($P < 0.001$). This lesion decreased body weight gain ($P < 0.001$) and caused irregular estrous cycles ($P < 0.05$). Ovarian analysis revealed increased follicular atresia ($P < 0.05$) and a reduced number of small healthy follicles ($P < 0.05$) in NK3-SAP rats. However, ovulation was not affected, as revealed by the unchanged number of corpora lutea. In the OVX+E2 model, E2-induced LH surge was amplified ($P < 0.01$) and advanced by 1 hour ($P < 0.05$). The PRL surge, in turn, was attenuated in NK3-SAP rats ($P < 0.01$). In the OVX model, basal LH secretion was unaffected by the NK3-SAP lesion, and PRL levels were undetectable in both groups. NK3-SAP and Veh rats presented similar number of TH-ir neurons in the ARC but the pTH-ir and pTH/TH ratio were increased in the median eminence of NK3-SAP rats ($P < 0.05$).

Conclusions and Support: Selective loss of KNDy neurons differently affects E2 regulation of LH and PRL secretion in female rats. Our results support a inhibitory role of KNDy neurons in the generation of the LH surge. The partial loss of KNDy neurons seems to facilitate the LH surge and ovulation even in a condition of irregular estrous cyclicity. The reduction of PRL surge, associated with the increased activity of tuberoinfundibular dopaminergic neurons, reveals that KNDy neurons inhibit neuroendocrine dopamine and this effect is implicated in the E2-induced increase in PRL secretion. This suggests a new pathway for the neuroendocrine control of PRL secretion, in which KNDy peptides orchestrate changes in the PRL release through dopaminergic neurons. Thus, KNDy neurons seem to exert multiple hypothalamic effects impacting the female reproductive function. Support: CNPq, CAPES and FAPEMIG.

ID: 3541

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

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Title: ESTROGEN-INDUCED PROLACTIN SECRETION IN FEMALE RATS INVOLVES DAILY DOPAMINERGIC SIGNAL AND ALTERED PITUITARY RESPONSIVENESS TO HYPOTHALAMIC INPUTS

Introduction: In rodents, 17β-Estradiol (E2) induces a PRL surge on the afternoon of proestrus (PRO). Although dopamine (DA) is known to tonically inhibit PRL release, the neuroendocrine mechanism involved in the E2 regulation of PRL release is not completely understood.

Objective: We used models of low and high physiological levels of E2 in female rats in order to investigate the essential neuroendocrine components responsible for the E2-induced increase in PRL secretion.

Methods: Ovariectomized (OV) rats (CEUA Nº100/2012) were treated with oil (OV; n = 6) or E2 at the doses of 4 (OVE-4, n = 5) or 80 (OVE-80; n =5) µg/kg b.w. Rats on diestrus (DI; n = 8) and PRO (n = 7) were used as physiological controls. Propyl pyrazole triol (PPT, n = 5) and diarylpropionitrile (DPN, n = 3) were used as selective agonists of estrogen receptor (ER)α and ERß, respectively. Blood samples were collected hourly between 13–18 h for hormonal measurements. Double-label immunohistochemistry to tyrosine hydroxylase (TH) and phosphorylated TH (pTH) was performed in the median eminence (ME). DA and 3,4- dihydroxyphenylacetic acid (DOPAC) levels were measured in the ME and neurointermediate lobe of pituitary (NIL). Fos immunoreactivity was investigated in hypothalamic areas. Expression of selected genes was measured by qPCR in the paraventricular nucleus (PVN) and anterior pituitary.

Results: Both doses of E2 promoted afternoon surges of PRL in OVE-4 and OVE-80 rats, similar in time (15–18 h) and magnitude (300–500 ng/mL) to that of PRO. There was no surge of PRL in OV or DI rats, which in turn displayed a small increase in PRL levels (20–50 ng/mL) at 18 h. By the time of the PRL surge, the pTH/TH ratio in the ME was lower in OVE-80 rats compared with OVE-4 and OV ($P < 0.05$) and did not differ between PRO and DI rats. No change in Fos expression associated with the PRL surge was found in the preoptic area, periventricular nucleus, or PVN. None of the E2 treatments altered oxytocin (OT) gene expression in the PVN either. Additionally, OV, OVE-4 and OVE-80 rats displayed an equal reduction in DOPAC and DOPAC/DA ratio in the ME and NIL at 18 h compared to other time points during the day ($P < 0.001$). On the other hand, both doses of E2 reduced the gene expression of ERα, ERß, and dopamine D2 receptor ($P < 0.01$) and increased the gene expression of OT receptor ($P < 0.01$) in the pituitary, whereas progesterone receptor mRNA was increased only by 80 µg/kg E2 ($P < 0.001$). Confirming the role of ERs, both PPT and DPN were able to induce an afternoon surge of PRL ($P < 0.01$), with 3 times higher levels in OV+ PPT rats ($P < 0.05$).

Conclusions and Support: Our findings demonstrate that both low and high physiological levels of E2 are able to generate PRO-like surges of PRL. The activity of hypothalamic neurons involved in the control of PRL secretion was not found to be altered in association with the occurrence of the PRL surge. Conversely, a daily afternoon decrease in DA inhibitory tone is observed regardless of the E2 status. In turn, E2 modulates ERα and ERß genes and stimulates the expression of dopamine D2 and OT receptor in the pituitary. Thus, these pituitary effects seem to alter lactotroph responsiveness to the inhibitory and excitatory hypothalamic inputs and, therefore, are permissive to the occurrence of the afternoon surge of PRL secretion. FINANCIAL SUPPORT: CNPq, FAPEMIG.

ID: 3545

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

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Title: TREATMENT WITH CINAMALDEHYDE RESTORES MOLECULAR AND FUNCTIONAL DESORDERS IN THE TESTICLE IN AN ANIMAL MODEL OF FRUTOSE-INDUCED METABOLIC DYSFUNCTION

Introduction: Several metabolic dysfunctions, such as obesity, type 2 diabetes, insulin resistance, dyslipidemia, and chronic subclinical inflammation, can affect reproductive physiology leading to infertility. Cinnamaldehyde, the main component of cinnamon oil, has hypoglycemic, hypolipidemic, anti-inflammatory and antioxidant effects. However, the cinnamaldehyde potential to improve male reproductive function has been poorly explored.

Objective: To evaluate if treatment with cinnamaldehyde is effective in reversing or mitigating molecular and functional changes in the testicle induced by fructose overload.

Methods: Adult male Wistar rats were divided into 3 groups: Control (CT), drinking water ad libitum; Fructose (FR), 20% fructose in drinking water ad libitum; Fructose + Cinnamaldehyde (CI), 20% fructose in drinking water ad libitum + cinnamaldehyde 40mg/kg of body weight, via gavage, for 8 weeks. All procedures were approved by the Ethics Committee of Animal Use of Fluminense Federal University #757). It was evaluated body mass gain and visceral fat depots mass; sperm parameters; glycemia and serum lipid profile by colorimetric assay; testicle mRNA levels by RT-qPCR.

Results: There were no differences in blood glucose, visceral fat mass and body weight gain among groups. However, fructose-overload induced higher serum levels of triglyceride ($p=0.0116$), total cholesterol ($p=0.0474$), LDL ($p=0.0480$), and VLDL ($p=0.0116$) compared to the control group. Cinnamaldehyde treatment decreased serum lipid profile to control levels. The FR group exhibit lower testicle width (FR vs CT, $p<0.001$), and cinnamaldehyde normalized this parameter. Although fructose reduced prostate mass (FR vs CT, $p=0.0220$), the CI group presented an enlarged prostate (CI vs CT, $p=0.0410$). There were no changes in the mass of the testicles, epididymis, seminal vesicle, or testicular height among groups. In the sperm evaluation, the FR group exhibited lower sperm concentration ($p=0.0103$), sperm viability ($p=0.0290$), and membrane functionality ($p=0.028$), compared with the CT group. Interestingly, cinnamaldehyde normalized all these damages induced by fructose overload. Analyzing the expression of steroidogenesis-related genes, the FR group showed a decrease in the expression of Star (FR vs CT, $p=0.0253$), Cyp19a1 (FR vs CT, $p=0.0260$), and Srd5a1 (FR vs CT, $p=0.0433$), and cinnamaldehyde treatment restored the expression of those genes to control levels. Both FR and CI groups showed lower expression of Srd5a2 (FR vs CT, $p=0.001$; CI vs CT, $p=0.0047$). There were no changes in the expression of Hsd3b2 and Cyp17a1 among groups. Concerning inflammation-related genes, the FR group showed higher expression of Tnfa (FR vs CT, $p=0.0138$), Il1b (FR vs CT, $p=0.0327$), and Il6 (FR vs CT, $p=0.0065$), that were normalized by the cinnamaldehyde treatment. Although there was no change in Bcl2 mRNA levels among groups, the expression of the pro-apoptotic gene Bax was lower in the CI group compared to the FR group ($p=0.0121$). Regarding cholesterol metabolism-related genes, the fructose overload induced an increase in Ldlr expression (FR vs CT, $p=0.0139$) that was normalized in the CI group. There was no change in Srebp2 expression.

Conclusions and Support: Fructose overload induced molecular and functional disorders in the testicle of rats, that were normalized by the cinnamaldehyde treatment, suggesting a protective effect of cinnamaldehyde in the male reproductive system under metabolic disturbances.

ID: 3556

Área: NEUROFISIOLOGIA

Forma de Apresentação: TRABALHO ORAL

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Title: PLASMA DYNAMIC AND NEUROPROTECTIVE ROLE OF LACTATE FOLLOWING NEONATAL HYPOXIA-ISCHEMIA

Introduction: Hypoxia-ischemia (HI) is an important cause of neonatal death and permanent neurological disabilities. Even though lactate (LAC) has shown neuroprotective effects in animal models of cerebral ischemia, understanding of its plasma dynamic is important to allow its use as a cerebral metabolic fuel in neonates that underwent hypoxic-ischemic events.

Objective: To investigate plasma LAC levels after experimental HI and following an intraperitoneal (i.p.) injection of LAC; to analyze if an i.p. administration of LAC affects brain LAC concentrations; to evaluate if LAC administration after HI reduces the volume of brain lesion.

Methods: Seven-day-old (P7) Wistar male and female rats were submitted to a surgery for ligation of the right common carotid artery followed by exposure to a hypoxic atmosphere (8% of oxygen) for 60 min. Blood samples were collected at 5, 20, 30 and 45 minutes after HI (n=8). Sham animals were kept in normoxia and had its blood collected at the same timepoints. Another group of animals (P7) with no previous manipulation received an i.p injection of either LAC or vehicle (phosphate-buffer saline, PBS) and had its blood collected at 5, 30, 45 and 90 minutes after the injection (n=6). Moreover, the hypothalamus of these animals was collected to determine brain lactate concentrations. To evaluate the volume of the brain lesion, additional animals (P7) were assigned to four experimental groups: HI (rats submitted to HI that received PBS), HI+LAC (rats submitted to HI that received LAC), SHAM (underwent a fictitious surgery and received PBS) and SHAM+LAC (SHAM rats that received LAC) (n=8). LAC was administered intraperitoneally following HI. Animals were euthanized in P9 and their brains were sliced (3mm thickness) and stained with TTC (triphenyltetrazolium chloride). The sections were digitalized and the volume of the brain infarct (ipsilateral to carotid occlusion) was expressed as a percentage of lesion relative to the volume of the hemisphere contralateral. Data were analyzed by two-way ANOVA followed by Bonferroni and expressed as mean±SEM. This study was approved by the Institutional Animal Care and Use Committee of the Hospital de Clínicas de Porto Alegre (#2018-0258).

Results: Plasma levels of LAC increased at 5 minutes following HI ($p<0.05$), and returned to baseline values after 30 minutes. Five minutes after an i.p. injection of lactate, plasma levels of lactate increased 4-fold ($p<0.05$) and returned to control levels in 45-90 minutes. Hypothalamic levels of LAC were higher in LAC-injected animals ($p<0.05$). Brain infarct was reduced in both male and female rats from HI+LAC group as compared to HI group ($p<0.05$).

Conclusions and Support: These results suggest LAC administered intraperitoneally reaches the brain and could act as an energy substrate, reducing the brain lesion in neonatal rats submitted to HI. Additional experiments are required in order to understand the mechanism of action by which LAC is protecting the brain. This study was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundo de Incentivo à Pesquisa e Eventos from Hospital de Clínicas de Porto Alegre (FIPE/HCPA), and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).

ID: 3560

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Title: P2X3 RECEPTOR EXPRESSION IN CARDIOVASCULAR TARGET ORGANS IN RATS WITH CARDIOVASCULAR DISEASE

Introduction: Cardiovascular diseases (CVD) are the leading causes of death in Brazil and worldwide. Previous studies have demonstrated increased purinergic P2X3 receptor subtype expression in the carotid body from hypertensive rats and human patients with CVD. In hypertensive rats, systemic antagonism of P2X3 receptors normalized carotid body dysfunction, reduced arterial pressure and basal sympathetic activity. Recent data from our laboratory showed that chronic systemic inhibition of P2X3 receptors prevented the progression of heart failure (HF) in rats supporting the novel idea that P2X3 receptors are a potential new therapeutic target for treating CVD. Nevertheless, to the best of our knowledge there are no reports describing expression levels of P2X3 receptors in the heart or blood vessels in CVD. Therefore, we tested the hypothesis that expression of P2X3 receptors changes in target organs, of rats with CVD.

Objective: To evaluate P2X3 receptor expression in the left ventricle, aorta, mesenteric artery and perivascular tissue of the aorta from HF rats, and rats fed with a high-fat diet (HFD).

Methods: All animal care and experimental procedures were approved by the Committee of Animal Research Ethics from Federal University of Santa Catarina (CEUA/UFSC, number 2351090518). Rat groups included: sham coronary ligation (Sham; n=3-5), HF (n=5-8), standard diet (n=4-6) and HFD (n=4-6). HF was induced by ligation of the left anterior descending coronary artery; rats were studied 6 weeks after the surgical procedure. Sham-operated rats underwent similar surgical procedures but did not undergo coronary artery ligation. The HFD consisted of standard rat chow, peanuts, milk chocolate and sweet biscuits in the proportion of 3:2:2:1. The rats were fed with the HFD for 7 weeks. P2X3 receptor expression was quantified by Western blotting.

Results: HF animals demonstrated increased cardiac (T-Test, t= 4.446, p= 0.001) and pulmonary index (T-Test, t= 3.448, p= 0.005), reduced left ventricle contractility (T-Test, t= 4.571, p= 0.001) and relaxation (T-Test, t= 4.060, p= 0.003). HFD showed higher body weight compared to the standard diet group (Two-way ANOVA, p=0.0001). The receptor was present in each of the organs studied (left ventricle, aorta, mesenteric artery and perivascular tissue of the aorta). However, no difference in a detectable level between rat groups was observed, i.e. HF rats compared with the Sham, or HFD compared to standard diet rats.

Conclusions and Support: We show that P2X3 receptor expression was detectable in cardiovascular structures such as heart, aorta, arteries and perivascular fat but neither HF nor a HFD altered expression levels, which is in stark contrast to that detected in the carotid body of rats with CVD. Support: CNPq, CAPES and FAPESP.

ID: 3564

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: TRABALHO ORAL

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Title: EFFECTS OF ANGIOTENSIN-(1-7) IN PREGNANCY-INDUCED CARDIAC HYPERTROPHY.

Introduction: It is widely known that Angiotensin-(1-7) [Ang-(1-7)] has protective effects against pathological cardiac hypertrophy. Recently, our group has demonstrated that Mas receptor has an important role in the development of pregnancy-induced cardiac hypertrophy in normotensive rats. However, the effects of Ang-(1-7) on gestational cardiac remodeling in hypertensive rats are unknown.

Objective: The aim of this study was to evaluate the effects of Ang-(1-7) on the gestational cardiac hypertrophy in hypertensive rats.

Methods: Normotensive (Wistar) and Spontaneously Hypertensive Rats (SHR, 280g-300g) were divided into following groups: i) Non-Pregnant Wistar; ii) Pregnant Wistar; iii) Non-Pregnant SHR; iv) Pregnant SHR and; v) Pregnant SHR treated with Ang-(1-7). The Ang-(1-7) (24 µg/kg/h, s.c., osmotic mini-pumps) was administered over the gestation period. Systolic blood pressure (SBP) was assessed by tail plethysmography (CEUA/UFG 039/14). Pregnant rats were euthanized on the twentieth day of gestation and gestational and fertility parameters were assessed. The medial part of the left ventricle (LV) were collected for histological analysis.

Results: Pregnancy increased the diameter of cardiomyocytes in WT-G when compared to WT (12.2 ± 0.13 vs 10.7 ± 0.09 μm in WT, $p < 0.05$). Pregnancy also increased the size of cardiomyocytes in SHR-G (17.20 ± 1.6 vs 14.02 ± 0.13 μm in SHR, $p < 0.05$). Treatment with Ang- (1-7) completely reversed this effect in SHR (12.60 ± 0.13 vs 17.20 ± 1.6 μm in SHR-G, $p < 0.05$). An increase in interstitial fibrosis was observed in the left ventricle of WT-G (10.82 ± 0.58 vs 6.04 ± 0.43 μm in WT, $p < 0.05$) and in SHR-G (16.91 ± 1.02 vs 12.33 ± 0.55% in SHR, $p < 0.05$). SHR-G Ang- (1-7) showed a decrease in interstitial vibrosis when compared to the SHR-G group (7.31 ± 0.49 vs 16.91 ± 1.02% in SHR-G, $p < 0.05$). Perivascular fibrosis in the left ventricle of SHR-G was greater (5.67 ± 0.55 vs 4.15 ± 0.39% in SHR, $p < 0.05$) and (5.67 ± 0.55 vs 4.03 ± 0.24% in WT, $p < 0.05$). Ang- (1-7) decreased the interstitial deposition of the extracellular matrix in SHR hearts (4.07 ± 0.41 vs 5.67 ± 0.55% in SHR, $p < 0.05$). Treatment with Ang- (1-7) did not change the gestational parameters (weight gain of pregnant rats, pre-implantation loss, post-implantation loss and number of fetuses) in hypertensive rats hypertensive pregnant rats through blood pressure-independent mechanisms.

Conclusions and Support: These data showed that treatment with Ang- (1-7) reduced the cardiac hypertrophy in hypertensive pregnant rats through blood pressure-independent mechanisms. Support: Capes, CNPq and FAPEG.

# Developmental Origins of Health and Disease (DOHaD)

ID: 3585

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: LOW-PROTEIN DIET DURING PERIPUBERTY IMPAIRS SPERMATIC PARAMETERS IN PUBERTAL WISTAR RATS BUT NOT AT ADULT LIFE

Embasamento/Background: Malnutrition is a condition caused by the excess or the absence of one or more micronutrients in a diet and affects people of every country in the world, being qualified by the World Health Organization as the greatest single threat to global public health. It is known that protein restriction during puberty/adolescence induces long-term metabolic changes, which may be related to reproductive malfunction. On the light of this facts and the importance of peripuberty as a critical period for the postnatal organ development of the male genital system, the aim of this study is to evaluate the immediate and late effects of the exposition to a low-protein diet during the peripubertal period into spermatic parameters.

Métodos/Methods: For that, male Wistar rats were divided into 2 groups: a protein-restricted (LP) and a normoproteic (NP) group. The rats in LP group received a low-protein diet (4%) and the ones in NP group received a normoproteic diet (23%) from PND 30 to PND 60. After the dietary period, rats of both groups were divided into 2 groups: NPp, NPa, LPp and NPa. Rats in LPa and NPa groups went through a dietary recuperation, in which they were fed ad libitum with a normoproteic diet from PND 60 to PND 120; and rats in LPp and NPp groups, were euthanized at PND 60 by decapitation with no anaesthesia. At PND 120, rats in LPa and NPa were anaesthetised with thiopental (0,08 mL) and euthanized by heart puncture. Then, sperm cells from the vas deferens were collected and destined to the analysis of sperm motility and evaluation of mitochondrial activity, in witch they are classified as DAB 1, 2 or 3, being 1 the most active and 3 the least. The right testis was collected for the analysis of spermatic count. The experimental protocol followed the ethical principles and it was approved by the Ethics Committee on Animal Use (OF. CIRC. CEUA-UEL. n 144/2019/Protocol n 477 – CEUA-UEM). The data was submitted to the normality Bartlett test and homogeneity Shapiro-Wilk test, then compared using an unpaired t test. Data was considered significantly different when $P<0.05$ and expressed as mean ± S.E.M.

Resultados/Results: The number of motile sperm cells showed to be decreased in the LPp group (2.58±1.01) in comparison to its control group, NPp (33.80±8.72). However, this reduction was not present in the LPa group (71.60±4.06) in comparison to its control group, NPa (66.33±2.99). It was observed a decrease in the number of cells classified as DAB 1 in the LPp group (160.66±2.01) in comparison to NPp group (111.22±5.43), and an increase in the number of cells classified as DAB 2 and DAB 3 in LPp group (35.17±1.32; 4.16±1.04; respectively) in comparison to NPp group (73.40±4.21; 15.38±2.61; respectively). Although, these alterations were not present in between the LPa and NPa groups. The parenchymal weight of the testes in group LPp (0.67±0.08) was significantly diminished in comparison to NPp group (1.21±0.03). However, this diminution was not observed in between the groups LPa (1.55±0.03) and NPa (1.56±0.03). The absolute number of sperm cells in the testes of rats in group LPp (33.31±2.50) were also reduced in comparison to NPp group (52.59±2.20), but this reduction was not observed in between the LPa (143.80±12.66) and NPa (136.80±13.79) groups. No difference was observed between the number of sperm cells by gram of testis, neither in between LPp (52.09±3.84) and NPp (43.84±2.49) groups, nor in between LPa (87.52±8.40) and NPa (92.29±8.43) groups. Also, a diminution on the daily spermatic production (DSP) was noted in group LPp (5.46±0.41) in comparison to NPp (8.62±43.84). However, this alteration on the DSP was not present in between LPa (22.43±2.26) and NPa (25.57±2.08) groups.

Conclusões/Conclusions: Reasoning from these partial results, we can infer that a protein restriction during peripuberty impairs the spermatic parameters analyzed in the pubertal male rat, however, this effect is mitigated in the adult male by a dietary recuperation.

Palavras Chave/Key-words: Malnutrition, protein deficiency, sperm cells, testis

ID: 3586

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal exposure to glycotoxins during lactation: outcomes for offspring glycemic homeostasis

Embasamento/Background: Glycotoxins and Advanced glycation end products (AGE) consumption have been associated to the development of disturbances in glycemic homeostasis, such as increased oxidative stress, β-cell dysfunction and insulin resistance. In rodents, the postnatal period is important for pancreatic development and maturation, therefore we hypothesized that maternal intake of methylglyoxal (MG), a glycotoxin, during lactation may impair pancreatic function of the offspring.

Métodos/Methods: Wistar pregnant rats were maintained in standard conditions until delivery. All animals had free access to standard chow and water. Delivery was considered day 0, in day 1 litter size were standardized for 8 pups per mother (4 Males and 4 Females) and separated into two groups whose dams were treated daily by gavage: Control (CO - saline 0,9% 1mL/kg – 4) and Methylglyoxal (MG - methylglyoxal 60mg/kg – 4). Treatment started on day 1 and halt at the end of lactation (day 21). The offspring were euthanized at 7, 14 and 21 days old for blood sample and tissue collection. A separated batch of animals were submitted to oral glucose tolerance test (GTT).

Resultados/Results: MG offspring presented decreased bodyweight ($p<0,05$) at weaning, and lower insulin levels at 14 ($p<0.05$) and 21 days old ($p<0.001$). Moreover, on day 21 it was observed decreased pancreatic islet area ($p<0.05$) and reduced activity of CAT and SOD enzymes in the pancreas. No difference was observed in basal glycemia, despite a tendency at 21 days-old ($p=0,0528$). The GTT revealed an increased glycemia at time 15' of the test ($p<0,05$) however no difference was observed in the analysis of the area under the curve.

Conclusões/Conclusions: Maternal exposure to glycotoxins during lactation impairs offspring pancreatic development and function early in life. It is noteworthy that this early impairment of glycemic homeostasis may increase susceptibility to the development of diabetes later in life.

Palavras Chave/Key-words: glycotoxins, oxidative stress, lactation, pancreas.

ID: 3587

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Materno-fetal Adipokines Profile in an Animal Model of Obesity

Embasamento/Background: Obesity is a chronic noncommunicable disease of epidemiological importance that affects the entire population. For the female public of reproductive age, obesity becomes an even greater problem due to the impact of excess weight on the intrauterine environment and, consequently, on fetal development and the health of future generations. Pregnancy causes physiological and metabolic changes to generate a fetus. However, obesity also causes changes that can alter the conditions expected for pregnancy, such as increased leptin secretion and decreased adiponectin secretion due to increased adipose tissue. Such changes can cause unfavorable outcomes, such as altered placenta development, inappropriate fetal growth, premature birth and adult morbidity. Thus, the objective was to investigate the hormonal profile in an animal model of maternal obesity induced by a high-fat and high-caloric diet.

Métodos/Methods: The experimental procedures were submitted for approval by the Ethics Committee of UNICAMP (CEUA: 5412-1). After four weeks of adaptation, swiss female mice were submitted to fed with standard (CT) or hyperlipidic (HF) diet during another four weeks. Then, the mating was performed. For each group of two females, it was assigned to a male, held together for three days at 12 hours intervals, when they were examined for the presence of signs of mating and detection of the vaginal plug (day E0.5 of pregnancy). Data on intake feeding and weight characterization were performed in the pregestational and gestational phases. After the gestational period, serum and amniotic fluid were extracted and collected for subsequent analysis by Magnetic Luminex® Assay.

Resultados/Results: The groups started with equivalent weights, the HF group showed greater weight gain due to having greater weight in the pre-gestational period and at the end of pregnancy. These results suggested a greater accumulation of adipose tissue in the HF group. The CT group and the HF group had similar caloric intake, suggesting that the composition of the diet had a significant role for weight gain in the HF group. Regarding the maternal hormonal profile, the HF group had a higher concentration of leptin in the serum, confirming the hypothesis of greater accumulation of adipose tissue although it was not possible to measure amniotic fluid (AF) levels. On the other hand, there were no differences in the presence of adiponectin in serum but the maternal consumption of a hight fat diet lead to an opposit adiponectin profile in AF with a tendency to decrease than control dams. Both adipokines have a wide range of important roles, ranging from maternal physiology to the fetal-maternal interface to the development and fetal growth. For these functions to be performed effectively and without the development of pathologies it is important to consider the ratio between leptin-adiponectin. The leptin-adiponectin ratio unfavorable could indicate insulin resistance, atherosclerosis, metabolic syndrome. In addition, there were no differences between the CT and HF groups regarding the presence of prolactin in serum and amniotic fluid.

Conclusões/Conclusions: According to all the results, it is possible to conclude that the concentration of leptin in the serum is statistically higher in the HF group, which is an important hormone for the development of the placenta and embryo. The diet represented an important factor in the modification of this parameter, suggesting impairment in the health outcome for the offspring.

Palavras Chave/Key-words: Pregnancy. Metabolism. Fetal programming. DOHaD.

ID: 3077

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Adipose Tissue of Mice Dams and Their Offspring is Affected by the Oxidative Stress as a Result of Dietary Interventions. Ana Carolina de Moura1, Mariana Fraga Gauthier1, Joana Fisch2, Vanessa Feistauer1, Silvana Almeida1, Renata Padilha Guedes1, Márcia

Embasamento/Background: Pregnancy per se is a condition of increased oxidative stress, as well as the obesity that is characterized by unbalanced oxidant-antioxidant status. When excessive weight and pregnancy are combined, massive oxidative stress may occur, which can be harmful to the mother and offspring's health. On the other hand, caloric restriction may exert a protective function because it enhances cellular autophagy, diminishes inflammation and oxidative stress.

Métodos/Methods: The Institutional Animal Care and Use Committee of UFCSPA (#388/15) approved this study. Thirty female BALB/c albino mice (60 days old) were separated in 3 different groups (n=10/group). To the control group (CONT) was administrated a standard mice chow ad libitum (energy content 3.4kcal/g); the restrictive diet group (RD) had 30% reduction in the standard chow amount, compared to the consumption of CONT; and the hypercaloric diet group (HD) was fed with a special chow ad libitum (energy content 4.9kcal/g). Diet adaptation lasted 25 days, after they were housed with males for mating. On the first postpartum day, litters were standardized at 6 pups. After weaning, the dams were euthanized. After delivery, the pups were standardized in 6 per group, totalizing 9 experimental groups. After weaning, male pups of each mother's group were named accordingly maternal/offspring diets: CONT/CONT, CONT/RD, CONT/HD, RD/CONT, RD/RD, RD/HD, HD/CONT, HD/RD, HD/HD. Around 100 days old, the offspring was euthanized and tissues were used for 2′,7′-dichlorofluorescein (DCF) and for thiobarbituric acid-reactive substances (TBARS) assays, and for the activities of superoxide dismutase (SOD) and catalase (CAT).

Resultados/Results: In the adipose tissue of dams SOD activity was significantly decreased in HD compared to CONT [$F(2,17)=3.409$; $p=0.050$]. In the adipose tissue of the offspring, regarding ROS production, we found both maternal and offspring diet effects, and also an interaction between these two factors [maternal diet effect: $F(2,62)=34.01$; $p<0.0001$; offspring diet effect: $F(2,62)=3.821$; $p=0.027$; interaction: $(F(4,62)=8.842$; $p<0.0001]$. ROS production was significantly increased in HD/CONT compared to CONT/CONT and RD/CONT ($p<0.0001$ for both comparisons). In HD/HD, ROS production was higher than RD/HD and CONT/HD ($p<0.0001$ for both comparisons). Concerning SOD activity, we found a maternal diet effect [$F(2,60)=38.99$; $p<0.0001$] and a significant increase in SOD activity in the offspring from HD dams, regardless of offspring diet. CAT activity also showed a maternal diet effect [$F(2,44)=3.997$; $p=0.025$]. CAT activity showed an increase in HD/RD compared to CONT/RD ($p=0.01$).

Conclusões/Conclusions: Our findings showed that the adipose tissue of the dams was slightly affected as a consequence of the diet modification, since HD group showed a decrease in SOD activity compared to CONT, which may predispose to oxidative stress. Thus, it is important to consider that adipose tissue has high concentration of antioxidant enzymes to manage the high production of ROS. In obese individuals, the expression and activity of antioxidant enzymes such as CAT, SOD, and glutathione peroxidase decreased in the adipose tissue. These data indicate that an increase in ROS production and a decrease in antioxidant enzymes in obesity can lead to oxidative stress in adipose tissue. The absence of oxidative stress in the adipose tissue of dams can be associated with the physiological adaptations following pregnancy and lactation. It has been proposed that lactation resets the metabolism, since it mobilizes the energy storages to milk production, preventing the development of metabolic and cardiovascular diseases. Thus, it is reasonable to suppose that we did not find a remarkable oxidative stress condition in the present study since we evaluated tissues from female mice following lactation. Financial Support: CAPES, CNPq, UFCSPA

Palavras Chave/Key-words: Restrictive Diet, Hypercaloric Diet, Superoxide Dismutase, Catalase

ID: 3590

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Endothelial Repercussion of Topiramate Exposure During Adolescence in Female rats: Short and Long Term Evaluation

Embasamento/Background: Topiramate (TOP) is a therapeutic agent approved for the treatment of epilepsy and migraine prophylaxis in adolescents. Currently, it has been recognized that exposure to drugs in important phases of biological development, such as adolescence, can program late changes in the health of an individual. Recently, it has been reported that treatment with TOP can favor the development of vascular diseases increasing vascular risk factors. However, at least in females, the effect of TOP treatment during adolescence on vascular endothelial function has not been investigated yet. Thus, this study aimed to assess whether exposure to TOP into adolescence interferes with the functions of the vascular endothelium in the short and long term in female rats.

Métodos/Methods: For this, female Wistar rats were exposed to TOP (41 mg/kg/day) or vehicle (CTR group) by gavage from postnatal day (PND) 28 to 50 (adolescence in rodents). During the exposition, the rats' weight was daily monitored to adjust the volume of medication and to follow body mass gain. After that, TOP and CTR groups were evaluated at PND 51 or PND 90 (in the estrus phase). The female rats evaluated at PND 90 were weighed weekly until the day of the experiment (PND 57, 64, 71, 78 and 85). In both periods, thoracic aorta reactivity to the vasoconstrictor phenylephrine (Phenyl) and vasodilators acetylcholine (ACh) and sodium nitroprusside (SNP) was evaluated in the presence (E+) or absence of endothelium (E-). Groups were compared by the maximum response (maxR) and pD2 for each drug. Data were expressed as mean ± standard error of the mean and analyzed by multiple t-tests, two-way ANOVA or test t. Differences were considered statistically significant when $p<0.050$ (CEUA: 9379.2018.26).

Resultados/Results: There was no difference in body mass gain during exposition or until PND 90. At PND 51, in aortic rings E+ and E-, the maxR (g) to Phenyl was similar between the groups [CTR E+: 1,61 ± 0,08 (11) vs TOP E+: 1,62 ± 0,08 (12); CTR E-: 2,63 ± 0,07 (11) vs TOP E-: 2,59 ± 0,12 (12)] as well as at PND 90 [CTR E+: 1,51 ± 0,09 (9) vs TOP E+: 1,34 ± 0,07 (9); CTR E-: 3,16 ± 0,07 (9) vs TOP E-: 3,28 ± 0,08]. Regarding maxR (% relaxation) to vasodilators, there was no difference in the response to ACh at PND 51 [CTR: 93,47 ±

1,25 (9) vs TOP: 92,45 ± 1,16 (8)] as well as at PND 90 [CTR: 92,59 ± 1,10 (8) vs TOP: 90,20 ± 1,19 (8)]. The response to SNP vasodilator was also similar in both periods [PND 51 = CTR: 96,24 ± 0,76 (9) vs TOP: 97,76 ± 0,63 (9); PND 90 = CTR: 95,04 ± 0,86 (12) vs TOP: 95,61 ± 1,05 (10)]. Moreover, pD2 for Phenyl, ACh and SNP was similar between the CTR and TOP groups, when evaluated at the end of exposition or in adulthood.

Conclusões/Conclusions: In the present study was demonstrated that TOP exposure during adolescence does not alter, in the short and long term, the body mass gain and aorta reactivity in healthy female rats, suggesting that TOP in the dose and period used is safe concerning these parameters.

Palavras Chave/Key-words: vascular reactivity; endothelium; adolescents.

ID: 3080

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Temporal Effects Of Maternal Vitamin D Deficiency On Brown Adipose Tissue Development In Rats Offspring

Embasamento/Background: Maternal vitamin D deficiency (VDD) has been linked to impaired development of different tissues in offspring, leading to adverse metabolic outcomes. However, much little is known about the implications of this condition on brown adipose tissue (BAT) physiology along the time. Therefore, we investigate the role of vitamin D on brown adipose tissue development in male rats offspring.

Métodos/Methods: Twelve 5-week-old female Wistar Hannover rats were fed either a standard diet (AIN93G) or modified diet (AIN93G without vitamin D) for six weeks. At the end of this period, they mated and both diets were maintained throughout gestation and lactation. At weaning, the male offspring was separated in four groups: 21-days and 180-days male offspring born and breastfed from mothers fed with standard (SD21; n=6 and SD180; n=15) or modified diet (VDD21; n=6 and VDD180; n=16). After weaning, the 180-days male offspring was fed with standard until the day of the eutanasya, when BAT and white adipose tissue (WAT) were harvested for analysis *P≤0,05 (CEUA 52/2018).

Resultados/Results: VDD groups showed a reduction in the calcidiol serum concentration at both ages (5.3±0.3 vs 29±0.9 in SD21 group and 23±1.1 vs 40±2 in SD180 group). At 21 days of age, VDD group weighed less (32±1 vs 42±2 g in SD21 group) and showed a great loss of white adipose tissue (WAT) mass (epididymal: 88±12 vs 184±27 mg in SD21 group; retroperitoneal: 120±15 vs 263±30 mg in SD21 group), without changes in BAT mass. However, BAT showed a decreased content of lipid droplets, with no alterations on the content of BAT noradrenaline as well as on thermogenic and mitochondrial proteins as estimated by Western blot. This was accompanied by lower serum insulin (0.8±0.1 vs 2.3±0.3 ng/ml in SD21 group) and calcium concentrations (7±0.1 vs 8.7±0.1 mg/dL in SD21 group). Most of these effects were reverted in the VDD180 group, which showed no differences in total body weight, but an increase in WAT (epididymal: 11.58±0.78 vs 7.98±0.53 mg in SD180 group, retroperitoneal: 9.73±0.68vs 6.92±0.62 mg in SD180 group), and BAT mass (382±34 vs 302±30 mg in SD180 group) as well as in serum insulin levels (6,7±0,6 vs 3,5±0,5 ng/ml in SD180 group), without differences in plasma calcium levels.

Conclusões/Conclusions: The data suggest that vitamin D deficiency during pregnancy and lactation results in a biphasic effect on BAT development, with lower lipids droplets associated with reduced insulin levels at weaning, followed by an increased BAT mass and a metabolic syndrome phenotype in adult life. Suport: FAPESP (2019/19993-6).

Palavras Chave/Key-words: Vitamin D deficiency; Brown adipose tissue development; Programming; Metabolic syndrome

ID: 3593

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Exposure to Sulfasalazine: Reproductive Parameters of Female Rat Offspring. Karina Nicole Sobota1; Simone Forcato Ferreira1; Ana Beatriz de Oliveira Aquino1; Daniela Cristina Ceccatto Gerardin1. 1State University of Londrina - Londrina/PR.

Embasamento/Background: Sulfasalazine (SAS) is recommended as the first line for the treatment of chronic inflammatory bowel diseases (Crohn's disease and ulcerative colitis). It is known that in men, SAS treatment causes decreases testosterone levels and increases luteinizing hormone (LH) levels. Although, SAS treatment is considered safe, during throughout gestational period because it is not teratogenic, SAS

and its metabolites cross the placenta achieving therapeutic concentrations in fetal circulation. Furthermore, it also is detected in milk and urine samples from infants. Based on this evidence, it could alter these hormones in females and cause reproductive alterations, since some environmental perturbations such as drug exposition during early development can increase the susceptibility of organisms to the development of diseases in adulthood. However, studies about the reproductive parameters of the female are scarce. The present study aimed to evaluate if maternal exposure to SAS might interfere with reproductive parameters of female rat offspring.

Métodos/Methods: Wistar female rats (n=10) were gavaged with SAS 300mg/kg/day from gestational day (GD) 0 until lactational day (LD) 21. Control dams (n=10) received carboxymethylcellulose (CMC, vehicle) at the same periods. During the gestational period, dams received supplementation with folic acid (FA) 3mg/kg/day, 2 h before the treatment with SAS due to this drug to inhibit folate uptake. The female pups' body weight was measured on post-natal day (PND) 1, 4, 7, 14, 21. The anogenital distance (AGD) was obtained on: PND 1, PND 21 and, the day of vaginal opening. AGD was measured through a Vernier caliper and normalized through its division by the cube root of body weight. On PND 21, one female pup per little (n=9-10/group) was euthanized by decapitation and had reproductive organs (uterus and ovaries) removed and weighed. In another subgroup, the vaginal opening was verified daily, from PND 25. From of day, which was observed the vaginal opening, the vaginal smear was performed to verify the first estrus. From PND 75, vaginal smears were obtained daily, always at the same time in the morning, over a period of 15 days. The coefficients of proestrus (Cp), estrus (Ce), and metaestrus/diestrus (Cmd) and, estrous cycle duration was calculated by the formula C=a/b 100%, where C is the coefficient of the cycle period, a is the number of days of the corresponding cycle period during the observation, and b is the total duration of the complete cycles (in days). Results were considered statistically significant if $p < 0.05$ and compared by Analysis of co-variance (ANCOVA), Student t-test or Mann-Whitney U (CEUA/UEL: 125.2018).

Resultados/Results: The body weight gain during lactation period (DPN 1 - DPN 21), AGD, reproductive organs weight at PND 21 were similar between groups, as well as the installation of puberty. Furthermore, the maternal exposure to SAS did not induce alterations in estrus cyclicity of female offspring (n=10/group), such as Ce [CTR: 26.67 (25.00-33.33); SAS: 26.67 (25.00-28.33)], Cmd [CTR: 53.33 (51.67-60.00); SAS: 53.33 (46.67-58.33)], Cp [CTR: 16.67 (6.67-21.67); SAS: 20.00 (11.67-26.67)], Estrus Cycle length (days) [CTR: 6.25 (4.69-15.00); SAS: 5.00 (3.75-9.37)], $p > 0.05$, Mann-Whitney U test.

Conclusões/Conclusions: Although the literature is described that SAS alters the fertility in men and rodents, this is the first study that investigated the effect of maternal exposure to SAS on the reproductive development of female offspring. In this way, more studies are required to investigate the effects of maternal exposure to SAS during critical periods of development.

Palavras Chave/Key-words: maternal exposure, chronic inflammatory disease, female fertility.

ID: 3594

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: ORAL

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Título/Title: Maternal High-fat Diet During Pregnancy and Lactation Contributes to Platelet Hyperactivation in Male Mouse Offspring

Embasamento/Background: Maternal over-nutrition increases the risk of diabetes and cardiovascular events in offspring. While prominent effects on cardiovascular health are observed, the impact of this on platelet physiology has not been studied. Here, we studied whether maternal high-fat diet (HF) ingestion can affect the platelet function in offspring.

Métodos/Methods: C57BL6/N mice dams were given a HF or control (C) diet for 8 weeks prior to and during pregnancy. Male offspring also received either C or HF diets for 26 weeks. Experimental groups were: C/C, dam and offspring fed chow; C/HF dam fed chow and offspring fed high-fat diet; HF/C and HF/HF. Phenotypic (body weight, % of body fat, etc) and metabolic (glycaemia, triglyceridemia, etc) tests were performed and blood collected for platelet studies.

Resultados/Results: Compared to C/C, offspring HF groups were obese, with fat accumulation, hyperglycaemia and insulin resistance. Maternal obesity led to an overall effect of increased mean platelet volume and reactivity in offspring. Platelets from HF/HF mice were hyperreactive, displaying higher fibrinogen binding after stimulation with different agonists, and increased platelet adhesion and spreading on collagen. Both maternal and offspring HF groups presented decreased levels of collagen receptor GPVI with increased oxidative stress. HF/HF mice had increased phosphorylation of PKC substrates, total tyrosine and AKT at Ser473 compared to C/C.

Conclusões/Conclusions: Maternal HF diet ingestion is able to programme platelet hyperactivation in male mouse offspring. Since platelet function can be programmed by early developmental periods, it is possible to use this window of intervention to reduce the risk of thrombotic events.

Palavras Chave/Key-words: Platelet; Developmental Biology; Oxidative stress; Metabolic Syndrome

ID: 3083

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Instituições:

Título/Title: Naringin Supplementation During the Third Week of Pregnancy Induces Redox Alterations in the Offspring's Cerebellum During Postnatal Development

Embasamento/Background: Naringin is a glycosylated flavonoid predominantly found in citrus fruits. Owing to its ability to promote a neuroprotective effect, especially through the regulation of redox homeostasis, naringin supplementation has been studied in several disease models in the central nervous system (CNS). However, there is a lack of research evaluating the possible impact of this supplementation during pregnancy on fetal development. We aimed to evaluate the effect of maternal naringin supplementation during the third week of pregnancy in the offspring's cerebellum redox homeostasis.

Métodos/Methods: Pregnant Wistar rats were divided into control group and naringin group, both treated by oral gavage. During the third week of pregnancy, the control group received distilled water, while the naringin group received the flavonoid at a dose of 100 mg/kg/day dissolved in water. On postnatal day 1, postnatal day 7, and postnatal day 21 male and female pups were euthanized. The cerebellum was dissected and stored at –80 °C. We evaluated the total content of oxidants by the dichlorofluorescein (DCFH) oxidation, reduced glutathione concentration (GSH), the activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and glyoxalase 1 (GLO1). Data was analyzed by two-way analysis of variance (ANOVA) for two independent variables (sex and naringin supplementation) in the software GraphPad Prism 6.0. The experimental design and procedures were approved by the local Ethics Commission on Animal Use (CEUA/UFRGS), protocol number 35332.

Resultados/Results: No changes were observed between the control group and the naringin group in postnatal day 1. On postnatal day 7, maternal naringin supplementation induced increased total oxidants level and SOD activity in the female offspring. Also, an increase in the total content of oxidants, GSH levels, increase activity of SOD and reduced activity of GPx was observed between control females and control males. On postnatal day 21, reduced GLO1 activity was observed in naringin males compared to control males. Also, reduced GSH content, GPx and GLO1 activity was detected between control females and control males.

Conclusões/Conclusions: As demonstrated, the redox alterations found on postnatal day 7 suggest that naringin induced a pro-oxidative milieu in the female offspring's cerebellum. Interestingly, these alterations were observed only in the female offspring, suggesting they are more susceptible to effects of maternal naringin supplementation. Therefore, future research should aim to understand the mechanisms underlying the alterations induced by maternal naringin supplementation in the offspring's brain redox homeostasis and how they might modify normal cerebellum development.

Palavras Chave/Key-words: flavonoids, pregnancy, brain, antioxidant.

ID: 3595

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Reproductive Parameters of Adult Female Rats Treated with TOP during Adolescence

Embasamento/Background: The Developmental Origins of Health and Disease suggest that the exposition to certain factors during critical stages of development, such as childhood and puberty, may influence features on adult individuals. Topiramate (TOP) is an antiepileptic drug approved by the Food and Drug Administration (FDA) in 2014 for prophylaxis treatment of migraines during adolescence, one of those critical stages. Female adult Sprague-Dawley rats treated with TOP (100 mg/kg/day) for 28 days displayed a significant reduction in the ovaries mass as well as embryos weight. Whereas the group treated for 84 days showed a decreased pregnancy percentage and implantation sites, as well as an increase in the ovaries mass and reduction of viable fetuses. These results demonstrated that TOP may act as a potential endocrine disruptor (ED) for the female reproductive system, since EDs are exogenous substances or mixtures, such as drugs, that alter the endogenous hormones and cause adverse effects on the organism

Métodos/Methods: Wistar female rats (n=8-9/group) were treated by gavage with TOP (41mg/kg/day) from postnatal day (PND) 28 to PND 50. The control group received water during the same period. To evaluate puberty installation, the vaginal opening was verified daily, from PND 26. Upon observing the vaginal opening, the vaginal smear was performed daily to verify the first estrus. The anogenital distance (AGD) was measured through a Vernier caliper on the day of the vaginal opening and the day of the euthanasia. Subsequently, the AGD was normalized through its division by the cube root of the body weight. From PND 75, vaginal smears were performed daily, always at the same time in the morning, over a period of 15 days. The coefficients of proestrus (CP), estrus (CE), and metaestrus/diestrus (CMD), and estrous cycle duration was calculated by the formula C=a/b 100%, where C is the coefficient of the cycle period, a is the number of days of the corresponding cycle period during the observation, and b is the total duration of the complete cycles (in days). On PND 100, the females were euthanized, and the reproductive organs (uterus and ovaries) were removed, weighed and used to obtain histological slides. The uterus was analyzed through the measurements of the uterine epithelium, endometrial stroma, myometrium, and perimetrium. Whereas the ovary was analyzed through the count of the corpora lutea as well as ovarian follicles at different stages of development. Data were compared by analysis of covariance (ANCOVA), Student´s t test or Mann-Whitney U ($p>0.05$), (CEUA/UEL: 9379.2018.26).

Resultados/Results: The treatment with TOP during adolescence did not alter body weight, AGD, reproductive organs weight, installation of puberty, estrous cycle, as well as uterus and ovaries histology (n=8-9/group), such as number of corpora lutea [CTR: 4.25 (3.30-6.38) ; TOP: 5.67 (5.00-6.00) ], primary [CTR: 23.43 ± 2.26; TOP: 28.42 ± 1.97], grow [CTR: 11.66 ± 0.85; TOP: 14.55 ± 1.27], and antral [CTR: 6.35 ± 0.62; TOP: 7.44 ± 0.93] follicles of adults rats.

Conclusões/Conclusions: The literature suggests that TOP can act as an ED in adult female rats' reproductive system, and that ED's administered during critical development stages can cause alterations in adult individuals. However, in the present study, the treatment with TOP during adolescence did not interfere in the reproductive parameters during adult life.

Palavras Chave/Key-words: Migraine; Toxicity; Teenager; Female

ID: 3597

Área: DOHaD and stress

Forma de Apresentação: Ê-POSTER

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Título/Title: Increased Light Period of the Maternal Circadian Cycle Increases the Number of Uterine Glands in the Adult Female Offspring

Embasamento/Background: The circadian cycle plays numerous roles in the physiological processes of an organism. Maternal melatonin is modulated by the circadian cycle and regulates the fetus rhythm. In addition, this molecule reduces the production of ROS (reactive oxygen species) by increasing the antioxidant enzymes at the embryonic stage. However, the impact of altered circadian cycle during prenatal development remains unclear. This study aimed to evaluate whether circadian cycle changes during pregnancy period may alter the development of the female reproductive system of the offspring in rats.

Métodos/Methods: Female Wistar rats were distributed into light-dark (LD) group, in which pregnant rats were exposed to a normal light-dark photoperiod during gestation (12h/12h), and light-light group (LL), in which pregnant rats were exposed to a photoperiod of constant light during gestation (24h). After birth, pups remained in normal light-dark photoperiod until adulthood. At PND90, uterus and ovaries were collected for morphometric and histological analyses and oxidative stress status assay.

Resultados/Results: Exposure to continuous light during gestation increased the glutathione reductase (GR) and glutathione S-transferase levels (GST) in uterus, while lipid peroxidation (LPO), glutathione peroxidase (GPx) and superoxide dismutase (SOD) did not change in uterus and ovaries. The number of uterine glands were increased in LL females. The ovary morphology was not altered.

Conclusões/Conclusions: The alteration in the maternal circadian cycle was able to increase the number of uterine glands and the antioxidant capacity of female offspring in adult life.

Palavras Chave/Key-words: Circadian cycle, female offspring, gestation, development

ID: 3599

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Maternal Hyperglycemia and Snack Intake Effects on Offspring Glucose Tolerance, Sucrose Preference and Body Weight at Different Life Stages

Embasamento/Background: The effects of maternal diabetes and diet manipulation have been thoroughly studied separately. Previous studies have shown that snack intake during pregnancy and lactation further impair glucose tolerance on hyperglycemic female rats. Nonetheless, there is no evidence of how diet manipulations may aggravate behavioral and metabolic impairments in the offspring of hyperglycemic dams. Since maternal metabolism and nutritional status are key factors for a healthy offspring intrauterine and postnatal development, the aim of the present study was to investigate the impact of mild hyperglycemia associated with snack intake on offspring glucose tolerance and sucrose preference.

Métodos/Methods: Newborn female Wistar rats were divided into Control (citrate buffer, s.c.) or STZ (streptozotocin, 100 mg/kg, s.c.) groups. All experimental procedures were approved by the local ethics committee (Protocol number 919). On postnatal (PND) 90, rats from both groups were mated and subdivided into four groups: females fed with standard chow (Control, n = 22; STZ, n = 23); and females fed with standard chow plus potato chips and 1,5% sucrose solution from pregnancy day 0 to lactation day 14 (Control-snack, n = 23; STZ-

snack, n = 23). Dams gave birth naturally, litters were culled to 8 pups (4 males, 4 females), and an oral glucose tolerance test and a sucrose preference test were performed in male and female offspring on PND 30, 90, and 360. After that, body weight, length, and anogenital distance were measured and animals were euthanized to measure fat pads.

Resultados/Results: Offspring from snack-fed dams, regardless of maternal metabolism, showed lower glycemic levels on PND 30 and 360 during the oral glucose tolerance test. However, in adulthood, maternal hyperglycemia impaired offspring glucose tolerance regardless of snack intake, showing an age-dependent effect. Maternal snack intake also reduced sucrose preference in male and female offspring on PND 90. Maternal metabolism and snack intake had greater short-term effects, seen in male and female offspring on PND 30. However, maternal hyperglycemia and snack intake had opposing outcomes. While the former increased body weight, Lee index, and retroperitoneal fat pad, the latter reduced the same parameters. Additionally, offspring from snack-fed dams had a lower body weight from puberty to senescence, showing there was no catch-up growth.

Conclusões/Conclusions: Despite of aggravating glucose tolerance in hyperglycemic dams, maternal snack intake was not effective to further impair metabolic and biometric parameters in the offspring at different life stages. Overall, snack intake and maternal hyperglycemia had opposing effects that counter-balanced each other. Further studies will analyze if offspring behavior is affected by this impaired maternal metabolism.

Palavras Chave/Key-words: maternal diabetes, snack intake, offspring, sucrose preference

ID: 3601

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Neonatal Overnutrition-Induced Obesity by Litter Reduction Increases Body and Testicular Weight and Decreases Motility of Male Wistar Rats

Embasamento/Background: It is known that nutritional changes during the perinatal period alter metabolic and / or endocrine regulation in childhood until adulthood. According to the World Health Organization, 1 in 5 children and adolescents are considered obese. In an experimental model, it has been observed that neonatal programming through litter exposure to stimuli during early development will result in effects on adult life. The increase in demand for fertility clinics in the last decade has been significant and the etiology of male infertility often remains unclear. Knowing the importance of the postnatal period for the maturation of the male reproductive system, the objective of this study was to evaluate the effects of obesity induced by neonatal overnutrition on testicular and sperm parameters of male Wistar rats.

Métodos/Methods: For this, animals were obtained from the mating of male and female rats from the Central Animal Farm, and on the postnatal day (PND) 3 , the litter size was adjusted to 3 puppies (SL - small litter) or 10 puppies (NL - normal litter) with each mother. After weaning, on PND 21, the males of NL or SL groups were kept in a vivarium until PND 60, when they were weighed and euthanized at 2 pm. The protocol was approved by the Ethics Committee on Animal Use of State University of Londrina (OF CIRC CEUA nº 87/2020). Ten animals from each experimental group had their right and left testicles removed and weighed on a precision analytical balance. From the body weight and testicular weight, testicular weight relative to body weight was calculated. Of the same 10 animals, the vas deferens were collected and washed, and its content was used to the analysis of sperm motility. The data was submitted to the normality Bartlett test and homogeneity Shapiro-Wilk test, then compared using an unpaired t test. Data was considered significantly different when $P<0.05$ and were expressed as numbers ± S.E.M. Statistical analyses were performed using GraphPad InStat (version 3.02).

Resultados/Results: The data showed that obesity induced by neonatal overnutrition (SL) reflected in the increase in body weight (284.5 ± 4.5) and testicular weight (1.46 ± 0.03) in the early adulthood (PND 60) compared to control group (258.6 ± 4.3; 1.36 ± 0.02; respectively). On the other hand, the relative testicular weight was not changed in the obese animals (0.52 ± 0.006) in relation to the control group (0.51 ± 0.009), showing that such testicular weight increase accompanied the rise in body weight. Likewise, the evaluation of sperm motility allowed us to conclude that obesity induced during the perinatal period increased the number of immotile sperm (26.8 ± 2.3) of young adult animals compared to control group (18.82 ± 2.2).

Conclusões/Conclusions: Although more analysis needs to be carried out to guarantee a more concrete conclusion, the present study showed that neonatal overnutrition-induced obesity by litter reduction was sufficient to alter testicular weight and sperm motility in these animals. Thus, it is concluded that overnutrition even during the neonatal period can impair the animal's fertility in the early adulthood in these experimental conditions.

Palavras Chave/Key-words: testis, sperm, postnatal development, Neonatal Overnutrition-Induced Obesity

ID: 3602

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Maternal DHA Supplementation During Pregnancy and Lactation Prevents the Development in Offspring of Glucose intolerance and Hepatic Steatosis Induced by Feeding a High-Calorie Diet.

Embasamento/Background: A large number of observational studies have shown that the consumption of Docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) enriched food or the nutritional supplementation with these n-3 long-chain polyunsaturated fatty acids (n-3 LCPUFAs), have positive health effects ranging from prevention and reversion of the cognitive deficits associated with neurological diseases and ageing to improvement and prevention of the metabolic syndrome. Based on these lines of evidence, maternal LCPUFAs supplementation during pregnancy has become a current clinical practice to improve neurological outcomes in the offspring. This study aimed at determining whether maternal supplementation during pregnancy with a mixture of DHA/EPA prevents in offspring the metabolic complications of obesity and to identify the mechanisms underlying the potential preventive effects.

Métodos/Methods: Pregnant Wistar rats received from the beginning of gestation to the end of lactation an oral daily dose of 350 µl/kg of a fish oil extract, corresponding to 160 mg/kg DHA and 23 mg/kg EPA, or 350 µl/kg of safflower oil as placebo. At birth, litter size was adjusted to eight pups per litter. Pups were weaned at 21 days and split into two sub-groups to be fed standard chow or a free-choice high-fat high-sugar (fc-HFHS) diet. Thus, four experimental groups each one consisting of 8 male animals from 8 different litters were formed: DHA/EPA-STD; DHA/EPA-fc-HFHS; placebo-STD; placebo-fc-HFHS. The anthropometric and metabolic characteristics of offspring were assessed at three months.

Resultados/Results: Compared to animals fed standard chow, rats exposed to the fc-HFHS diet exhibited increased body weight and liver weight along with enhanced body fat and leptin in serum independently of maternal diet. Maternal DHA/EPA supplementation prevented both the glucose intolerance and the rise in serum insulin resulting from consumption of the fc-HFHS diet. In addition, animals from the DHA/EPA-fc-HFHS group showed decreased hepatic triglyceride accumulation compared to placebo-fc-HFHS rats. This latter protective effect was correlated with decreased hepatic expression of genes regulating the lipogenesis, β-oxidation and glycolysis metabolic pathways. DHA/EPA-fc-HFHS animals exhibited also decreased expression of pro-inflammatory genes and, conversely, enhanced hepatic levels of mRNAs coding for anti-inflammatory genes.

Conclusões/Conclusions: Maternal n-3 LCPUFA supplementation protects the offspring against hepatic steatosis and improves glucose intolerance following high-calorie feeding by inhibiting lipogenesis and reducing inflammation.

Palavras Chave/Key-words: Pregnancy, Docosahexaenoic acid (DHA), Obesity, Offspring.

ID: 3603

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Fish Oil Supplementation During Pregnancy Did Not Reprogram Obesity Phenotype Or Food Preference Of Rat Offspring Induced By Maternal High-Fat Diet

Embasamento/Background: Background: Maternal high-fat diet (HF) during the perinatal period induces obesity in the offspring. Obesity is associated with unbalanced energy metabolism and endocannabinoid system (ECS) over activation. ECS consists mainly of the endocannabinoids derived from n-6 fatty acids, cannabinoid receptors (CB1 and CB2) and metabolizing enzymes (FAAH and MAGL). ECS activation in the central nervous system (CNS) is associated with increased homeostatic and hedonic eating, resulting in hyperphagia and higher motivation for palatable foods. We have demonstrated that maternal HF diet during the perinatal period results in early obesity with sex-specific changes in the ECS and leptin signaling in the hypothalamus of the offspring, associated with increased n-6/n-3 ratio. We hypothesized that maternal supplementation with fish oil, an important source of n-3 fatty acids, during pregnancy could reprogram the metabolic changes induced by maternal consumption of HF diet.

Métodos/Methods: All animal procedures were approved by CEUA/CCS/UFRJ (protocol 059/19). Female rats received standard diet (C; 9% fat) or high-fat diet (HF; 28% fat) during 8 weeks before mating. A subgroup of the HF progenitor rats received supplementation with fish oil (HFFO; 3% EPA and DHA) exclusively during gestation. After birth, all progenitors were fed their original diet (C or HF) until weaning (postnatal day 21). Metabolic parameters of male and female offspring were analyzed from birth to adult life and food preference was assessed in adolescence (postnatal day 45) and adulthood (postnatal day 150). *$p<0.05$.

Resultados/Results: Maternal HF diet decreased body weight of the female pups compared to the control group at birth ($p<0.05$), with no changes in male pups. In addition, maternal supplementation with fish oil decreased glycemia in female pups, compared to female HF pups ($p<0.05$). These alterations were not associated with changes in the expression of inflammatory markers (TNF-alpha and IL1b mRNA) in the hypothalamus of the offspring. During lactation, maternal HF diet increased body weight in male and female offspring ($p<0.05$) associated with greater white adipose mass ($p<0.05$) at weaning. Weanling HF offspring showed an increase in plasma glucose compared to C offspring ($p<0.05$), without improvement by maternal supplementation with fish oil. In the food preference tests, HF offspring showed a higher preference for high-fat diet since adolescence (postnatal day 45) until adulthood (postnatal day 150) demonstrating that the maternal HF diet programmed a pattern of food preference. However, the maternal supplementation with fish oil did not alter the offspring's preference for any type of diet offered.

Conclusões/Conclusions: We demonstrated that the maternal HF diet induced overweight, increased adiposity and increased plasma glucose in the offspring after weaning, accompanied by greater food preference for the HF diet from adolescence to adulthood. This preference for HF diet may be related to changes in the SEC in offspring at birth already demonstrated by our group, since the SEC and CB1 signaling in the hypothalamus reinforces a motivation to consume highly palatable foods. Fish oil supplementation did not alter the obesity phenotype observed in offspring programmed by a maternal HF diet. In addition, the maternal HF diet or its supplementation with fish oil did not induce changes in expression of the cytokines at birth, suggesting that in the neonate offspring the inflammatory profile is still controlled.

Palavras Chave/Key-words: High-fat diet; obesity; fish oil; food preference

ID: 3604

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Effect of Leuconostoc Mesenteroides SD23 Intake on Obese Rat Mothers During Pregnancy and Lactation on the Maternal and Offspring Gut Microbiota and Morphological Adaptive Changes of Small Intestinal

Embasamento/Background: Obesity during pregnancy and lactation leads an increased risk of the offspring (F1) developing metabolic disorders in addition to the adverse effects on the mother. A large number of studies have demonstrated that maternal obesity (MO) is associated with alterations in the composition and diversity of the intestine microbial community. Recently researches suggested that probiotics might be a novel approach to counteract these F1 MO effects. The aim of this research was to analyze the impact of Leuconostoc SD23, a probiotic isolated from aguamiel (edible sweet sap obtained from Agave salmiana, a traditional Mexican) by modulating the composition of the gut microbiota in the mothers and their F1, and morphological adaptive changes of small intestinal in the mothers.

Métodos/Methods: From weaning through lactation, female Wistar rats ate chow (C; 5% fat) or high energy obesogenic diet (MO; 25% fat). Half of the C and MO mothers received a daily dose of probiotic orally (1 x 1010 CFU/mL) for one month before mating and through lactation (CP and MOP). Morphological adaptive changes of small intestinal (jejunum), and fatty acid profile were determined in the mother, and change in the gut microbiota was determined in both mothers at the end of lactation and F1 at postnatal day 21.

Resultados/Results: At the end of lactation, small intestinal morphology in mothers was altered in MO, by an increase in villus height, higher crypt depth and low numbers of goblet cells per area compared with C, CP and MOP. These changes are likely to increase intestinal absorption and permeability with subsequent metabolic inflammation; increasing energy harvest from the HFD. Administration of Leuconostoc SD23 is effective in reducing villus height, crypt depth and higher numbers of goblet cells per area in MOP. MO increased the content of total saturated fatty acids (SFA) compared with C, CP and MOP. In the mothers the composition of maternal gut microbiota Firmicutes/Bacteroidetes ratio (F/B), considered as an early biomarker for obesity, was higher in MO than to C, CP and MOP. In F1, the Proteobacteria phylum, considered as early priming of the innate and adaptive immune system, was lower in male and female MO compared to C, CP and MOP. The Verrucomicrobia phylum associated with fat storage, was higher in male MO compared to C and CP, and was not different to MOP. In female MO was higher compared to C, CP and MOP.

Conclusões/Conclusions: MO during pregnancy and lactation is accompanied with gut microbiota dysbiosis with a simultaneous development of metabolic disorders, which could affect microbiota transmission from the mother to F1 and further result in F1 metabolic disturbances. Maternal probiotic intervention improved gut microbiota in both mothers and F1. Financial Support: SEP-CONACyT-2016 (287912), and Newton Fund RCUK-CONACyT (Research Councils UK – Consejo Nacional de Ciencia y Tecnología - I000/726/2016 FONCICYT/49/2016).

Palavras Chave/Key-words: Probiotics; obesity; programming; microbiota

ID: 3605

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: The Effects of Gestational Metformin Treatment on Early Overnutrition-Induced Metabolic Dysfunction in Adult Male Rat Offspring.

Embasamento/Background: Metformin has been used to treat gestational diabetes. Metformin crosses the placenta and has been associated with beneficial effects on glucose offspring tolerance and fat mass accumulation during an obesogenic diet. We have previously studied the long-term effects of metformin exposure during lactation in early over nourished rats. In this model, metformin treatment prevents metabolic dysfunctions in adult rats. Given these favorable changes after early metformin exposure, we aimed to evaluate whether gestational metformin may program offspring to resist adult metabolic dysfunctions development caused by postnatal overfeeding.

Métodos/Methods: Pregnant rats received 300mg/kg/day of metformin (Met) via gavage throughout pregnancy until delivery, while control pregnant rat received a 0.9% saline (Sal) solution in the same volume and period. After birth, male Wistar rats were raised in small litters (SLs, 3pups/dam) and normal litters (NLs, 9 pups/dam) to obtain early overfeeding and normal feeding during lactation. Thus, four offspring groups were formed: NL and SL offspring of Met dams and NL and SL offspring of Sal dams. All offspring groups were weaned at day 21. At 180 days of age, their body composition, food intake, glucose tolerance and lipid profile were assessed.

Resultados/Results: Adult rats over nourished during lactation had increased body weight, adiposity, food intake, glycemia levels, glucose intolerance and altered plasma lipid profile ($P<0.05$) compared with NL rats. Maternal Met treatment had no effect on body weight, adiposity, food intake and plasma lipid profile in adult SL offspring. However, SL-Met rats showed improved glucose tolerance ($P<0.05$) despite similar adiposity when compared with SL-Sal. Unexpectedly, total cholesterol, triglycerides and total VLDL cholesterol were increased in NL-Met offspring despite no effect on body weight and glucose homeostasis compared with NL-Sal ($P<0.05$).

Conclusões/Conclusions: Gestational metformin improves glucose tolerance in adult SL offspring, although Met treatment has not prevented weigh gain, high adiposity and altered lipids profile induced by early overfeeding.

Palavras Chave/Key-words: Metformin, pregnancy, small litter, metabolic programming

ID: 3606

Área: DOHaD and stress

Forma de Apresentação: Ê-POSTER

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Título/Title: Gestational Malnutrition Affects Milk Eating Pattern of the Newborn Rats

Embasamento/Background: In early stages of life development, environmental insults such as maternal undernutrition have been shown as triggering health damage, which affects not only the subjects that underwent such stress, but also their offspring, which subsequently displays it as non-communicable diseases. In this study, we aimed to evaluate the effects of maternal caloric restriction during the last third of gestation on the milk feeding behavior of lactating newborn rats.

Métodos/Methods: Experimental procedures were approved by the Ethics Committee (number: 23108.724433/2017-16). At 75-days-old, female Wistar rats were mated, and after that, conception was detected by vaginal smear observation, in which the presence of spermatozoa determined the beginning of pregnancy. On day 14th of pregnancy, food was reduced by 50% of the amount normally fed, ad libitum, by control rats (FR50 group) until delivery, while the control rats (CONT group) was fed ad libitum. The rats were kept nursing 8 pups per 21 days, when weaning was given. Body weight was assessed at birth and weaning. On days 6th, 11th and 16th of lactation the milk intake by 4 hours fasted rat offspring was measured.

Resultados/Results: The FR50 rats was born smaller than CON rats (birthweight around 9% smaller, $P<0.01$). On the other hand, weaned FR50 rats was heavier than CON rats (body weight around +7% higher, $P<0.01$). Regarding milk consumption, in comparison with CONT group, FR50 rat offspring were hyperphagic during the first half of lactation. At day 6th of age, milk intake by FR50 rats was 44% higher than that in CONT rats ($P<0.05$), which remained on the day 11th of age (71%, $P<0.01$). Interestingly, on the day 16th of age, the milk intake was not different between FR50 and CONT rats ($P>0.05$).

Conclusões/Conclusions: Caloric restriction during the last third of gestation was able on changing the behavior of milk consumption in newborn rats, increasing it during the first two weeks of life, which suggests a risk factor for long-term metabolic syndrome.

Palavras Chave/Key-words: Intrauterine malnutrition, feeding behavior, metabolic programming, hyperphagia.

ID: 3607

Área: DOHaD and aging

Forma de Apresentação: ORAL

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Título/Title: Cardiac Alterations in Obese Mothers' Offspring Could be Associated to Sex-Specific Developmental Programing of Adipose Tissue Distribution

Embasamento/Background: Maternal obesity (MO) predisposes to offspring (F1) cardiovascular disease and increased adipose tissue accumulation in a sex-specific manner. However, the relation of visceral fat distribution to the cardiovascular function in male and female F1 is poorly defined. We aimed to evaluate the association between left ventricular (LV) structure and function with visceral adiposity in male and female F1 from obese mothers.

Métodos/Methods: Female (F0) Wistar rats, were weaned to chow (C) or high fat diet (MO) at 21 days (d) and mated with non-experimental males at 120 d. Males and females F1 from different litter (n=8/group) were weaned to C diet at postnatal day (PND) 21. LV ejection fraction (EF), diastolic (Dd)/systolic diameter (Sd), intraventricular septum (IVS) and posterior wall (PW) thickness were determined by echocardiographic assessment in anesthetized rats at PND 550. Two days later, same animals were euthanized, heart and retroperitoneal fat depot weighed. Serum triglycerides (TG) and Insulin Resistance Index (IRI) were determined. Data were analyzed by Two-Way ANOVA and linear regression. $P<0.05$ was considered significant.

Resultados/Results: F1 body weight was increased in males vs. females, but similar in C and MO groups within males and females. Increased TG, insulin and IRI were observed between MO vs C in males and females. Retroperitoneal fat mass was higher in MO vs. C males but similar in MO and C females. Heart weight was increased in males vs. females and in MO vs C males but similar between C vs. MO females. Echocardiographic assessment showed similar EF, Dd and Sd in all F1 with increased IVS and PW in MO vs C males and females and lower IVS and PW in MO females vs MO males. Retroperitoneal fat mass exhibited moderated correlation vs. heart weight ($R=0.4$, $P=0.03$) and strong correlation vs. IVS ($R=0.6$, $P<0.001$) and vs. PW ($R=0.5$, $P=0.005$).

Conclusões/Conclusions: Maternal obesity lead to sex-specific alterations in the offspring LV structure, which are compatible with the hypertrophic cardiomyopathy. In addition to metabolic alterations in the offspring, such as dislipidemia and insulin resistance, LV structure alterations could be mediated by the visceral adipose tissue distribution. Further studies are needed to elucidate the underlying mechanism regarding cardiac alterations of obese mother´s offspring in relation to visceral adipose tissue.Financial support. Newton RCUK-CONACyT (FONCICYT/49/2016).

Palavras Chave/Key-words: Hypertrophic Cardiomyopathy, Adipose Tissue, Maternal Obesity

ID: 3096

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: A Maternal Diet Enriched In Extra Virgin Olive Oil Does Not Prevent Reduced Uteri Weight and Decidual PPAR Levels in The Offspring of Diabetic Rats. Cintia Romina Gatti*, Sabrina Lorena Roberti*, Dalmiro Gomez Ribot, Romina Higa, Alicia Jawerbaum Centro d

Embasamento/Background: Maternal diabetes increases the risks of maternal, fetal and placental complications and leads to the programming of metabolic and cardiovascular diseases in the offspring. These alterations are in part related to a maternal diabetes-induced prooxidant-proinflammatory intrauterine environment, which may alter the uterus in the female offspring. Our recent studies have shown that a dietary supplementation with extra virgin olive oil (EVOO) is able to reduce markers of the prooxidant-proinflammatory state in the placenta and different fetal organs in experimental models of diabetes and pregnancy. EVOO is highly enriched in oleic acid, a monounsaturated fatty acid that activates Peroxisome Proliferator Activated Receptors (PPARs). PPARs are involved in decidualization and anti-inflammatory processes. The aim of this work was to evaluate the uterus of the offspring of diabetic rats that receive or not an EVOO enriched diet during pregnancy, evaluating the weight of decidualized and not-decidualized uteri at a prepubertal age, as well as addressing PPARs expression in the decidua at a postimplantation stage.

Métodos/Methods: A mild pregestational diabetic rat model was induced in F0 females by neonatal administration of streptozotocin (90 mg/kg sc). Control and diabetic females were mated with healthy males and were fed or not with a 6% olive oil enriched diet from day 1 of pregnancy until parturition. The offspring were fed a standard diet and the uteri of the female offspring (F1) were evaluated a) at a prepuberal stage: 30 day postnatal, with or without induction of decidualization with PMSG (50 UI) and hCG (50 UI) and b) on day 9 of pregnancy. At the prepuberal stage non-decidualized and decidualized uteri were weighted, and on day 9 of pregnancy, the expression of PPARalpha, PPARgamma and PPARdelta was evaluated in the decidua.

Resultados/Results: At a prepubertal stage, the offspring of diabetic rats (Diabetic Group) showed a reduction in weight in the non-decidualized uteri (36%, $p<0.05$ vs. Control Group). This alteration was not prevented by the EVOO enriched diet (27%, $p<0.05$ EVOO-Diabetic Group vs. EVOO-Control Group). The induction of decidualization increased the weight of the uteri of the diabetic rat offspring compared to the non-decidualized Diabetic Group (60%, $p<0.001$). The maternal diet enriched in EVOO did not change the weight of the uteri in the decidualized groups. At the postimplantation stage evaluated (day 9 of pregnancy), there were no changes in the number of implantations and resorptions in the evaluated groups. In the decidua, we found reduced protein expression of PPARalfa, PPARgamma y PPARdelta (60%, 40%, 51% reduction respectively, $p<0.05$ vs. Control). The maternal EVOO diet did not change PPARs expression in the evaluated groups.

Conclusões/Conclusions: Maternal diabetes led to a reduced uteri weight in the prepubertal offspring of female diabetic rats, an alteration that was not prevented by the EVOO enriched diet. The reduction in weight is not observed in the decidualized uteri, suggesting an overstimulation of the decidual process in the diabetic group. During pregnancy, no changes were observed in the number of implantations and resorptions, but the expression of the three PPAR isotypes are reduced, which may affect the decidual function. The EVOO-supplemented diet did not change PPAR levels in the evaluated groups, and further works addressing PPAR target genes are needed to address the putative capacity of EVOO-supplemented diet to activate PPARs despite their reduced levels.

Palavras Chave/Key-words: uteri - decidua - olive oil - PPAR

ID: 3608

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: EFFECT OF THE PRÉ- AND POSTNATAL HIGH-FAT DIET ON THE METABOLISM AND ELECTRICAL ACTIVITY OF THE AUTONOMIC NERVOUS SYSTEM IN ADULT RATS.

Embasamento/Background: Energetic homeostasis is regulated by neuroendocrine hypothalamic pathways, which maintain a synchronism between energy consumption and expenditure. Breaking this synchronism leads to the development of metabolic syndrome (MS), characterized by the presence of obesity, hyperglycemia, hyperinsulinemia, hypertension, dyslipidemia, thus predisposing to heart disease and type 2 diabetes. Studies in rodents using a high-fat diet (HFD), in critical periods of development demonstrate predisposition of offspring to MS. In this context, this research aimed to trace the metabolic profile of offspring adult rats that received HFD during prenatal, lactation, and puberty periods and establish the periods of development with greatest impact on metabolic programming in adulthood.

Métodos/Methods: We analyzed adult male offspring rats submitted to nutritional insult (HFD) in different periods of life: Maternal HFD during pregnancy (PREG/HFD), Maternal HFD during lactation (LAC/HFD) and HFD during puberty period (PUB/HFD). Control groups received normal fat diet throughout the experimental protocols (CTL/NF). Adult rats were killed at postnatal day (PND) 120. Biometric, Biochemical, and Electrophysiological parameters were evaluated.

Resultados/Results: The results showed that adult offspring rats metabolic programmed during lactation and adolescence had a significant increase in adiposity, blood pressure, and dysfunction in sympathetic and parasympathetic autonomic nervous system. However, adult offspring rats submitted to maternal HFD during lactation was more sensitive to the effect of the diet, with hyperphagia, dyslipidemia, hyperglycemia and glucose intolerance. Adult Offspring programmed during pregnancy had no obesity and diabetogenic phenotype.

Conclusões/Conclusions: Our data suggest that lactation and adolescence are more critical than pregnancy to influence neuroendocrine axe to disrupt metabolism late in life.

Palavras Chave/Key-words: Metabolic Syndrome, hypothalamus, metabolic programming.

ID: 3609

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Cardiometabolic Syndrome in Adult Rats Programmed by High-fat Diet During Adolescence

Embasamento/Background: Background: Exposure to high fat diet during gestation and lactation programs cardiometabolic syndrome in adulthood. Adolescence also has been considered a susceptible window of development; however little is known about the high fat exposure during this life period. The present study aims to evaluate whether high fat diet exposure during adolescence induces cardiometabolic syndrome in adulthood.

Métodos/Methods: Methods: The research ethics committee approved the study under CEUA nº 1527130815. Thirty day-old Wistar rats were exposed to a high fat (HF, 35% lard w/w n:24) diet until 60 days of age then fed a normal fat diet (NF, 4.5% w/w of fat n:24) for a further sixty days. Control animals received the NF diet throughout life. Body weight and food consumption were evaluated throughout the protocol. At 120 days of age biometric, metabolic (oGTT and ipITT) histological analysis and cardiovascular parameters were evaluated. Statistical comparisons were performed by Student´s T test.

Resultados/Results: Results: The HF animals showed lower food intake (2526±40,40 vs 2225±18,44 p<0,0001) and higher caloric intake (1446±23,01 vs 1598 ±29,83; p<0,0038) during exposure to HF compared with control group. At 120 days of life, HF animals showed an increase in weight (+ 14%; p <0.002), in fat pads (mesenteric:+ 22%; p <0.03 and retroperitoneal: + 34%; p <0.001), hypertriglyceridemia (+ 34%, p <0.01), hyperglycaemia (+ 14%, p <0.04), reduced insulin sensitivity (-30%, p <0.04) and glucose intolerance compared to control animals. Systolic (SBP), diastolic (DBP) and mean (MBP) blood pressure were increased in HF animals (+ 10%, + 4% and + 17%, respectively; p <0.009, p <0.004 and p <0.01), but heart rate remained unchanged. After intravenous injections of atenolol (4 mg/kg) and methylatropine (3 mg/kg), the bradycardia and tachycardia response, respectively and intrinsic heart rate were similar between groups. The baroreflex sensitivity (ΔHR / ΔMAP) in response to phenylephrine (8 µg / kg, iv) and sodium nitroprusside (50 µg / kg, iv) was similar between groups. The depressor response hexamethonium (30 mg/kg, iv), a ganglionic blocker, greater in the HF group (+26%; p <0,01). In histological analysis in heart showed increased perivascular and interstitial fibrosis (+42%; +%62 respectively; p<0,02 and p<0,0001) and left ventricular hypertrophy (+29%; p<0,0001).

Conclusões/Conclusions: Conclusions: Exposure to HF diet during adolescence programs cardiometabolic syndrome in adulthood, characterized by cardiometabolic changes, hyperactivity of the vascular sympathetic nervous system and cardiac structural changes. To our knowledge, our results are the first to demonstrate the characterization of cardiometabolic syndrome in this type of experimental model. These data further highlight the importance of maintaining sound dietary intake during the adolescent developmental window.

Palavras Chave/Key-words: Key-words: high fat diet; high blood pressure; metabolism; adolescence. Funding: CNPQ and Capes.

ID: 3610

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Exposure To Glycotoxins During Lactation Leads Offspring To Cardiac Hypertrophy And Fibrosis Early In Life.

Embasamento/Background: Lactation constitutes an important phase of development, and disturbances occurred during this period may increase the risk for cardiometabolic diseases later in life. The consumption of Advanced Glycation End products (AGEs) is related to increased oxidative stress, inflammation and higher risk for cardiovascular disease. Methylglyoxal (MG), an AGE precursor, may be involved in the development of diabetic cardiac myopathy. Therefore, we hypothesized that maternal exposure of MG during lactation may predispose the offspring to the development of cardiac remodeling early in life.

Métodos/Methods: Pregnant Wistar rats were maintained in standard conditions until birth. All animals had free access to standard chow and water. Delivery was considered day 0, in day 1 rats litter size were standardized for 8 pups per mother (4 Males and 4 Females) and separated into two groups: Control (CO), whose mothers received saline 0,9% (1mL/kg), and Methylglyoxal (MG), treated with methylglyoxal (60mg/kg). Both groups were treated daily by gavage, starting at day 1 after birth and halt at the end of lactation. At weaning (day 21), offspring from CO and MG groups were weighed and euthanized. Blood and heart samples were collected for lipid profile and histological analysis, respectively.

Resultados/Results: MG pups show reduced bodyweight at weaning and increased heart interstitial fibrosis (p<0,01), which is accompanied by increased cardiomyocyte diameter (p<0,05). No difference is observed in perivascular fibrosis or heart weight. MG animals have decreased triglycerides levels when compared to CO (p<0,05). No difference is observed in total cholesterol or HDL.

Conclusões/Conclusions: Maternal intake of an AGE precursor during lactation, leads neonatal offspring to cardiac remodeling, with increased tissue fibrosis, cardiomyocyte hypertrophy, and increased triglycerides. Therefore, we suggest that these neonatal alterations may be an important predictor, increasing the risk to the development of cardiomyopathy later in life.

Palavras Chave/Key-words: Glycotoxins, Fibrosis, Methylglyoxal, Heart.

ID: 3613

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Early Weaning Models Induce Long-term Effects on the Hypothalamic-Pituitary-Gonadal Axis and Steroid Receptors in Wistar Rats

Embasamento/Background: According to the World Health Organization (WHO), globally, only 40% of infants under six months of age are exclusively breastfed; this information is a concern for public health since literature shows that insults during initial states of early development may cause metabolic alterations throughout life. Our group and other scientists have shown over time how early weaning may cause alterations to offspring. In our experimental models of pharmacological and non-pharmacological early weaning (respectively PEW and NPEW), animals become obese in adult life with a dysfunctional control of glucose, dyslipidemia and hormone deregulation.

However, there are few data regarding how early weaning may affect sex hormones and the hypothalamic-pituitary-gonadal axis in adult life on animals from both sexes. Thus in this study, we intend to investigate the long-term effects of early weaning on the HHG axis and sex steroids receptors in peripheral metabolic tissues of offspring at postnatal day (PND) 180.

Métodos/Methods: Female Wistar rats and their offspring were separated in 3 groups: NPEW, in which lactating mothers were bandaged in order to prevent suckling's access to milk. PEW, in which mother received bromocriptine injections, a dopamine agonist in order to stop milk production, thought prolactin inhibition, in a concentration of 0.5 mg twice a day; both manipulations occurred in the last 3 days before weaning; control, in which there were no intervention on dams in order to restrain offspring suckling, resulting in a standard weaning at PND21. The offspring were analyzed at PND180. Plasma testosterone, progesterone and estradiol levels were evaluated by ELISA. The protein expressions of androgen and estrogen receptors (AR and ER, respectively) were measured on liver, adipose tissue, pituitary and hypothalamus by Western blotting.

Resultados/Results: The results shown here are preliminary. Analysis of the plasma sex hormones of the male offspring showed that, while progesterone and estradiol were unchanged, testosterone was higher on the NPEW group in comparison to control (+92%, $p<0.05$). Female offspring analysis showed no alteration of progesterone nor testosterone; however, estradiol was lower on PEW group compared to control and NPEW (control vs PEW -36%, $p<0.05$; NPEW vs PEW -37%, $p<0.05$). The AR was higher on the liver of the PEW males when compared to control (+34%, $p<0.05$). The ER was lower on the white adipose tissue of the NPEW males, when compared to control (-38%, $p<0.05$).

Conclusões/Conclusions: Both early weaning models programs the plasma sex hormones in adult life in both sexes, although differently. These findings can be due to alterations in the hormone secretion of HHG axis. The results from androgen and estrogen receptors will help to understand the effect of sex hormones on GnRH and gonadotropins as well as on peripheral tissues.

Palavras Chave/Key-words: Early weaning, Hypothalamic-pituitary-gonadal axis, metabolic programming, sexual hormones

ID: 3614

Área: DOHaD and abuse drugs

Forma de Apresentação: Ê-POSTER

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Título/Title: Long-term Effects of Maternal Nicotine Exposure During Breastfeeding on the Hypothalamic-Pituitary-Gonadal Axis and Steroid Receptors in the Rat Progeny

Embasamento/Background: Insults early in life, when organs are developing and differentiating, can lead to the onset of several endocrine-metabolic changes in adulthood. Studies have shown that environmental exposure to endocrine disruptors is associated with changes in the short and/or long term, resulting in metabolic programming. Among these disruptors, it is known that maternal exposure to nicotine during breastfeeding lead to the development of obesity and reproductive disorders in the adult ofsspring. Here, we hypothesized that the offspring from exposed nicotine dams could be long-term programmed for a disturbed hypothalamic-pituitary-gonadal (HPG) axis and steroid receptors, in a tissue-specific and sex-dependent manner.

Métodos/Methods: For this study, lactating dams were separated on 2 groups: nicotine-exposed (NIC) in which dams where implanted with osmotic minipumps that released 6 mg/kg of nicotine daily for 14 days (postnatal day 2 to 16) and control group, in which dams were implanted with osmotic minipumps that released saline for the same period. Offspring were analyzed at 180-day-old. Until now, we evaluated plasma concentrations of luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone, progesterone and estradiol by ELISA. We measured the protein expression of androgen receptor (AR) in the liver by Western blotting.

Resultados/Results: In NIC males, plasma LH and testosterone levels had a reduction of 22% and 31% ($p<0.05$), respectively, with no changes in FSH, progesterone and estradiol. In NIC females, plasma FSH increased by 85% ($p<0.05$) when compared to the control group, but with no changes in LH, testosterone, progesterone and estradiol levels. The AR protein expression is decreased by 37% ($p<0.05$) in the liver from male NIC rats, without differences in female offspring.

Conclusões/Conclusions: Our partial results suggest that exposure to nicotine solely during breastfeeding induces changes in the HPG axis on both sexes. NIC male offspring developed a hypoandrogenism due to a failure of LH levels and the lower AR expression suggest a reduction of testosterone action in the liver of these animals. The results of androgen receptor in other tissues as well as estrogen receptors can give some clues regarding the effect of sex hormones in this programming model.

Palavras Chave/Key-words: Nicotine; Metabolic programming; Sex Hormones; Obesity.

ID: 3616

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: HIGH-FAT DIET INTAKE DURING PUBERTY INDUCES NON-ALCOHOLIC FATTY LIVER DISEASE IN ADULT MALE RATS Beatriz Gonçalves dos Santos1 ו; Rosiane Aparecida Miranda2 ו; Larissa Cristina dos Santos Ribeiro1; Lucas Araújo Ferreira1; Maiara Vanusa Guedes Ribeiro

Embasamento/Background: Purpose: To evaluate whether high-fat diet intake during puberty is able to program obesity and related hepatometabolic dysfunctions.

Métodos/Methods: Methods: All procedures performed in this study were approved by ethics committee approval (CEUA-UEM protocol number 1527130815). Male Wistar rats 30-day-old (PN 30) were randomly assigned into two groups and were fed with: standard chow (NF group) or high-dat diet (HF group) during the 30 days until PN 60. Subsequently, both groups were fed a standard chow from until completing 120-day-old (PN 120), when morphometric and hepatometabolic analyses when performed following euthanasia.

Resultados/Results: Results: At PN 120, HF presented overweight, hyperphagia, increased adiposity, hyperglycaemia, hyperinsulinaemia and hypertriglyceridemia. Plasma glucose levels during intravenous glucose tolerance test (ivGTT) and intraperitoneal insulin tolerance test (ipITT) were also higher in HF, whereas kitt was significantly low, suggesting reductions in insulin sensitivity. HF animals displayed a significant increase in blood glucose levels during the pyruvate tolerance test, indicating increased in gluconeogenesis. Further, HF group shows increase in hepatic lipid inclusion, as revealed by morphometry. PEPCK and FAS protein expression were higher in the livers of the HF animals.

Conclusões/Conclusions: Conclusion: Here we showed for the first time which, HF during puberty causes an obesity phenotype at adult life, leading to glucose dyshomeostasis and non-alcoholic fatty liver disease. The hepatic metabolic dysfunctions found in HF animals may rely in the overexpression of some proteins involved in gluconeogenesis and lipogenesis processes.

Palavras Chave/Key-words: Keywords: High-fat diet, puberty, obesity, NAFLD.

ID: 3617

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Prenatal Androgen Exposure Alters Male Sperm Count, Motility, and Offspring Growth but does not affect Fertility.

Embasamento/Background: Prenatal androgen exposure affects females' reproductive and metabolic parameters, leading to phenotypes that resemble those of Polycystic ovary syndrome (PCOS) in women. PCOS is a multifactorial pathology, and prenatal androgen excess is considered one of the main factors contributing to the syndrome development in females. In the past years, it has been reported that male relatives of PCOS women may show altered metabolic and endocrine parameters. However, few studies had focused on the effects of prenatal androgen exposure on males and the intergenerational effect of androgens. This study aimed to investigate the impact of androgen exposure on males' reproductive parameters and outcomes and the possible paternal contribution to intergenerational effects until neonatal development.

Métodos/Methods: Pregnant females (F0) were treated daily on gestational days 16 to 19 with a dose of 1mg of testosterone. A control group was daily injected with vehicle in the same window of injection. The offspring from androgenized mothers were the prenatally androgenized (PA) group, and those from mothers injected with vehicle were the control group (C). Male offspring (F1) weight was weekly measured from day 7 to adulthood (90 days of life). We performed a glucose tolerance test during adulthood, and after-euthanasia epididymis and testis were weighted. We also analyzed epididymal sperm count and motility analysis, and morphological studies were assessed. Spermatozoa were classified as normal or abnormal. Morphological abnormalities were divided into head defects (considering amorphous head, head with amorphous curvature or curvature absence), and tail defects were analyzed only considering the presence of simple or double tail or the absence of the tail. The fertility rate was evaluated. For this, PA-F1 and C-F1 males were mated with naïve females. A randomly selected group from both treatments was euthanized at 14 days of pregnancy and embryo weight, and embryo crown-rump length was assessed. Another group was left to deliver, and offspring (F2) parameters were analyzed at postnatal day 6 (PND6).

Resultados/Results: No differences were found in the growth curve nor the glucose tolerance test in males from the PA-F1 groups as compared to C-F1. PA-F1 males showed decreased average testis weight and lower sperm motility and count than C-F1 males. No differences were found regarding the percentage of abnormal sperm in PA-F1 animals as compared to C-F1. Moreover, fertility studies revealed no alterations in the mating index, the fecundity and fertility index of PA males if compared to controls. Regarding F2, we found no differences in embryos' weight. However, embryos from PA-F1 fathers showed an increased embryo crown-rump length compared to the offspring of C-F1 fathers. At PND6, F2 offspring from PA-F1 males showed decreased body weight and body length in females and males. No differences in the anogenital distance were found between F2 from PA-F1 males and those from C-F1.

Conclusões/Conclusions: Our results show that prenatal androgen exposure impairs male sperm parameters without affecting fertility rate. Moreover, the offspring of PA-F1 fathers showed an altered growth, with increased length during intrauterine development and a decreased body weight and length at the neonatal stage in both sexes. Financial support: FONCYT-ANPyCT-MINCYT-PICT 632/2016

Palavras Chave/Key-words: androgen excess, reproduction, intergenerational effects.

ID: 3618

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Overfeeding Combined with Poor Maternal Diet During Impair Long-term Metabolism in Male Wistar Rats.

Embasamento/Background: The early life nutritional environment affects the development of metabolism, mainly in the maturation of the central nervous systems (CNS) and endocrine organs; we investigated the effects of maternal low-protein diet combined with postnatal early overfeeding on the male offspring's pancreatic beta-cell function in later life.

Métodos/Methods: Only male rats were used; delivery was considered post-natal-day 0 (PN0). Wistar rats' dams were divided into control (NP) or low-protein diet (LP). LP dams remained on the diet until PN14, after which all animals were supplied with the control diet. At PN2, litters were adjusted to 9 (normal litter - NL) or 3 (postnatal overfeeding - PO) pups, resulting in 4 experimental groups: NP-NL, NP-PO, LP-NL and LP-PO. Litters were weaned on PN21. At PN83, a batch of animals from all experimental groups, the Glucose Decay Constant index (KITT) was calculated from the results of Intraperitoneal Insulin Tolerance Test (ipITT), one week after, the animals underwent surgery for cannula implantation, followed by intravenous glucose tolerance test (ivGTT). At PN90, animals were euthanized and tissues collected.

Resultados/Results: LP-PO animals' present a biometric profile similar to the control (NP-NL) group. In the ivGTT, LP maternal diet elevated the glycemia ($p<0.01$). KITT analysis showed that LP maternal diet animals are more sensible to insulin ($p<0.0001$) and postnatal overfeeding enhances the sensibility to insulin ($p<0.0001$), making the LP-PO group the most affected. All groups demonstrated reductions in pancreatic islet size compared to control group ($p<0.05$).

Conclusões/Conclusions: Presenting a normal weight phenotype, the postnatal overfeed offspring whose mothers received the low-protein diet presented morphological impairment in the endocrine pancreas, accompanied by glucose intolerance and high insulin sensitivity.

Palavras Chave/Key-words: Key-words: lactation; maternal diet; early postnatal overfeeding; metabolism developmental plasticity. Financial Support: CAPES e CNPq.

ID: 3619

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Diabetes-Induced Fetal Programming and Post Weaning Consumption Of High Fat Diet In Rats –Preliminary Results Verônyca Gonçalves Paula1,2, Yuri Karen Sinzato1, Eduardo Kloppel1, Rafaianne Queiroz de Moraes-Souza1,2, José Eduardo Corrente3, Gustavo T

Embasamento/Background: Diabetes mellitus is one of the factors that negatively affect the intrauterine environment during pregnancy, causing changes in development and metabolism. In combination with other factors might compromise dams and fetuses in the short and long-term. Objective: To evaluate the influence of the hyperglycemic intrauterine environment and post-weaning consumption of a high-fat diet on the glycemic and lipid profile of adult rat offspring.

Métodos/Methods: Female rats received citrate buffer (C) or streptozotocin (D) on day 5 post-natal. In adulthood, these rats were mated to obtain female offspring, who were fed a standard diet (SD) or high-fat diet (HFD) from weaning to adulthood (n=7 rats/group): OC/SD and OC/HFD: female offspring of control mothers and received SD or HFD, respectively; OD/SD and OD/HFD: female offspring of diabetic mothers and received SD or HFD, respectively. At adulthood (day 115 of life), the Oral Glucose Tolerance Test (OGTT) was performed. Next, the rats were anesthetized and sacrificed to obtain blood samples for biochemical measurements. P-value must be lower than 0.05 for the conclusion that the difference was statistically significant.

Resultados/Results: The OC/HFD, OD/SD, and OD/HFD groups showed an increase in fasting blood glucose compared to the OC/SD group. The OD/HFD group showed an increase in fasting blood glucose compared to the OD/SD group. At 30 and 60 minutes, all groups had increased blood glucose levels compared to the OC/SD group. The rats OD/HFD group also showed greater blood glucose compared to the OC/HFD group. At 120 min, blood glucose levels in all groups differed significantly from the OC/SD group, being more evident in the OD/HFD group. The OD/SD and OD/HFD groups showed an increase in cholesterol, triglyceride, and very-low-density lipoprotein (VLDL) concentrations and a decrease in AST activity when compared to their respective controls.

Conclusões/Conclusions: Our results showed that both the hyperglycemic intrauterine environment and the HFD consumption were able to promote glucose intolerance in adult offspring. In addition, the offspring of diabetic mothers, regardless of the type of diet, also presented dyslipidemia, confirmed by the hypertriglyceridemia and hypercholesterolemia, contributing to an altered lipid metabolism of these adult offspring. This fact suggests a more exacerbated influence on impaired fetal programming by maternal diabetes. Financial Support: FAPESP (Process number 2016/25207-5), and CNPq Research Fellowship (coordination of Prof. Dr. Débora Cristina Damasceno), and grant of the Ph.D. scholarship by the Coordination for the Improvement of Higher Education Personnel (CAPES).

Palavras Chave/Key-words: fetal programming; diabetes; high-fat diet; dyslipidemia

ID: 3621

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Influence Of Gestational Diabetes On The Production Of Anti-Insulin Antibodies And Cytokines In Colostrum And Saliva.

Embasamento/Background: Maternal hyperglycemia may interfere with the composition and with the concentration of immunological mediators in colostrum. However, there is little evidence on the concentration of antibodies and cytokines in colostrum of mothers who developed gestational diabetes. Thus, our aim was to evaluate the concentration of anti-insulin IgA antibodies and the cytokine concentration in colostrum compared to the saliva of pregnant women who developed gestational diabetes.

Métodos/Methods: . It was a case-control study conducted at the Hospital Materno Infantil of the Federal University of Maranhão. The protocol was registered at Plataforma Brasil and approved by CEP-HUUFMA (No. 3.301.629). The study evaluated 74 women, 37 in the gestational diabetes group and 37 in the non-diabetic group. The colostrum was collected manually, always in the morning, 48 hours after delivery and the saliva collection was performed after 2 hours fasting and oral hygiene with filtered water. Saliva and colostrum were centrifuged (2,000 rpm) and the supernatant used to determine the antibodies and cytokines concentrations by Enzyme-linked immunosorbent assay (ELISA) and Cytometric Beads Array (CBA). The biochemical determination of glucose, cholesterol, triglycerides, urea and amylase concentrations were performed in an automated system. Statistical analysis used the Student's t-test for samples with normal distribution and Mann-Whitney test to compare ordinal or continuous variables without normal distribution.

Resultados/Results: The average age of women with gestational diabetes was 31 years. Among newborns of diabetic mothers, 27% had fetal macrosomia and 30% were hypoglycemic, within the first 24 hours of life. The highest concentrations of glucose, cholesterol, calcium, anti-insulin IgA and IL-10 occurred in colostrum in women with gestational diabetes. This group also showed a reduction in IFN-γ and TGF-β concentrations. The total concentration of triglycerides, total protein, IgA, TNF-α and IL-17 was not different between the two groups. The increase in anti-insulin IgA in colostrum showed a positive correlation with TNF-α. In contrast the increase of anti-insulin antibodies showed a negative correlation with TGF-β. This seems to be the first report concerning the increase of anti-insulin antibodies in colostrum from women with gestational diabetes and their influence on the cytokine concentration.

Conclusões/Conclusions: Considering that anti-insulin antibodies are among the most frequent humoral markers in the loss of self-tolerance, our results indicate that immunological evaluations are important to qualify the milk of women with gestational diabetes, since the repercussion of this increase in the immune system of the babies is not known. Those results opens new perspectives for further studies aiming to follow-up of these women and their children during a longer period.

Palavras Chave/Key-words: Colostrum, Saliva, Anti-insulin, Gestacional diabetes

ID: 3110

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Caloric Restriction During Pregnancy Influences Biochemical, Mitochondrial and Behavioral Aspects in Rat Pups

Embasamento/Background: Alterations in the intrauterine environment lead to consequences that last lifelong and may be related to oxidative stress, mitochondrial function and influence on physical and neuromotor development as well as feeding behavior throughout life. In this context, pregnancy overweight is a growing concern, which may increase the risk of chronic diseases in adult life. Thus, caloric restriction (CR) may exert neuroprotection if well controlled, since undernutrition during pregnancy also leads to complications in the fetus' health. This hypothesis is based on the large evidence on CR benefits for adult animals. Our aim in this work was to assess the effect of 20% CR during pregnancy on redox homeostasis in the hippocampi of pups, as well as on developmental and behavioral evaluation.

Métodos/Methods: In order to evaluate CR effect on the 21 days of pregnancy, we divided dams into two groups: control and CR. CR group received 20% less chow and the micronutrients consumption was equalized between groups via oral gavage. Pups' prefrontal cortex were evaluated on postnatal days (PND) 0, 7, 21, and 60 for hippocampal redox homeostasis parameters, such as oxidants content, antioxidant

enzymes activity and oxidative stress parameters.. During development, a battery of physical and neuromotor milestones were assessed. In order to assess feeding behavior, we evaluated the motivation to seek palatable food on PND21 and 60. This project was approved by the local ethics commission (CEUA-UFRGS) under the number 30044.

Resultados/Results: We observed an increase in oxidants content at birth in CR group, evidenced by dichlorofluorescein (DCFH) content. In this age, all antioxidant enzymes were similar to control group. Mitochondrial mass and membrane potential were decreased. Throughout life, DCFH oxidation returned to control levels, although it was increased on PND60.We observed antioxidant enzymes activation in latter ages: Superoxide dismutase (SOD) was increased on PND7 and 21, catalase (CAT) was increased on PND7, glutathione peroxidase (GPx) and glutaredoxin (Grx) were increased on PND60. On PND60, mitochondrial mass and membrane potential were increased. Of note, even with increased mitochondrial activity, mitochondrial superoxide levels were decreased on PND60. Malondialdehyde (MDA) content was decreased on PND60, as well as the carbonyl levels, indicating decreased oxidative stress. There was no alteration on physical and neuromotor development between groups. For feeding behavior, there was no alteration on PND21, and on PND60, although pups took the same time to reach food and start eating, CR pups ate less palatable food than their control counterparts.

Conclusões/Conclusions: Data presented in this work demonstrated gestational CR benefits for pups. Of note, CR was moderate and micronutrients consumption was equalized. Thus, the only intervention was calorie reduction. Moreover, standard laboratory animals (control group) are sedentary and overfed, sadly a consistent match for a good part of western society. In this context, redox homeostasis was improved, as well as mitochondrial activity and oxidative stress was prevented. Pups had no delay on development and ate less palatable food in adulthood in the feeding behavior test we performed.

Palavras Chave/Key-words: Nutrition, pregnancy, oxidative stress, caloric restriction

ID: 3622

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Implications of Maternal Diabetes and Post-Weaning Consumption of High-Fat Diet in Pregnancy of Offspring: Preliminary Results Larissa Lopes da Cruz1,2, Verônyca Gonçalves Paula1,2, Yuri Karen Sinzato1, Eduardo Kloppel1, Rafaianne Queiroz de Moraes-So

Embasamento/Background: Diabetes mellitus is a common medical condition before and during pregnancy and causes adverse pregnancy outcomes worldwide. The number of diabetic women has increased, and this contributes to abnormal fetal development. Considering the high consumption of high-lipidic diet in the last years, the objective of this study is to evaluate the influence of the hyperglycemic intrauterine environment and post-weaning consumption of a high-fat diet on the glycemic profile and reproductive performance of adult rat offspring.

Métodos/Methods: Female rats received citrate buffer (C) or streptozotocin (a drug to induce diabetes for pancreatic beta-cell - D) on post-natal day 5. In adulthood, these rats were mated to obtain female offspring, who were fed a standard diet (SD) or high-fat diet (HFD) from weaning to adulthood (n=7 rats/group): OC/SD and OC/HFD: female offspring of control mothers and received SD or HFD, respectively; FODM/SD and OD/HFD: female offspring of diabetic mothers and received SD or HFD, respectively. At adulthood (day 115 of life), the Oral Glucose Tolerance Test (OGTT) was performed and female rats were mated with non-diabetic males. On day 21 of pregnancy, the rats were anesthetized and the uterus was removed for counting of the numbers of corpora lutea, implantation sites, resorptions (embryonic deaths), live and dead fetuses. The rates of pre-and post-implantation loss were also calculated. P-value must be lower than 0.05 for the conclusion that the difference was statistically significant.

Resultados/Results: The experimental groups (OC/HFD, OD/SD, OD/HFD) showed increased area under curve (AUC) and high circulating glucose levels (140.30; 152.70 and 164.50 mg/dL/min, respectively) compared with the OC/SD group (110.14 mg/dL/min). Also, OD/HFD group showed an increase in AUC compared with the OC/HFD. After mating, the groups OC/HFD, OD/SD, and OD/HFD presented a lower number of full-term pregnant rats compared with the OC/SD rats. There were no statistical differences in corpora lutea, implantation sites, and resorption (embryo death). The rats OC/HFD, OD/SD, and OD/HFD presented lower gravid uterus weight and higher embryonic losses before implantation compared with OC/SD group, being more pronounced in OD/HFD rats. However, the implanted embryos managed to develop, as verified by the number of live fetuses and embryonic loss percentage after implantation.

Conclusões/Conclusions: Our results show that fetal programming induced by maternal diabetes, associated or not to an inadequate diet, was able to promote glucose intolerance in adult offspring, leading to reproductive damage.

Palavras Chave/Key-words: Fetal programming, hyperlipidic diet, diabetes, reproductive outcomes.

ID: 3623

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Transgenerational Effect Of Hyperglycemia In Daughters And Granddaughters Of Diabetic Rats After Glucose Overload And Its Repercussions In Newborns And Placentas. Franciane Quintanilha Gallego Souza1, Vinícius Soares Barco1, Verônyca Gonçalves Paula1,

Embasamento/Background: Background: Maternal hyperglycemia provides an abundant supply of glucose to the fetus. Adaptations will be induced during fetal development that may have consequences for the metabolism of the offspring in adult life. The mechanisms of this transgenerational effect have been studied in several animal models and can be related to observations in the human offspring of diabetic mothers, however, few studies are evaluating the transgenerational effect in granddaughters of diabetic dams. Objective: To analyze glycemia after glucose overload in adult daughters and granddaughters of rats with diabetes and the repercussions on the growth of their newborns and placentas.

Métodos/Methods: Methods: Mild diabetes was induced in female Sprague Dawley rats by streptozotocin (beta cytotoxic drug) at the neonatal period. The non-diabetic females received the citrate buffer (vehicle). At adulthood, the control and streptozotocin-induced rats were submitted to an oral glucose tolerance test (OGTT) and included as mildly diabetic. Following, the rats were mated to obtain their female offspring (OD), which were maintained up to adult life to perform the OGTT. Next, the rats OD were mated to obtain granddaughters of mildly diabetic rats (GDD), which also were maintained up to adulthood for OGTT similar to other rats on day 115 of life. At full-term pregnancy, the OC, OD, and GDD rats were anesthetized and killed to obtain their newborns and placentas for weighing. The glycemic levels from OGTT in different time-points of OC, OD, and GDD were compared and presented as mean and standard deviation. For comparative analysis of OGTT glycemia, fetuses, and placentas, Tukey´s Multiple Comparison Test was used. For all statistical comparisons, a minimum confidence limit of 95% ($p<0.05$) was considered.

Resultados/Results: Results: At the beginning of OGTT (fasting), rats in the OD group showed an increase in glucose concentrations compared with the control group (OC). After 30 minutes of glucose overload, the OD and GDD groups had an increase in blood glucose, with values higher than 140 mg/dL, characterizing a glucose intolerance status. The OD group continued to show higher glycemic values after 60 and 120 minutes of glucose overload. The OD and GDD rats showed lower fetal weight and percentage of newborns adequate for gestational age (AGA) and a greater percentage of newborns small for gestational age (SGA). Considering the placentas, it was verified a lower placental weight and efficiency in the OD group.

Conclusões/Conclusions: Conclusion: The preliminary results indicate that fetal development in a hyperglycemic intrauterine environment generates a diabetogenic tendency in the other generation of rats, affecting maternal glycemic metabolism in both daughters and granddaughters of diabetic rats. In addition, it promotes impaired fetal growth induced by a decreased placental efficiency and intrauterine growth restriction, contributing to smaller fetuses. Financial Support: FAPESP (Process number 2016/25207-5), and CNPq Research Fellowship (coordination of Prof. Dr. Débora Cristina Damasceno), and grant of the Ph.D. scholarship by the Coordination for the Improvement of Higher Education Personnel (CAPES).

Palavras Chave/Key-words: rats, diabetes, offspring, transgenerational.

ID: 3624

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Effects of Maternal Hyperglycemia on Offspring Hyperglycidic Diet Preference on Infancy

Embasamento/Background: Changes on maternal metabolism can increase offspring susceptibility to develop obesity and associated metabolic disorders. This risk is also related to offspring nutrition in postnatal life. When animals are given access to different kinds of food, feeding behavior is influenced by food choice/preference. Brain circuits involved in central regulation of food intake and preference starts developing in the second half of pregnancy and continues until the first 4 weeks of postnatal life in rats, thus making them vulnerable to alterations in maternal metabolism during pregnancy and lactation. However, the effects of maternal hyperglycemia during pregnancy and lactation on offspring food preference have not been explored yet. Therefore, the present study aimed to evaluate the effects of maternal hyperglycemia on offspring hyperglycidic diet preference on infancy.

Métodos/Methods: In order to achieve this goal, pregnant Sprague-Dawley rats were rendered hyperglycemic by an intraperitoneal administration of 35 mg/kg streptozotocin (STZ) diluted in citrate buffer (0.1M, pH4.5) on pregnancy day 7 (STZ group, n = 5). Control group (n = 9) received only citrate buffer. Around pregnancy day 21 the rats delivered naturally, and the litters were culled to 8 pups (4 male and 4 females). On postnatal day (PND) 30, one male and one female per litter were housed on individual cages and fasted for 12 hours. Food preference was then evaluated by offering two different kinds of powdered diet: standard chow (3825kcal/kg, 63.5% carbohydrates, 22% proteins and 4.5% fat) and a highly palatable hyperglycidic diet (3891.5 kcal/kg, 77.37% carbohydrates, 13.64% proteins and 2.79%

fat), which consisted in standard powdered chow enriched with granulated sugar (sucrose, 38%). fasting animals were given access to both diets in the early dark phase of the cycle, and food intake was assessed 1, 12 and 36 hours later. Food preference was determined as the percentage of consumed hyperglycidic diet in relation to the total amount consumed of both chows (standard chow plus hyperglycidic chow). All experimental procedures were approved by the local ethics committee (protocol number 1134).

Resultados/Results: There was no difference on acute food preference (1h measure) between groups, however at both 12 and 36h offspring from STZ dams presented a higher preference for the hyperglycidic diet.

Conclusões/Conclusions: These results show that maternal hyperglycemia can alter offspring food preference, which can contribute to the susceptibility to obesity and the development of metabolic disorders later in life. Further studies will be developed to better understand food preference for other macronutrients in the offspring of hyperglycemic dams and also evaluate this preference during offspring adulthood. Financial support: Research grant by Fundação de Amparo à Pesquisa do Estado de São Paulo – FAPESP (2019/01306-2).

Palavras Chave/Key-words: Maternal hyperglycemia; offspring; food preference.

ID: 2857

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: BISPHENOL-A EXPOSURE AGGRAVATES WHITE AND BROWN ADIPOCYTE HYPERTROPHY INDUCED BY HIGH-FAT DIET CONSUMPTION IN OVARIECTOMIZED MICE

Embasamento/Background: Bisphenol-A (BPA) is an endocrine disrupter (ED), which has estrogenic, antiestrogenic and anti-androgenic actions. Recently, we demonstrate that BPA exposure in postmenopausal mice aggravates hepatic steatosis, but whether this ED can impair adipose tissue in this period of life in females, needs further investigations. Objective: Herein, we evaluated the effects of BPA exposure on white and brown adiposity in ovariectomized (OVX) female mice fed on a high-fat diet (HFD).

Métodos/Methods: Adult Swiss female mice were OVX and submitted to a normolipidic diet or HFD and drinking water without (OVXCTL and OVXHFD groups respectively) or with 1 µg/mL BPA (OVXCBPA and OVXHBPA groups respectively), for 3 months. The rectal temperature was measured weekly throughout the experimental period, subsequently, the adiposity and the morphology of the retroperitoneal white adipose tissue (rWAT) and of the interscapular brown adipose tissue (iBAT) were performed (CEUA UFRJ Macaé approval: MAC035). Data were analyzed by Shapiro-Wilk and compared using ANOVA or Kruskal-Wallis ($P<0.05$).

Resultados/Results: OVXHFD females displayed increased body weight (BW; 59 ± 3 g), food consumption (6 ± 0.7 Kcal/24h), rWAT (1 ± 0.2mg/g BW), perirenal white fat pad (0.5 ± 0.04mg/g BW), and iBAT weights (0.6 ± 0.04mg/g BW), when compared with OVXCTL (47 ± 2g; 3 ± 0.6 Kcal/24h; 0.5 ± 0.07; 0.2 ± 0.02 and 0.3 ± 0.03mg/g BW, respectively). BPA exposure did not modify these parameters in OVXHBPA (58 ± 2g; 6 ± 0.8 Kcal/24h; 1 ± 0.2; 0.4 ± 0.05 and 0.8 ± 0.2mg/g BW, respectively), when compared to OVXHFD. The rectal temperature of OVXHFD females was slightly greater (37.3 ± 0.04 ºC), through the experimental period, when compared to OVXCTL (36.9 ± 0.05 ºC). BPA exposure did not alter this parameter in OVXHBPA group (37.5 ± 0.05 ºC), in comparison to OVXHFD. Morphological analysis of rWAT revealed adipocyte hypertrophy in OVXHFD females which was evidenced by an increased adipocyte diameter (70 ± 0.4 µm) and a reduction in the number of adipocytes/field analyzed (60±2), when compared to OVXCTL (54 ± 0.4µm and 87 ± 2, respectively). BPA exposure aggravated fat deposition in OVXHBPA, since the rWAT exhibited an increase of 22% in adipocyte diameter (86 ± 2µm) and reduction of 11.6% in the number of adipocytes/field (53 ± 0.9), in comparison to OVXHFD females. OVXCBPA females also increased the adipocyte diameter (60 ± 0.2 µm) and reduced the number of adipocytes/field (70 ± 2) in rWAT, when compared to OVXCTL. Furthermore, OVXHFD females displayed increased adipocyte area (503 ± 12µm2) and number of lipid vacuoles (9 ± 0.1), but a reduction in the number of adipocytes/field (84 ± 3) in iBAT, when compared to OVXCTL (319 ± 4 µm2; 6 ± 0.09 and 119 ± 5, respectively). BPA exposure in OVXHBPA aggravated the hypertrophy of iBAT adipocytes, increasing in 30% the adipocyte area (656 ± 8 µm2), 67% the number of lipid inclusions/adipocyte (10 ± 0.1) and reduced in 16% the number of brown adipocytes/field (70 ± 1), in comparison to OVXHFD.

Conclusões/Conclusions: Exposure to BPA in the postmenopausal worsens the deposition of lipids in rWAT and iBAT associated with the normolipidic diet, but this effect is exacerbated when associated with HFD. These data warn that postmenopausal ED can lead to the onset of chronic diseases predisposed by increased adiposity. Support: CAPES.

Palavras Chave/Key-words: Bisphenol A; HYPERTROPHY; OVARIECTOMY; HIGH-FAT DIET

ID: 3625

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Effects of chronic central leptin infusion on the reproductive tract of male offspring of rats with mild hyperglycemia. Cruz, A. G.; Oliveira, G.P.; Silva, G.V.; Rodrigues, L.P.; Martins, M.G.; Woodside, B.; Kiss, A. C. I.

Embasamento/Background: The intrauterine development of mammals is completely dependent on the flow of maternal nutrients and metabolic alterations, such as diabetes, can modify this balance. Maternal hyperglycemia can compromise several aspects of the offspring, including their metabolism and reproductive function. Offspring from diabetic dams have impaired leptin levels, a hormone related to energetic homeostasis and reproduction regulation. Leptin acts as a metabolic signal carrying information to the central nervous system regarding fat reserves and modulating the reproductive axis. Adequate energy storages are crucial for the maintenance of the reproduction, reinforcing that metabolism and reproduction are connected. However, there are no studies regarding the relationship between leptin and the reproductive function of the male offspring of hyperglycemic rats. Our hypothesis is that chronic leptin infusion will attenuate some of the deleterious effects of maternal hyperglycemia on male offspring reproductive function.

Métodos/Methods: All experimental procedures were approved by the local ethics committee (Protocol number 1134). Sprague-Dawley female rats were mated with control males and on pregnancy day (PD) 7 mild hyperglycemia was obtained through the administration of streptozotocin (STZ) (STZ group (n=6), 35 mg/kg intraperitonially, diluted on citrate buffer 0.1M pH 4,5). Control animals received only citrate buffer (n=6). On 21st day of pregnancy, the rats gave birth naturally and litters were culled to 4 males and 4 females on the post-natal day (PND) 1. Two male offspring from each litter were used and each received a different treatment (saline or leptin), thus the litter was the experimental unit. The following experimental groups were formed: Control-Saline (n=6) and Control-Leptin (n=6), STZ-Saline (n=6), STZ-Leptin (n=6). Around PND 82 a cannula was implanted in the cerebral lateral ventricle, connected by a polyethylene tube to an osmotic pump (Alzet® model 2001) filled with either saline 0,9% or leptin (1 µg of leptin per day at a rate of 1 µl/hour for 7 consecutive days) that was inserted subcutaneously into the dorsal region of the animal. On the PND 89, the rats were killed and the organs of the reproductive tract were collected.

Resultados/Results: Maternal hyperglycemia changed some aspects of the male offspring reproductive tract and offspring from hyperglycemic dams responded differently to the chronic leptin infusion compared to the control group.

Conclusões/Conclusions: Our data showed that maternal hyperglycemia can compromise male offspring reproductive function and those offspring are more sensitive to the central effects of leptin. Experiments are currently being carried out to increase the number of animals on each experimental group. Moreover, other reproductive parameters will be assessed, such as the sexual behavior and sexual preference.

Palavras Chave/Key-words: hyperglycemia, reproduction, leptin, rats

ID: 3370

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Intrauterine and Lactational Exposure to Acetaminophen Did Not Interfere with Aortic Endothelial Function of Male and Female Adult Rats. Jezuino, J. S.1, Silva, D.G.1, Vidigal, C.B1, Moura, K.F.1, Novi, D.R.B.S.1, Moreira, E.G.1, Gerardin, D.C.C.1, Ceravo

Embasamento/Background: Acetaminophen is the analgesic drug most recommended by physicians during all stages of gestation. Although considered safe for the fetus, this drug crosses freely the blood-placental barrier and its metabolites could be secreted by maternal milk. A study performed with pregnant women showed that the use of acetaminophen during pregnancy was associated with an increased risk of preeclampsia, thromboembolism, and gestational hypertension. Moreover, it has been described that male rats treated with acetaminophen presented endothelial dysfunction related with increased oxidative stress. However, the vascular safety for the exposed progeny of mothers treated with acetaminophen during gestation and lactation has not been described. Thus, the objective of this study was to investigate if maternal treatment with acetaminophen could cause vascular dysfunction in male and female adult offspring.

Métodos/Methods: Pregnant Wistar rats were treated by gavage with 350 mg/kg/day of acetaminophen or water from gestational day (DG) 6 to DG 21 (PARG and CTRG) or from DG 6 to lactation day (LD) 21 (PARGL and CTRGL). It was evaluated in male and female offspring (75 days) the aortic reactivity to Phenylephrine (Phe), Acetylcholine (ACh) and Sodium Nitroprusside (SNP) in the presence (E+) or absence (E-) of endothelium. Data were expressed as maximal response (maxR, mean ± SEM) and compared by test t or one-way ANOVA (*$p<0.05$). Research approval by the Animal Research Ethical Committee: CEUA nº 7900.2017.82.

Resultados/Results: In male offspring the maxR to Phe in rings E+ or E-, in both periods of exposure, was similar among groups [E+: PARG 2,15±0.19 (7) vs CTRG 1.87±0.15 (7); E-: PARG 2.98±0.20 (8) vs CTRG 3.49±0.22 (7)], [E+: PARGL 2.11±0.17 (10) vs CTRGL 2.23±0.15 (9); E-: PARGL 3.17±0.16 (10) vs CTRGL 3.50±0.11 (9)]. The maxR (% of relaxation) to ACh was also similar among groups (PARG vs CTRG [87.28±2.41 (8) vs 86.04±2.19 (7)], and PARGL vs CTRGL [91.48±1.63 (9) vs 89.37±1.60 (7)]), as well as the response to SNP (PARG vs CTRG [95.41±0.89 (8) vs 93.52±1.30 (8)] and PARGL vs CTRGL [95.57±0.74 (10) vs 94.35±0.70 (9)]). In female offspring maxR to Phe in rings E+ or E-, in both periods of exposure to acetaminophen was similar among groups [E+: PARG 1.58±0.18 (9) vs CTRG 1.61±0.12 (7); E-: PARG 3.90±0.56 (10) vs CTRG 3.08±0.18 (7)], [E+: PARGL 1.74±0.12 (11) vs CTRGL 1.71±0.15 (11); E-: PARGL 3.27±0.18 (11) vs CTRGL 3.46±0.20 (11)]. The maxR to ACh was similar among groups (PARG vs CTRG [91.50±1.74 (10) vs 90.15±3.70 (7)], and PARGL vs CTRGL [89.32±2.10 (10) vs 89.83±1.52 (12)]), as well as the response to SNP (PARG vs CTRG [94.09±0.81 (9) vs 94.11±2.77 (8)] and PARGL vs CTRGL [93.81±0.83 (11) vs 96.16±0.90 (12)]).

Conclusões/Conclusions: These results demonstrated that intrauterine and lactational exposure to acetaminophen did not interfere with the vascular endothelial function in male and female adult offspring, suggesting that this exposure period and the utilized dose are safe for progeny.

Palavras Chave/Key-words: vascular reactivity; maternal treatment; endothelial dysfunction.

ID: 3626

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Exposure to a highly palatable diet exacerbates maternal glucose intolerance of hyperglycemic rats

Embasamento/Background: The incidence of obesity and diabetes has increased worldwide lately. Although changes in lifestyle have clearly contributed to this increase, there is considerable evidence that maternal nutrition during pregnancy and lactation can contribute to this scenario. On this way, the increased incidence of obesity and diabetes in young women of childbearing age is a concern. Several pregnant women have some kind of metabolic disorder, such as diabetes or obesity. Although evidence suggests that appropriate maternal nutrition during pregnancy is a key factor in the current and future health of the young, pregnant women, even obese ones or those with metabolic disorders such as diabetes, tend to exceed the recommended caloric intake and the consequences to the mother herself and her offspring need to be thoroughly investigated. Experimental studies have systematically explored the effects of maternal diabetes and nutrition separately. Nonetheless, there is currently no evidence of the effects of their association. In the present study, our goal was to evaluate the effects of maternal mild hyperglycemia associated with inappropriate nutrition during pregnancy and lactation on maternal glucose tolerance and offspring growth. Our hypothesis is that inappropriate nutrition will aggravate maternal diabetes during pregnancy, which will compromise offspring growth in a greater degree than seen previously for models of maternal diabetes or high-fat diet alone.

Métodos/Methods: In order to test this hypothesis, female Sprague-Dawley rats were mated and assigned on pregnancy day (PD) 0 either to standard chow (n=16) or standard chow plus snacks (n=16) (potato chips and 1,5% sucrose solution) from PD 0 to lactation day (LD) 14. Maternal food intake and body weight were daily measured. Mild hyperglycemia was induced through the administration of streptozotocin (STZ, 35 mg/kg, i.p. diluted on citrate buffer 0.1M ph 4,5) on PD 7. Experimental groups were formed as follows: Control (normoglycemic and standard chow, n=8), Control-snack (normoglycemic and standard chow + snacks, n=8), STZ (hyperglycemic and standard chow, n=8), and STZ-snack (hyperglycemic and standard chow + snacks, n=8). An oral glucose tolerance test (OGTT) was performed on PD 15. Dams gave birth naturally and litters were culled to 8 pups (4 males, 4 females) on postnatal day (PND) 1. Litter weight gain was followed daily from PND 1 to 14. All experimental procedures were approved by the local ethics committee (Protocol number 1134).

Resultados/Results: The experimental model of STZ administration was effective to induce glucose intolerance during pregnancy and snack consumption exacerbated this effect. Nonetheless, this association did not change litter weight gain.

Conclusões/Conclusions: In conclusion, exposure to a highly palatable diet exacerbated maternal glucose intolerance. However, litter weight gain was not further impaired. Additional studies will be developed employing the current experimental model to evaluate the effects on several offspring behavioral and metabolic parameters.

Palavras Chave/Key-words: maternal hyperglycemia, diet, offspring, rat

ID: 3627

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Development of fetuses from rats with diabetes-induced fetal programming and post-weaning consumption of high-fat diet: Preliminary results

Embasamento/Background: Background: Diabetes during pregnancy causes to maternal-fetal complications. The number of diabetic women has increased, and this contributes to abnormal fetal development. In addition, inadequate eating habits are the major factors for the development and progression of metabolic disorders. Objective: To evaluate the development of fetuses from rats with the hyperglycemic intrauterine environment and post-weaning consumption of a high-fat diet.

Métodos/Methods: Methodology: Female rats received citrate buffer (C) or streptozotocin (D) on day 5 post-natal. In adulthood, these rats were mated to obtain female offspring, who were fed a standard diet (SD) or high-fat diet (HFD) from weaning to adulthood (n=7 rats/group): OC/SD and OC/HFD: female offspring of control mothers and received SD or HFD, respectively; OD/SD and OD/HFD: female offspring of diabetic mothers and received SD or HFD, respectively. At adulthood (day 115 of life), the Oral Glucose Tolerance Test (OGTT) was performed and female rats were mated with non-diabetic males. On day 21 of pregnancy, the rats were anesthetized and the fetuses and placentas were removed for weighed. The placental efficiency was measured (fetus weight/placental weigh). P-value must be lower than 0.05 for the conclusion that the difference was statistically significant.

Resultados/Results: Results: All the experimental groups (OC/HFD, OD/SD, OD/HFD) presented increased area under the curve (AUC) compared to the OC/SD group at the 115 of life. Also, after pregnancy, these groups showed decreased fetal weight and placental efficiency and an increased percentage of fetuses classified with small and adequate for gestational age in relation to the OC/SD group. The OD/HFD group showed a more exacerbated decrease in fetal and placental weight, and an increase in placental efficiency compared with the OD/SD group.

Conclusões/Conclusions: Conclusion: Our preliminary results show that fetal programming induced by maternal diabetes, associated or not to an inadequate diet, was able to promote glucose intolerance in adult offspring, leading to impaired fetal and placental development.

Palavras Chave/Key-words: fetal programming; diabetes; high-fat diet; fetal development.

ID: 3628

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Effects of leptin central infusion on food intake of offspring of rats with mild hyperglycemia

Embasamento/Background: Maternal diabetes is a metabolic disorder that confronts the fetus with an abundant supply of glucose, inducing adaptations that increase the susceptibility of offspring to developing diabetes and obesity in adulthood. Postnatal feeding behavior can also contribute to the development of several metabolic disorders. Studies have shown that the exposure to an unbalanced intrauterine environment, due to maternal diet or metabolic, manipulations during pregnancy and lactation, can lead to changes in the offspring pathways that regulate food intake. Food intake is regulated by a complex system that includes peripheral and central factors. One of the hormones that plays an important role is leptin, a hormone secreted by adipose tissue and an important signal that acts on the hypothalamus regulating the homeostasis of energy balance. Although several studies have shown the impact of maternal diabetes on a number of offspring parameters, the effects on the central food intake control have not yet been fully elucidated. Thus, the aim of the present study was to evaluate the effect of chronic central infusion of leptin on food intake of offspring of rats with mild hyperglycemia.

Métodos/Methods: Sprague-Dawley rats were used. Female rats were mated with control males and on pregnancy day (PD) 7 mild hyperglycemia was obtained through the administration of streptozotocin (STZ group (n=6), 35 mg/kg i.p. diluted on citrate buffer 0.1M ph 4.5). Control animals received only citrate buffer (n=6). On the 21st day of pregnancy, rats gave birth naturally and litters were culled to 4 males and 4 females on the post-natal day (PND) 1. On PND 75 two male offspring from each litter were used and each received a different treatment (saline or leptin). Thus the experimental groups were formed according to the presence or absence of maternal hyperglycemia and treatment with saline or leptin, as follows: Control saline (n=6), Control leptin (n=6), STZ saline (n=6), STZ leptin (n=6). On PND 82 animals underwent surgery for implantation of a cannula in the cerebral lateral ventricle (Alzet® model 2001) which released saline 0,9% or leptin (1 µg of leptin per day at a rate of 1 µl/hour for 7 consecutive days). Body weight and food intake were daily monitored for 7 days before and 7 days after surgery. On PND 89, rats were killed and cannula placement was evaluated. All experimental procedures were approved by the local ethics committee (Protocol number 1134).

Resultados/Results: The chronic central leptin infusion was able to decrease the food intake in offspring from both experimental groups. However, this effect was more pronounced on offspring of STZ dams.

Conclusões/Conclusions: Our data show that offspring from mild hyperglycemic dams present differences on food intake control and are more sensitive to the central effects of leptin. More studies will be carried out to unravel the pathways involved on those changes.

Palavras Chave/Key-words: rats, leptin, food intake, hyperglycemia

ID: 3117

Área: DOHaD and aging

Forma de Apresentação: ORAL

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Título/Title: Maternal Obesity Programs Systemic Metabolic State and Adiposity Degree of the Offspring Impacting on Age-related Skeletal Muscle Decline in a Sexually Dimorphic Manner

Embasamento/Background: Skeletal muscle weakness and atrophy are consequences of aging that may be negatively programmed in offspring by maternal obesity (MO). To determine if maternal obesity alters the progress of offspring age-related decline in muscle strength and metabolic dysfunction, we studied first generation offspring (F1) of a high fat diet-induced maternal obesity rat model to evaluate adiposity, muscle strength and systemic metabolic state at early and late life stages.

Métodos/Methods: We studied male and female F1 exposed to maternal high fat diet (MOF1) or control maternal diet (CF1) in young (postnatal day, ~ p220) and aged (~ p615 ) adults (n = 5 to 8/ group) to evaluate muscle force (forelimb grip strength: FGS and forelimb grip

strength body weight (BW) adjusted: FGS adj), adiposity degree (BW, body fat: BF, and adiposity index: AI), and metabolic parameters (triacyl glycerides: TAG, cholesterol: Chol, glucose: Gluc, insulin: Ins, and homeostasis model assessment of insulin resistance: HOMA-IR). Analysis was by unpaired t-tests, quadratic least square regression models, and combinatorial data analyses (CD).

Resultados/Results: Bivariate analysis of male and female F1 by group and age identified BW, FGS, BF, AI, TAG, Ins, and HOMA-IR as outcomes with differences between male MOF1 and CF1 young adult groups ($p < 0.05$). No differences in groups of aged males were found. BW, FGS, FGS adj, BF, AI, Col, and Ins differed between female young adult MOF1 and CF1. In aged females, BW, FGS adj, BF, AI, and TAG were different between MOF1 and CF1 groups. FGS adj and BF were correlated ($R2 = 0.721$, $RA2 = 0.619$, $p = 0.003$) such as FGS adj and AI ($R2 = 0.706$, $RA2 = 0.597$, $p < 0.001$) in female MOF1 and CF1 at both ages. In male MOF1 and CF1 also at both ages, a correlation was observed between FGS adj and BF ($R2 = 0.514$, $RA2 = 0.325$, $p = 0.041$). Discriminant analyses of male and female F1 per group and age identified BW, FGS, Col, Gluc, Ins, and HOMA-IR as variables with maximized mean differences ($\Lambda = 0.017$, $p < 0.001$) in male F1, such as BW, FGS, BF, AI, and TAG were the variables with maximized mean differences ($\Lambda = 0.006$, $p < 0.001$) in female F1.

Conclusões/Conclusions: From early life, MO programs F1 obesity-related systemic metabolic imbalances and increased adiposity phenotypes in a sexually dimorphic manner. In male F1, the main changes were in obesity-related phenotypes associated with metabolic disparities of glucose and cholesterol, while the greater degree of adiposity was strongly correlated with decreased skeletal muscle force in female F1. Further studies are needed to identify underlying mechanisms related to muscle fiber composition and inter- and intramuscular fat deposition to elucidate biological and endocrine mechanisms involved.

Palavras Chave/Key-words: maternal obesity, obesity-related phenotype, aging, offspring

ID: 3629

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Effects of Gestational Protein Restriction on Hypothalamus Pituitary Adrenal Axis of Adult Male Rats Offspring

Embasamento/Background: Appropriate conditions during pregnancy are crucial to adult health. Low-birth weight is closely associated with environment insults during gestation and has been extensively related to the development of cardiovascular diseases and psychiatry disorders, such as anxiety and stress. The hypothalamus-pituitary-adrenal (HPA) axis is the central mechanism for stress response, and studies have shown that adversities during gestation could modulate the axis. In our model, gestational protein restriction promotes an increased plasmatic level of corticosterone and catecholamines in male offspring. These hormonal changes may influence the establishment of high blood pressure phenotype also presented in this programmed model. Adrenal and pituitary glands are vital components of the HPA axis. Studies have demonstrated the sympathetic nervous system's involvement in controlled integration and modulation of the stress response. Moreover, maternal behavior in rats during early life could also influence HPA axis activity, leading to stress-related phenotype. The current study aimed to evaluate early life maternal behavior and the morphological and functional parameters of the adrenal and pituitary gland in gestational protein-restricted male offspring, trying to elucidate HPA axis changes and catecholaminergic dysfunction previously described in this model.

Métodos/Methods: Wistar rats were matched, and sperm in the vaginal smear confirmed pregnancy. Dams were submitted standard protein (NP group; 17% of protein) or low-protein chow (LP group; 6% of protein) throughout gestation. On the day of delivery, the dams were weighted, and anogenital distance was measured. The litter was reduced to 8 dams, prioritizing males and diet returns to rodent standard chow. On the day of birth until weaning, maternal behavior parameters were evaluated and scored. 16-wk old male offspring were euthanased, and the adrenal and pituitary gland was collected to western blot and immunohistochemistry analysis.

Resultados/Results: The LP offspring showed low birth weight compared with NP, but this difference is absent at weaning, and no difference in maternal behavior between groups was found. Glucocorticoid and mineralocorticoid receptors, which are pivotal for glucocorticoid action, increase in the pituitary, adrenal gland of 16wk-old LP offspring, and a 98.8% increase CRH receptor and 63,3% of ACTH immunostaining content in LP pituitary were found, compared with NP offspring. Adrenal morphological analysis showed a 39.67% increased NeuN (marker for chromaffin cells) adrenal medulla and, glomerulosa, fasciculate, and reticular layers staining accompanied by a 168.77% increase of PCNA reactivity in LP offspring. Furthermore, the study found increased 5HT1A receptor (48,69%) in the adrenal gland, which is associated with inhibitory catecholamines secretion; and increase of immunostaining content of 5HT1A and 5HT2A receptors within pituitary lobes, which could modulate HPA axis activation at the pituitary level via serotoninergic innervation of hypothalamic CRH neurons.

Conclusões/Conclusions: Protein restriction in utero results in adult offspring, morphological and functional changes in the adrenal glands, and hormonal modulation associated with increased stress response and adrenergic hyperactivity, possibly participating in the genesis and maintenance of high blood pressure in this programmed model.

Palavras Chave/Key-words: low-protein diet; HPA axis; catecholamines, stress response

ID: 3630

Área: DOHaD and stress

Forma de Apresentação: Ê-POSTER

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Título/Title: Sleep Restriction During Peripuberty Does Not Influences on Prostate Inflammatory Profile in Rats

Embasamento/Background: During puberty, a complex process of sexual development occurs. Sleep plays a critical role in immune system maintenance and influences cytokines under normal and pathological conditions. In the male reproductive system, cytokines are produced by somatic and spermatogenic cells under physiological stimuli and influence physiological process. The aim of the present study was to evaluate whether sleep restriction (SR) during the peripubertal phase could influence the inflammatory profile in prostate tissue.

Métodos/Methods: OF. CIRC. CEUA/UEL nº 046/2014. Male Wistar rats at peripubertal phase (post-natal day, PND40) were randomly distributed into 2 groups (6 animals/group), and subjected to an experimental period between PND 40 and 61. Animals from the control group (C) were maintained in polypropylene cages with laboratory grade pine shavings as bedding throughout the experiment. Rats in the SR group were exposed to SR by the modified multiple-platform method. These rats were placed inside a water tank for 18 h (beginning at 16:00) containing 20 circular platforms (each 6.5 cm in diameter) with the water level within 3 cm of the upper surface. When they reached the paradoxical sleep phase, muscular atonia caused them to fall into the water and awake. On day 22 of the experiment (PND 62), the animals were anesthetized with a combination of ketamine and xylazine and euthanized by cardiac puncture. Prostate was collected and used for measure interleukin-6 (IL-6) levels, N-acetyl-β-D-glucosaminide (NAG) and Myeloperoxidase (MPO) activity.

Resultados/Results: There was no alteration on IL-6 levels, NAG and MPO activity in the prostate of rats submitted to SR during peripuberty when compared to Control group.

Conclusões/Conclusions: At this experimental condition, SR during peripuberty did not influences de inflammatory profile in the prostate of male rats.

Palavras Chave/Key-words: Sleep loss, puberty, prostate, development  Financial Support: CAPES - PROEX - AUXILIO 690/2018 PATOLOGIA EXPERIMENTAL

ID: 3631

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal High-Fat Diet Promotes Alterations in Glycolytic Skeletal Muscle Metabolism of Male Offspring and Affect Their Response to Fructose-Drinking Challenge in Adult Life

Embasamento/Background: Maternal nutritional stress at certain stages of growth and development can alter the structure and function of skeletal muscle throughout life of future generations. Skeletal muscle is an extremely plastic tissue and is susceptible to stress; thus, in this study, we investigated if perinatal maternal high-fat diet would influence skeletal muscle lipid metabolism and its mitochondrial ultrastructure of male adult offspring and disturb their response to a challenge with fructose intake at adulthood.

Métodos/Methods: Female Wistar rats were fed a standard diet (mSTD: 9% fat) or isocaloric high-fat diet (mHFD: 29% fat) 8 weeks prior to mating, during pregnancy and lactation. After weaning, male offspring received a standard diet and, from 120 to 150 days of age, half of the animals from each group received 15% of fructose-drinking water (mSTD-F and mHFD-F). At 150th day, we collected the glycolytic extensor digitorum longus (EDL) muscle for molecular characterization and mitochondrial ultrastructure analysis by transmission electron microscopy.

Resultados/Results: mHFD male offspring were overweight ($p<0.05$), presented higher visceral adiposity ($p=0.009$), and hyperleptinemia ($p=0.02$). Furthermore, fructose-receiving offspring exhibited hyperleptinemia ($p=0.02$) and hypertriglyceridemia ($p<0.0001$). Despite that, in EDL muscle, fructose intake decreased muscle mRNA expression of lipoprotein Lpl, only in mHFD (-29.2%, $p=0.02$) vs mHFD water. Conversely, we observed a suggestive increase in muscle fatty acid uptake since both mHFD ($p=0.03$) and fructose ($p=0.01$) increased the protein expression of FABP4 transporter, mostly in mHFD-F (+2.3x, $p=0.02$, vs mHFD water). In addition, fructose increased the Slc27a1 (FATP1) transporter mRNA only in mSTD offspring (+1.3x, $p=0.04$, vs mSTD water). Regarding muscle lipogenesis markers, fructose decreased mRNA expression of Scd ($p=0.01$), irrespective of maternal diet, while mHFD increased protein content of FAS ($p=0.02$). However, mHFD augmented mRNA levels of the lipid oxidation transcription factor Ppard, which could contribute to the non-alteration of muscle triglyceride content observed. Concerning muscle mitochondrial respiratory chain genes, mHFD reduced mRNA expression of Sdhb (complex II) ($p=0.03$), markedly in mHFD-F, whereas it increased Atp5f1b (ATP synthase) mRNA ($p=0.02$). Finally, fructose increased mRNA expression of mitochondrial transcription factor Tfam, a key regulator of the mitochondrial genome transcription. These data suggest enhanced ATP synthesis by mHFD and mitochondrial biogenesis by fructose, and could be compensatory mechanisms for the reduced number of total mitochondria and the increase of injured mitochondria content, besides increased mitochondrial area, mainly in mHFD-F (-27.5%, $p=0.01$; +1.5x, $p=0.0001$; +1.8x, $p=0.03$, respectively, vs mSTD-F).

Conclusões/Conclusions: We conclude that mHFD programmed the glycolytic skeletal muscle EDL of male adult offspring to respond to fructose by altering the lipid metabolism pathways, which may serve as adaptative mechanisms to avoid triglycerides accumulation in the muscle. On the other hand, marked mitochondrial ultrastructural changes of mHFD were exacerbated by fructose intake, and were accompanied by changes in mitochondrial-related genes expression that would suggest mitochondrial respiratory chain dysfunction.

Palavras Chave/Key-words: maternal high-fat diet, fructose intake, skeletal muscle

ID: 3121

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Evaluation of Reproductive Behaviors of Female Rats Exposed to Sulfasalazine in utero and during Lactation. Simone Forcato Ferreira1; Ana Beatriz de Oliveira Aquino1; Karina Nicole Sobota1; Ana Carolina Inhasz Kiss2; Daniela Cristina Ceccatto Gerardin1. 1

Embasamento/Background: According to the Developmental Origins of Health and Disease (DOHaD), maternal exposure to drugs might affect the morphological and functional development of organs, increasing the risk of disease development at adulthood. Sulfasalazine (SAS) is a drug commonly prescribed as the first line for the treatment of inflammatory rheumatic and bowel diseases, such as ulcerative colitis and Crohn's disease. Although SAS crosses the placenta and can be present in the fetal circulation in therapeutic concentrations, this drug has been considered safe, including during the first gestational due to not be teratogenic. It is known that SAS inhibits the cystine/glutamate antiporter system Xc and alters the motivation of rodents in behavioral experiments. Therefore, it could also interfere in the motivation of other behavior tests such as maternal behavior. In this way, the present study aimed to evaluate the reproductive behavior (sexual and maternal behavior) of female offspring exposed to SAS during the early stages of the development of rats.

Métodos/Methods: Wistar female rats were treated (n=10) with SAS 300mg/kg/day. Control dams (n=10) received carboxymethylcellulose (CMC, vehicle). During the gestational period, dams received supplementation with folic acid (FA) 3mg/kg/day, (2h before of the treatment with SAS), since SAS inhibits folate uptake. Both groups were treated from gestational day (GD) 0 until the lactational day (LD) 21, by gavage. From postnatal day 90, the female pups (n=10/group) were evaluated for sexual behavior. The test lasted until ten mounts had been observed. The females were evaluated such as frequency of each lordosis magnitude, on a scale of 0–3, which 0 means absence of lordosis and 3 maximum lordosis. Moreover, were calculated the lordosis quotient (LQ=[number of lordosis / total mounts]×100) and the mean lordosis score (LS=total number of lordosis points/total number of lordosis responses). The maternal behavior of these rats was evaluated on LD 5. The mother-pup interaction was recorded for 30 min. In this test, were evaluated the following parameters: the latency to retrieve the first pup for the nest; the total number of retrieving, and of contact pup; time spent on nest building; on pup licking/grooming, nursing, and on self-grooming. Results were considered statistically significant if $p \leq 0.05$ and compared by Analysis of ANOVA, Kruskal-Wallis, Student t-test, or Mann-Whitney U (CEUA/UEL: 125.2018).

Resultados/Results: In sexual behavior evaluation, the Student t-test showed that maternal exposure to SAS induced a significant increase in the lordosis score (CTR: 2.02 ± 0.08; SAS: 2.30 ± 0.11*, n=10/group) and in magnitude 3 of lordosis (Mann-Whitney U, p=0.03). The parameters of the maternal behavior of female offspring were similar between groups.

Conclusões/Conclusions: These results show that exposure to SAS during early development induced significant alterations in the sexual behavior of female offspring in adulthood. In rats, maternal care during the early stages of a pup's life plays an important role in the development and/or reproductive behavior of offspring in adulthood. Thus, the results observed might be related to the alterations in the maternal behavior of dams induced by SAS (data not shown). Financial Support: CAPES (Doctoral fellowship to SFF), and Araucaria Foundation (scientific initiation fellowship to ABOA).

Palavras Chave/Key-words: maternal exposure, system Xc, sexual behavior, maternal behavior.

ID: 3634

Área: DOHaD and abuse drugs

Forma de Apresentação: Ê-POSTER

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Título/Title: Characterization of Central and Peripheral Endocannabinoid System in Adult Rat Offspring Programmed by Maternal Nicotine Exposure During Lactation

Embasamento/Background: Nicotine exposure during lactation compromises the offspring phenotype at a long-term in both sexes: male offspring show obesity, hyperleptinemia, hypercorticosteronemia and normophagia while female offspring show normal body weight, leptinemia and corticosteronemia but hyperphagia. Endocannabinoid system (ECS) is involved in some important processes in central nervous system (CNS) and in peripheral metabolic organs that could be affected by nicotine exposure. We hypothesized that the offspring exposed to nicotine during breastfeeding was imprinted for a deregulated central and peripheral ECS later in life, which could be affecting several aspects of their metabolism.

Métodos/Methods: Lactating Wistar rats were implanted with osmotic minipumps releasing nicotine (NIC, 6 mg/Kg/day) or 0.9% saline (control) from postnatal day (PN) 2 to 16. Male and female offspring were analysed at PN180. We evaluated protein expression of N-acylphosphatidylethanolamide-phospholipase D (NAPE-PLD), diacylglycerol lipase (DAGL), cannabinoid receptors type 1 and 2 (CB1 and CB2), fatty acid amide hydrolase (FAAH), monoacylglycerol lipase (MAGL) in lateral hypothalamus (LH), paraventricular nucleus of the hypothalamus (PVN), liver and visceral adipose tissue (VAT).

Resultados/Results: In LH, both NIC male and female offspring did not show any changes in markers of ECS. In PVN, NIC males increased NAPE-PLD and FAAH protein expression (+40% and +34%, $p<0.05$, respectively), without differences in NIC females. On the periphery, ECS showed some alterations: NIC males had lower NAPE-PLD protein expression in the liver (-37%, $p<0.05$) and CB1 in the VAT (-35%,

p<0.05). In contrast, NIC females had lower CB1 protein expression in the liver (-40%, p<0.05) and higher DAGL protein expression in the VAT (2-fold, p<0.05).

Conclusões/Conclusions: Our results suggest that the endocannabinoids biosynthesis is higher in CNS of NIC male offspring, as we detected increased NAPE-PLD and FAAH protein expression, enzymes responsible for anandamide synthesis and inactivation, respectively. On the other hand, peripherally, NIC males seem to be less responsive to ECS. Regarding the females, despite they did not show changes of ECS in CNS, they diverge on peripheral tissues, suggesting lower action in the liver and higher action in the VAT. Thus, the changes in ECS markers are sex- and tissue-dependent and could explain, at least in part, the phenotype of the offspring in this programming model.

Palavras Chave/Key-words: Nicotine; Lactation; Endocannabinoid System; Metabolic Programming.

ID: 3635

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Effects of Consumption of Olive Oil During Gestation and Lactation About Emotional Behavior and Energy Metabolism of Adult Offspring Submitted to Maternal Separation

Embasamento/Background: Maternal nutrition during pregnancy is a relevant factor for the intrauterine environment because can have a direct impact on fetal development. Depending on the type of nutrient ingested by mother there may be a metabolic program that can mitigate the effects of stress early in life. Maternal separation (MS) is an animal model of early life stress which consists of the rupture of the mother-pup bond. This intervention can change emotional behavior in adulthood in a sex-specific way. In addition, MS can induce changes in the dorsal hippocampus (DH) that seem to be closely correlated with the development of depression. Mitochondrial dysfunction seems to act as a key factor in the pathophysiology of depression. Olive oil (OO) may be a strategy for preventing depression because containing nutrients that act on the modification of biomolecules involved with energy metabolism. This study aims to investigate the possibility that a diet with OO during pregnancy/lactation affect the emotional behavior and energy metabolism in the DH of the offspring in the adulthood submitted to MS.

Métodos/Methods: Female Wistar rats on the first gestational day were allocated into 2 groups according to the diet: mothers fed standard chow + soybean oil (SO) or mothers fed standard chow + OO. On the day of the offspring's birth the groups were subdivided according to MS protocol into: Intact SO; Intact OO; Separate SO and Separate OO. MS occurred from the postnatal day 1 to 10, for 3 hours/day. After weaning, the pups were divided into males and females according to the groups and received standard chow until adulthood. The caloric consumption and body weight were analyzed in this period. From 60 days of age the animals were submitted to the open field test, forced swimming test, and euthanized. The DH was collected for biochemical analyzes.

Resultados/Results: Anova of repeated measures or three-way showed that MS caused an increase in male body weight, which was prevented by the consumption of OO (P<0.001). There were no differences in the caloric intake (P>0.05). MS increased the immobility time in the forced swim test (P<0.05) characterizing depressive behavior and caused a reduction in mitochondrial mass (P=0.008) and potential (P=0.004) both in males. In the analysis of energy-sensing proteins in the DH, it was seen that MS caused a reduction in the sirtuin-1 immunocontent in males (P=0.002), and that OO reduced the activation of AMPK also in males (P<0.05).

Conclusões/Conclusions: OO consumption prevented the weight gain induced by MS but was not able to prevent depressive behavior. However, consumption of OO during gestation and lactation seems to program the metabolism in adulthood in a sex-specific way. Financial Support: CNPq.

Palavras Chave/Key-words: Maternal separation; Depression; Energy metabolism; Sex-specific.

ID: 3636

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Long-Term Cardiovascular Effects of Male Rats Treated With Topiramate During Infancy

Embasamento/Background: Critical periods of development as pregnancy, post-natal age, infancy and adolescence have been targeted of studies in order to understand the origin and progress of chronic diseases in adult life. The developmental theory of origin of health and disease (DOHaD) refers to how stressors during different stages of life can have long-term impacts in the individual health or its in their prole. Then, drug administration can promote metabolic, endocrine and epigenetics changes that can influence in health programming of the individuals as soon as your descendants. Second-generation antiepileptic drugs, as Topiramate (TOP), are approved since 1999 by Food and Drug Administration for the epilepsy treatment in children from two years old and in 2014 for migraine prophylaxis from twelve years old. Is

already know that antiepileptic drugs are related with cardiovascular function impairments, as arrythmias. Previous data has established that TOP administration in adult individual has been associated to increased homocysteine and apoB in plasma, both atherosclerosis markers. However, it is still unknown if the administration of TOP during infancy could influence the health in long-term and the possible impacts of its multiple mechanisms of action in cardiovascular system. Thus, our purpose was to investigate the long-term effects in cardiovascular baseline parameters, as mean arterial pressure (MAP), systolic arterial pressure (SAP), diastolic arterial pressure (DAP) and hear rate (HR), after treatment with TOP during infancy.

Métodos/Methods: Then, Wistar two female and one male rats were submitted to mating, overnight and maintained in the same conditions (12/12 hr dark/light cycle; room temperature at 22ºC; 5 animals per cage; rodent chow and water ad libiditum). The next morning, the female rats were submitted to vaginal smear. Pregnancy were confirmed when cornified cells and sperm were presented in microscope visualization (DG 0) and these animals were followed up in whole gestational period. In the zero post-natal day (DPN 0), the offspring were counted, weighed and the gender identified. A minimum number of 8 and a maximum of 10 rats were maintained to ensure homogeneity in the breastfeeding period and the exceeding number in the litter was euthanized by beheading in guillotine. The weaning of remaining offspring carried out until DPN 21. Male litter rats were treated with water (CTR group; n=17) or TOP 41mg/kg/day (TOP group; n=14) during the infancy period (DPN 16 – 28). Arterial cannulation (DPN 119) and the baseline cardiovascular records (DPN120) were performed in adult life to obtain cardiovascular parameters in basal state. The records were obtained and analyzed using LabChart 7.0 (ADInstruments, Bella Vista, Australia).

Resultados/Results: The results showed that there were no differences in cardiovascular parameters between both groups MAP (CTR: MAP =104, 9 ± 2,78 mmHg; TOP: MAP = 98,62 ± 1,68 mmHg; p = 0,0555; t = 1,995), HR (CTR: HR = 344,2 ± 10,24 bpm; TOP: HR = 357,1 ± 8,471 bpm; p = 0,3367; t = 0,9768), SAP (CTR: SAP = 121,4 ± 4,269 mmHg; TOP: SAP = 113,8 ± 3,019 mmHg; p = 0,1501; t = 1,478) and DAP (CTR: DAP = 92,30 ± 2,819 mmHg; TOP: DAP= 86,90 mmHg ± 2,173; p = 0,1338; t = 1,542).

Conclusões/Conclusions: In conclusion, the treatment with TOP were not able to cause long-term cardiovascular alterations in baseline parameters. These data suggest a safe use of TOP in a critical period with no negative cardiovascular effect in the baseline parameters in adult life.

Palavras Chave/Key-words: Topiramate, Infancy, Cardiovascular Baseline Parameters, Health Programming.

ID: 3637

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: HIF Signaling Pathway During the Nephrogenesis of Rats Submitted to a Protein-Restricted Diet During Pregnancy

Embasamento/Background: Fetal programming is the response of an embryo and fetus during the crucial gestation period to environment insults, such as undernutrition that could promote permanent morphological and physiological changes in later life. Maternal dietary protein restriction during whole pregnancy is associated with low fetal birthweight and leads to programmed kidney morphological and physiological changes. Previous studies have demonstrated that HIF-1α (Hypoxia Induced Factor) is known to be essential for organogenesis by regulating the expression of numerous factors involved in angiogenesis, cellular proliferation, and apoptosis; however, no direct link between maternal protein-restriction, HIF expression and, impaired nephrogenesis has been established. Therefore, in the current study, we considered the modulation of pro-apoptotic and anti-apoptotic factors during nephrogenesis since organogenesis depends upon a tight balance between proliferation, differentiation, and cell death. Pregnant rats on a low protein diet during pregnancy are shown to produce offspring with high lifelong blood pressure related to a decreased number of nephrons. One of the factors associated with reduced nephron formation is the activation of the HIF signaling pathway during nephrogenesis, which compromises not only the absolute amount of nephrons but the maturation of tubular cells. Therefore, this study aimed to determine the HIF signaling pathway's evolution during the nephrogenesis of rats submitted to a protein-restricted diet during pregnancy.

Métodos/Methods: Wistar rats were matched using the harem system, and pregnancy was confirmed by the presence of sperm in the vaginal smear. Confirmed pregnancy, dams were submitted to isocaloric standard protein chow (NP group; 17% of protein) or low-protein chow (LP group; 6% of protein) throughout gestation. On the 17th gestational day, male embryos were collected, and embryonic kidneys were analyzed by immunostaining.

Resultados/Results: Increased HIF1α immunoreactivity was found during nephrogenesis and high pathway proteins - HSP90, NOS2, and decreased transcriptional factor Elf-4. Thus, we believe that the increased activation of the HIF signaling pathway is associated with a decrease in the number of nephrons and the reduction of ureteric bud branch in rats submitted to a low-protein diet and, consequently, the development of diseases in adulthood, such as hypertension. Here, we hypothesized that one of the mechanisms by which low-protein diets develop fewer nephrons is related to the increase in the concentration of not degraded HIF-1 alfa and the decrease in the transcriptional factor Elf-4 and in the proteins of the signaling pathway, which inhibits the adaptive response to the adverse environment: consequently, the renal cells' maturation and inhibition of the division of the nephrogenic progenitors' cells.

Conclusões/Conclusions: The current study supports the premise that offspring from dams exposed to a restricted protein diet express high levels of HIF during pregnancy, which turn fetus vulnerable to impaired renal development.

Palavras Chave/Key-words: fetal programming; low-protein diet; nephrogenesis; HIF-1α, kidney, HSP90, NOS2

ID: 3384

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Topiramate Treatment In Childhood Alters Biometric Parameters In Male And Female Adult Rats.

Embasamento/Background: It has been recognized that adverse conditions during early life may later affect the health of the individual. Topiramate (TOP) is a drug approved by the FDA (Food and Drug Administration) for the treatment of epilepsy in children from 2 years of age. It has been described that treatment with TOP reduces weight gain and adiposity. However, it is unclear whether these effects are similar between male and female subjects. In addition, the long-term effects of TOP treatment into childhood have not been investigated. The present study evaluated, in male and female rats treated with TOP during childhood some biometric parameters. The evaluation was performed in two different times: 24h after the last dose administrated and in adult life.

Métodos/Methods: The study was approved by the Ethics Committee of the UEL (9379.2018.26). Male and female Wistar rats were treated with TOP 41.0 mg/kg/day or water (CTR) by gavage during childhood (from the postnatal day (PND) 16 to 28). It was evaluated in male (PND 29 and 120) and female (PND 29 and 85) the Lee index (body weight1/3(g)/nasal-anal length (cm)×100); weight of retroperitoneal, perigonadal and brown adipose tissue; weight of right and left adrenal and liver (all values expressed as weight per 100g of body). Statistical analyses were performed using SPSS and the variables analyzed by test t, the results are presented as mean ± standard error of the mean. Differences were considered statistically significant if *p<0.05.

Resultados/Results: 24 hours after the last gavage, TOP male showed significant decreased in retroperitoneal adipose tissue [TOP:0.071 ± 0.005 (7) vs CTR:0.157 ± 0.016 (6)], brown adipose tissue [TOP: 0.132 ± 0.006 (7) vs CTR:0.157 ± 0.010 (6)] and increased left adrenal [TOP:0.014 ± 0.001 (7) vs CTR: 0.010 ± 0.001 (6)] when compared with male CTR. Adult male treated with TOP during childhood had a decrease in retroperitoneal adipose tissue [TOP: 0.659 ± 0.088 (11) vs CTR: 1.043 ± 0.088 (10)], perigonadal adipose tissue [TOP: 0.188 ± 0.057 (11) vs CTR: 1.262 ± 0.044 (10)] and increased left adrenal [TOP: 0.005 ± 0.000 (11) vs CTR: 0.006 ± 0.000 (10)] when compared with CTR adult male rat. The other parameters evaluated in male were similar between CTR and TOP. Regarding the biometric parameters evaluated in female rats 24 hours after the last gavage, there was no difference between the CTR and TOP groups. Adult female treated with TOP during childhood showed a decrease in brown adipose tissue [TOP: 0.071 ± 0.004 (12) vs CTR: 0.084 ± 0.002 (12)] when compared with CTR; other parameters were similar between groups.

Conclusões/Conclusions: Treatment with TOP during childhood resulted in acute and late changes in biometric parameters in male rats, whereas in female rats, only late changes were observed. More studies are needed to understand the consequences of these alterations on body health.

Palavras Chave/Key-words: anticonvulsant, disease programming, body index, adipose tissue

ID: 3640

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: ORAL

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Título/Title: MATERNAL POSTNATAL EARLY OVERFEEDING INDUCES OFFSPRING SEX-SPECIFIC HYPERGLICEMIA AND HYPOTHALAMIC INSULIN RESISTANCE DURING ADULTHOOD

Embasamento/Background: Early postnatal overfeeding induced by small litter is a risk factor for metabolic disorders. These animals develop overweight, hyperphagia and compromise of cardiac functions as adults. However, it is still not well described in the literature on the persistence of metabolic effects in the second generation. Our aim was to investigate the effects of maternal postnatal early overfeeding on metabolic parameters in the second generation (F2) offspring.

Métodos/Methods: At delivery (PN1), female Wistar rats (F0) were divided into two groups: normal litter (NL, 9 pups) and small litter (SL, 3 pups) during lactation. At weaning (PN21), the female offspring (F1) were fed standard chow and weighed daily. In adulthood (PN70), females were mated with normal male rats. During gestation and lactation (F1) they fed standard chow. After the weaning, both male and female offspring (F2) from NL dams (NLO) and from SL dams (SLO) were fed standard chow. At PN120, male and female offspring (F2) were fasted overnight and euthanized after anesthesia. Liver, pancreas, white and brown adipose tissue, hypothalamus and blood samples were collected. All procedures were approved by the UFG Ethics Committee (protocol 043/17). Financial Support: CAPES, CNPq and FAPEG;

Resultados/Results: Male and female SLO developed obesity, showing increased milk intake during the breastfeeding period, higher food intake after weaning and increased body's adiposity (mesenteric, retroperitoneal and perigonadal fat). However, only F2 male SLO offspring had an increase (+27%) in the glucose plasmatic concentration. Pancreas H&E's staining revealed that both F2 male and female SLO offspring had a higher pancreatic islet area surface. Nevertheless, the western blotting analysis of the insulin signaling pathway in the hypothalamus revealed that only F2 male SLO offspring had lower expression of PI3K and diminished levels of p-AKT when relativized by the AKT total expression. However, no difference was found between female offspring groups.

Conclusões/Conclusions: Early maternal postnatal overfeeding causes obesity and a sex-specific hyperglycemia and central insulin resistance in the male offspring during the adulthood. Nevertheless, both F2 male and female SLO offspring presented increase in the pancreatic islet area, only the F2 male SLO offspring showed central insulin signaling resistance by the lower expression of PI3K and p-AKT/AKT.

Palavras Chave/Key-words: fetal programming; metabolic; obesity;

ID: 3641

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Goji Berry (Lycium barbarum) Supplemented In Rats During Lactation Improves Biometric and Plasma Parameters in Methabolic Programming Model

Embasamento/Background: Epidemiological and experimental data have suggested that super or underfeeding during the pre and/or postnatal period can play a significant role in the development of obesity and related diseases, since in these periods feeding can influence various processes of hypothalamic development responsible for energy metabolism. In rodents a model used to alter post-natal nutrition is through manipulation of litter size. Many are the researches that try to find solutions to reduce or even minimize the accumulation of body fat and natural supplements have their use encouraged by nutrologists in the aid of fat reduction, among them the Goji berry (GB), recognized by the presence of polysaccharides and antioxidant components. Recent studies by our research group have observed reversal of metabolic syndrome parameters in rats submitted to a diet rich in carbohydrates treated with GB.

Métodos/Methods: That said, our objective was to evaluate whether supplementation with Goji berry (GB) in Wistar rats during lactation could prevent metabolic disorders of adult offspring raised in reduced litters. Biometric parameters such as food and water intake, body weight gain, organ and tissue weight and plasma parameters such as fasting glycemia, intravenous glucose tolerance test (IvGTT), plasma lipid profile, AST and ALT liver damage markers and frutosamine (CEUA 9659220318) were evaluated. The experimental groups (n=8) were made up of male rats from litters of nine puppies (NL); from three puppies (SL) and SL whose mothers received GB (250mg/kg of body weight) during lactation (SLGB), per gavage. After lactation the offspring received free supply of water and standard chow until 90 days of age.

Resultados/Results: Adult rats SL showed a significant increase ($p<0.05$) in food and water consumption, when compared to NL animals. The supplementation with GB reverted the body weight gain and reduced the weight of white fat deposits, as well as the adiposity index, when compared to the SL groups. In contrast, treatment with GB indicated an increase in the weight of the gastrocnemius muscle, which in turn kept the BMI similar among the three groups. Liver and testicles showed no significant differences in weight between the three groups. Regarding plasma biochemical parameters, SL adult rats showed a significant increase in glucose tolerance during ivGTT, increased triglyceride levels, total cholesterol, LDL and VLDL in relation to the control group. GB supplementation during lactation (SLGB) was able to promote significant changes in the adult offspring such as reduced glucose tolerance during ivGTT, reduced plasma triglyceride levels, total cholesterol, LDL and VLDL, and atherogenic index when compared to the SL group. The results showed that there was no significant difference ($p>0.05$) in fasting glycemia, plasma levels of HDL, AST, ALT and frutosamine between the three groups.

Conclusões/Conclusions: These preliminary results suggest that the components of GB can influence the development of energy metabolism control centers, which makes it an important adjuvant in the prevention of metabolic syndrome.

Palavras Chave/Key-words: metabolic syndrome, dyslipidemia, Goji Berry.

ID: 3642

Área: DOHaD and aging

Forma de Apresentação: ORAL

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Título/Title: Melanin-Concentrating Hormone (MCH) Neurons in the Lateral Hypothalamic Area of Aged Rats Are Not Modified by Maternal Food Restriction

Embasamento/Background: The Developmental Origins of Health and Disease (DOHaD) hypothesis is related to the adjustments performed by the organism to insults occurring at key stages of its development, which may lead to long-lasting consequences to the structure and function of multiple organs. Maternal nutrition during critical periods of individual development is essential, since nutrient deficiency during pregnancy and lactation causes significant changes in body weight, energy balance, food intake and neuropeptides expression. The melanin-concentrating hormone (MCH) is a neuropeptide widely expressed in the lateral hypothalamic area (LHA) that is involved in the regulation of energy balance and feeding behavior, in which MCH plays an orexigenic role. However, there is no information about the long-lasting effects of maternal food restriction on MCH neurons in the LHA. Our aim was to analyze the number and distribution of MCH neurons and their ultrastructure in the LHA of aged rats whose mothers were subjected to food restriction during pregnancy and lactation.

Métodos/Methods: After pregnancy confirmation, female Wistar rats were divided in two groups: control group (CG), ad libitum standard chow, and caloric restriction group (RG), 50% chow restriction compared to the control group during pregnancy and lactation (All experimental procedures were approved by the local ethics committee, Protocol number 722). After birth, male pups from both groups were divided into two 540-day-old subgroups (n = 8): CG540 and RG540. Body weight, body length, brain and adipose tissue (visceral and retroperitoneal) weights, food intake after weaning and glucose metabolism were also evaluated. Brains were processed to analyze the number, distribution and ultrastructure of MCH neurons in the LHA, according to immunohistochemistry protocols for light (n = 5) and transmission electron microscopy (n = 3). The MCH neurons mapping and number estimate in the LHA were performed using 3-D reconstruction and stereological study (Neurolucida and Stereoinvestigator softwares, version 11). Quantitative data were statistically analyzed ($p<0.05$).

Resultados/Results: Our data indicated that maternal caloric restriction during pregnancy and lactation decreased body weight, body length, brain weight and visceral and retroperitoneal adipose tissues throughout life. No differences between groups were observed in the glucose metabolism and food efficiency, although the relative food intake was increased in RG540. Stereological data have shown no difference in the number of MCH neurons, area and volume of the LHA of RG540. No changes were observed in the MCH neurons distribution in RG540, with both groups showing the majority of MCH neurons in the LHA caudal part, including mammillary and tuberal regions. No ultrastructural alterations in MCH neurons were seen after maternal caloric restriction during pregnancy and lactation. Both groups showed typical ultrastructural characteristics of peptidergic neurons, highlighting the presence of lipofuscin granules, which are expected in aged animals.

Conclusões/Conclusions: In conclusion, maternal food restriction during pregnancy and lactation changed biometric parameters in the offspring and their food intake, although there was no catchup growth in the restricted offspring. However, maternal undernutrition did not alter MCH neurons and their distribution in the LHA of aged rats, with no effects on their ultrastructure. The MCH system was analyzed for the first time in aging rats after programming by maternal food restriction. Since MCH distribution is highly conserved in vertebrates, we believe that it is less prone to alterations as other feeding-related neuropeptides, which may explain why no changes were seen in its number and distribution in the offspring of restricted dams.

Palavras Chave/Key-words: transmission electron microscopy, maternal food restriction, hypothalamus, neuropeptides

ID: 3135

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Instituições: Título/Title: FoxO1 in Embryonic Heart: Its Regulation by mTOR and Its Alteration by Maternal Diabetes. Romina Higa, Hugo Sato, Cintia Gatti, Sabrina Roberti, Alicia Jawerbaum.Laboratorio de Reproducción y Metabolismo (CEFYBO-CONICET) Universidad de Buenos Aires

Embasamento/Background: The transcription factor FoxO1 has a role in heart development by being involved in the metabolism, oxidative stress, endothelial dysfunction, inflammation and apoptosis of the cardiomyocyte. It phosphorylation in Ser 256 induces its nuclear exclusion and inactivation and this mechanism can be modulated by mechanistic target of rapamycin (mTOR). Maternal diabetes affects the embryonic, fetal and perinatal development and programs metabolic and cardiovascular alterations in the adult offspring. We have recently reported cardiovascular alterations related to the FoxO1 pathway in the adult offspring from diabetic rats. Angiopoietin-2 is an endothelial secreted factor involved in vascular development and inflammatory processes. We aim to evaluate the in vitro regulation of FoxO1 phosphorylation by mTOR in the heart of the embryo and the in vivo expression of angiopoietin-2, a FoxO1 target gene, in the heart of the embryo and offspring from diabetic rats.

Métodos/Methods: Heart explants obtained from embryos of control rats at day 12 of pregnancy were incubated with a mTOR inhibitor (Torin, 1μM) during 3 hours and phosphorylation of ribosomal protein S6 (Ser-235/236) and FoxO1 (Ser-473) was measured by Western Blot. The experimental model of diabetes was obtained by streptozotocin administration to adult rats (50mg/kg). Control and diabetic rats were euthanized at day 12 of pregnancy, embryonic hearts were collected and stored for P-FoxO1 and total FoxO1 measurement by Western blot and expression of angiopoietin-2 by qPCR assays. In the adult male offspring from diabetic rats, heart was obtained for measurements of the mRNA expression of angiopoietin-2 by qPCR assays.

Resultados/Results: The mTOR inhibitor Torin decreased P-rpS6 (mTORC1 downstream target) (74%, $p<0.05$) and P-FoxO1 in embryonic hearts from control rats (28%, $p<0.05$). In the embryonic hearts of diabetic rats, P-FoxO1/total FoxO1 ratio was reduced when compared to controls (55%, $p<0.05$). Expression of FoxO1 and its target gene angiopoietin-2 was increased in the embryonic hearts of diabetic rats when compared to controls (1.9 and 1.5 fold respectively, $p<0.05$). mRNA levels of angiopoietin-2 (1.5 fold, $p<0.05$) was also found increased in the heart of adult offspring from diabetic rats.

Conclusões/Conclusions: mTOR modulates FoxO1 activity in the embryonic heart. In the heart of embryos from diabetic rats, there are increased levels of active FoxO1 and mRNA expression of angiopoietin-2, a target gene related to altered vascular development. Similar changes in the expression of angiopoietin-2 were observed in the hearts of embryos and adult offspring from diabetic rats suggesting that programming of cardiac alterations initiates during organogenesis.

Palavras Chave/Key-words: FoxO1, Embryo´s heart, maternal diabetes, mTOR

ID: 3395

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: ORAL

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Instituições:

Título/Title: Involvement of Reactive Oxygen Species and Cyclooxygenases Pathway in Vascular Dysfunction of Male Adult Rats Treated with Topiramate During Childhood

Embasamento/Background: Background: Topiramate (TOP) is a drug approved by the FDA (Food and Drug Administration) for the treatment of epilepsy in children after 2 years of age. It has been described that events that occur during important stages of body development, such as childhood, may influence the health of the individual later in life. In this context, our group demonstrated that treatment with TOP during childhood alters vascular function in adult male rats, characterized by an increased contractile response independent of the endothelium, without interfering with vasodilation. However, the mechanisms involved with such changes have not been investigated yet. Aim: To investigate the mechanisms involved with vascular dysfunction in adult male rats treated with TOP during childhood.

Métodos/Methods: Methods: The study was approved by the Ethics Committee of UEL (9379.2018.26). Male Wistar rats were treated with 41.0 mg/kg/day TOP or water (CTR) by gavage during childhood (postnatal day, PND 16-28). In adulthood (from PND 120), the thoracic aorta reactivity to phenylephrine (Phenyl) in rings with endothelium was evaluated in the presence of indomethacin (10-6 M), apocynin (10-5 M) or tempol (10-5 M); the comparison between groups was made using the maximum response (maxR) and pD2 (-log of the concentration that causes 50% of the maxR) for the Phenyl. In another group of animals, the histology (aortic thickness) and Western Blot (analysis of the expression of cyclooxygenases: COX-1 and COX-2; and subunits of vascular NADPH oxidase: NOX-2 and p47phox) were performed in the thoracic aorta. The variables were analyzed with one-way ANOVA followed by Bonferroni post-test and independent test t; the results are expressed as mean ± standard error of the mean, differences were considered statistically significant when $p<0.05$.

Resultados/Results: Results: As previously described TOP aortic rings with endothelium presented increased response to Phenyl, when compared with CTR aortic rings. The aortic rings incubation with apocynin and indomethacin reduced maxR to Phenyl in TOP group [Phenyl: 2.87 ± 0.12 (11); indomethacin: 2.09 ± 0.14 (11); apocynin: 2.28 ± 0.13 (11), $p<0.05$], while incubation with tempol did not change maxR to Phenyl [tempol: 2.46 ± 0.13 (11), $p>0.05$]. The blockers did not interfere with the maxR in aortic rings of CTR group. Aorta isolated from TOP rats presented greater thickness compared to the CTR rats [TOP: 69.88 ± 1.24 (8); CTR: 63.90 ± 1.26 (7), $p<0.05$]. TOP group shows an increase in NOX-2 [TOP: 0.29 ± 0.03 (5); CTR 0.20 ± 0.02 (6), $p<0.05$] and p47phox [TOP: 0.22 ± 0.04 (5); CTR: 0.10 ± 0.03 (5), $p<0.05$] expression when compared with CTR group's aorta and COX 1 and 2 expression were similar between groups.

Conclusões/Conclusions: Conclusion: Adult male rats treated with TOP during infancy presented vascular dysfunction, characterized by hyperreactivity to Phenyl in the presence and absence of endothelium. This vascular dysfunction is probably related with smooth muscle cells hypertrophy caused by increased COX expression and reactive oxygen species generated by NADPH oxidase.

Palavras Chave/Key-words: Keywords: developmental theory of health and disease, vascular reactivity, childhood.

ID: 3397

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: ORAL

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Título/Title: MALATHION EXPOSURE DURING JUVENILE PERIOD UNTIL PUBERTY HAS NO EFFECTS TO THE ONSET OF PUBERTY OR ORGANS WEIGHTS OF FEMALE WISTAR RATS QUADRELI, D.H.; ERTHAL, R.P.; LUIZ, K.G.; FRIGOLI, G.F.; FERNANDES, G.S.A.

Embasamento/Background: The prevention of diseases that have Aedes aegypt mosquito as a vector, such as dengue and zika virus, depends on inceticide control. The organophosphate spraying policy has been applied worldwide, with malathion being widely used. Although there are studies relating the female reproductive system to malation, none of them related the onset of puberty in females with exposure to low doses of malathion. Knowing the importance of the juvenile and peripuberal periods in establishing the female reproductive cycle as a critical period for the development of the male genital system, the objective of the present study was to verify the effects of low doses of malathion during the juvenile and peripuberal periods of rats females on puberty, body weight and reproductive organs.

Métodos/Methods: In order to do so, 30 juvenile female Wistar rats (21 days old) were distributed into three experimental groups (n= 10 animals/group): control (saline), malathion 10 (saline + malathion 10 mg/kg) (M10) and malathion 50 (saline + malathion 50 mg/kg) (M50). The doses correspond to 0,5% and 2,5%, respectively, of oral DL50 for rats (oral DLC50 =2000mg/Kg). The rats were exposed to malathion or vehicle between postnatal day (PND) 22 and PND 60 by gavage (oral route), covering the juvenile and peripubertal periods of sexual development. During the experiment, vaginal opening day and first estrus day were measured to determine the onset of puberty. At PND 60, the rats were weighted, anesthetized and euthanized. The uterus and right ovarian were collected and weighted. The protocol was approved by the Ethics Committee on Animal Use of State University of Londrina (OF CIRC CEUA nº 01/2020). The data were compared using ANOVA followed by Dunnet's post-hoc test. Differences were considered significant for $p<0.05$. Statistical analyses were performed using GraphPad InStat (version 3.02).

Resultados/Results: The evaluation of the vaginal opening day and first estrus day of the females showed that the exposure of juvenile females to low doses of malathion was not enough to impair the onset of puberty. In addition, body, uterine and ovarian weights were not changed in groups exposed to malathion compared to the control group.

Conclusões/Conclusions: In conclusion, from these partial results we can infer that in these experimental conditions and parameters evaluated, the low doses of malathion did not impair the postnatal development of female rats exposed during the juvenile and peripuberal periods.

Palavras Chave/Key-words: Malathion, female reproductive system, postnatal development, onset of puberty.

ID: 3399

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: EFFECTS OF PROTEIN RESTRICTION ON GENERAL NUTRITIONAL PARAMETERS AND PANCREAS AND GUT WEIGHTS IN MALE MICE

Embasamento/Background: The excess and the lack of nutrients can trigger morphofunctional damages in the gastrointestinal system. These changes have been correlated with the development of diseases such as obesity and type 2 diabetes mellitus. It has been reported that protein restriction alters endocrine pancreatic morphofunction and insulin action. However, there is little information regarding protein undernutrition effects on intestine morphofunction, and whether the gut in undernutritoncontributes to the impairments in glucose homeostasis observed in malnourished subjects. The objetive of this study is to evaluate glucose tolerance, insulin sensitivity, pancreas and gut weight of protein-restricted mice.

Métodos/Methods: C57Bl/6 male mice from 30 to 120 days-old were randomly distributed into: control (CT) group, which fed ona diet containing 14% protein; or protein-restricted group (RP), which fed on a diet containing 6% protein. Data were analyzed by Shapiro Wilk, following comparisons with Student t or Mann-Whitney U test ($P < 0.05$; CEUA UNICAMP approval nº 5564-1/2020).

Resultados/Results: RP mice displayed hyperphagia (364.2 ± 2.1 g.weeks-1) and higher kilocalories intake (96.5 ± 0.5 kcal/week) during the experimental period, when compared to CT (298.8 ± 7.1 g.weeks-1 and 79.3 ± 1.9 kcal/week, respectively). However, RP mice exhibited lower body weight (BW; 24.6 ± 0.6 g), feed efficiency (29.3 ± 0.3%), Lee Index (304.6) and mesenteric fat pads (6.9 ± 0.9 mg/g BW)at the end of experimental period, when compared to CT (27.2 ± 0.5 g, 41.4 ± 0.2% and 312.6 ± 1.5, 12.0 ± 2.0 mg/g BW; respectively). In addition, RP mice displayed higher total cholesterol levels (92.1 ± 5.2 mg/dL), without modifications in triglyceridemia (55.91 ± 2.5 mg/dL) or glycemia (70.3 ± 2.1 mg/dL), than CT mice (66.2 ± 7.5, 55.2 ± 4.0 and 72.4 ± 3.0 mg/dL, respectively). Protein restriction significantly increased in 30% the insulin sensitivity (5.7 ± 0.2%min) in RP group, when compared to CT (4.4 ± 0.2%min). Furthermore, RP mice exhibited reductions of 22%, 23.3%, 12.1% and 16.5% in pancreas (8.0 ± 0.3 mg/g BW), cecum (12.3 ± 1.3 mg/g BW), small (45.8 ± 3.0 mg/g BW) and large intestines (26.8 ± 2.2 mg/g BW) weights, respectively, when compared to CT (10.4 ± 0.7 16.0 ± 0.5; 52.1 ± 1.8 and 32.1 ± 0.8 mg/g BW, respectively). But, only the length of the small intestine (31.5 ± 0.3 cm) was reduced in RP mice, when compared to CT (35.3 ± 1.7 cm).

Conclusões/Conclusions: Protein restriction induced hypotrophy both in pancreas and gut.Despite diminished pancreas weight, RP mice displayed normoglycemia due to augmented insulin sensitivity. Further investigations are necessary to clarify the correlation between intestine morphofunction and the impaired glucose homeostasis in protein restriction. Support: FAPESP.

ID: 3151

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Adrenalectomy Attenuates Metabolic Effects Induced by Postnatal Overnutrition in Male Rats.

Embasamento/Background: Postnatal nutrition in rodents can be modified by manipulating litter size. Its known that litter size reduction induces neonatal overfeeding by increasing milk intake, leading to early development of obesity, which persists until adulthood. Glucocorticoids are pointed as possible mediator for the development of obesity, since circulating glucocorticoids are increased in different models of obesity and bilateral adrenalectomy (ADX) can reduce obesity in these models.This study aimed to evaluate the effects of ADX and glucocorticoid replacement on metabolic changes promoted by neonatal overfeeding induced by reduction of litter size.

Métodos/Methods: For this, male Wistar rats (n=77) were obtained by mating of females and males provided by the Central Vivarium of the State University of Londrina (UEL). On postnatal day 3 (DPN), 3 pups (small litter - SL) or 10 pups (normal litter - NL) were kept with each female. On PND 60, animals underwent bilateral adrenalectomy (ADX) or fictitious surgery (sham), and half of ADX animals received corticosterone (CORT- 25 mg/L) in the drinking fluid. Body weight and food intake were daily monitored during 14 days after surgery. On the 13th day, animals were subjected to glucose tolerance test (GTT), and on the following day, animals were euthanized by decapitation for trunk blood collection and visceral adipose tissues removal. The experimental procedures were approved by the Ethics Committee on the Use of Animals undergoing experimentation for approval (CEUA:3457.2109.11). Compared to sham animals, ADX reduced body weight gain, food intake, weight and area of adipocytes of epididymal and retroperitoneal adipose tissues, plasma levels of corticosterone, triglycerides, total and HDL cholesterol in NL group.

Resultados/Results: Compared to ADX, replacement with corticosterone enhanced body weight gain, food intake, adipocyte area of epididymal adipose tissue, plasma concentrations of corticosterone, triglycerides, total cholesterol, HDL and LDL cholesterol in NL animals. However, in NL animals, ADX+CORT group showed lower weight and adipocyte area of retroperitoneal adipose tissue, and higher levels of total and LDL cholesterol, compared to sham group. In sham animals, litter size reduction promoted decrease of food intake and increase of body weight gain, weights and area of adipocytes of epididymal and retroperitoneal adipose tissues, plasma levels of corticosterone, free fatty acids, total and LDL cholesterol, glucose intolerance, compared to their respective NL animals. ADX was able to attenuate SL-induced changes on these parameters, since ADX decreased body weight gain, food intake, weight and area of adipocytes of epididymal and retroperitoneal adipose tissues, glucose intolerance, as well as plasma levels of corticosterone, triglycerides, total and HDL cholesterol and free fatty acids in SL animals compared with respective sham g In SL animals, CORT replacement increased body weight gain, adipocyte area of epididymal and retroperitoneal adipose tissues, plasma concentrations of free fatty acids and HDL cholesterol, compared with ADX animals. On the other hand, in SL animals, ADX+CORT group showed lower food intake, weights of epididymal and retroperitoneal adipose tissues, adipocyte area of retroperitoneal adipose tissue, AUC of GTT, plasma concentrations of corticosterone and free fatty acids, compared to sham animals.

Conclusões/Conclusions: In summary, adrenalectomy attenuated the anabolic effects observed after neonatal overnutrition induced by litter reduction, and corticosterone replacement could reverse most of ADX-related changes. Thus, glucocorticoids are likely to contribute to metabolic responses ascribed to neonatal overfeeding.

Palavras Chave/Key-words: energy homeostasis, glucocorticoids, litter size reduction, white adipose tissue.

ID: 3412

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Aluminium Chloride Impairs the Prostate Development During the Peripuberal Period

Embasamento/Background: In November 2015, the rupture of the mining waste dam in the municipality of Mariana, MG, caused immense environmental and social damage. The residues reached an enormous extent, contaminated the soil and water, where high concentrations of several metals were found, among them aluminum (Al). The Al is one of the most abundant metals in the earth's crust, having several applications, for example, in medicines, cosmetics and industrial products. Therefore, people are regularly exposed to this environmental contaminant. However, although some people consider it a "safe" metal, it is already known that it is capable of causing toxicity to a variety of organs, including the brain, bones, kidneys and blood, but it is not yet known whether Al can be toxic to the prostate tissue. This study aimed to evaluate whether exposure to aluminium chloride (AlCl3) during the peripubertal period affects ventral prostate development in rats.

Métodos/Methods: Male Wistar rats (30 days old) were distributed into three experimental groups: control (sterile 0.9% saline solution), AL7 (7 mg AlCl3/kg) and AL34 (34 mg AlCl3/kg). Animals were treated intraperitoneally from postnatal day (PND) 36 to 66 (peripubertal period). At PND67, the animals were anaesthetized and euthanized. Blood was collected for testosterone levels. The ventral prostate (VP) was removed, weighed and processed for histochemistry and immunohistochemistry to detect androgen (AR). Stereological and histopathological analyses and determinations of myeloperoxidase (MPO) and N-acetyl glycosidase (NAG) activity and IL-6 levels were performed. The experimental protocol followed the Ethical Principles in Animal Research adopted by Brazillian Council for Control of Animal Experimentation and it were approved by the Ethics Committee on Animal Use of State University of Londrina (OF. CIRC CEUA/UEL 059/2015).

Resultados/Results: The AL34 group presented a reduction in body weight, proving a systemic effect. The same group showed an increase in MPO activity compared to the other groups, indicating a possible systemic inflammatory condition. Prostatic tissue compartments were reorganized in groups AL7 and AL34, delaying the luminal development of prostatic acini but not with the number of acini. This interference in acini in the AL34 group was probably due to the reduction of AR-positive cells. There was no significant difference in prostate weight, NAG activity, testosterone or IL-6 levels.

Conclusões/Conclusions: In conclusion, the exposure to aluminium chloride during the peripubertal period impairs the prostatic development.

Palavras Chave/Key-words: Aluminium chloride, ventral prostate, microscopic analysis, cell count.

ID: 3414

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal, Placental and Umbilical Cord Vitamins in Birth Weight Alteration Salazar Monreal LG1, Salazar Contreras MJ1, Mora-Peña JS1, Gómez-Zapata HM, González-Domínguez MI2, Lazo de la Vega Monroy ML1, Barbosa-Sabanero G1. 1.Departmen

Embasamento/Background: Maternal nutrition during pregnancy, malnutrition, or overeating, leads to structural and metabolic changes in the developing fetus. This may be not only reflected in the first months of life but also in later stages, conferring a greater risk for metabolic diseases in adult life. Therefore, fetal development is sensitive to micronutrient availability, such as vitamins, which play a key role in cellular metabolism, differentiation, and growth. Vitamin B12, folic acid, and biotin concentrations have been associated with birth weight, which is a prognostic factor for metabolic diseases in adult life. However, little is known about the status of these vitamins in the umbilical cord and placenta compared to maternal levels.

Métodos/Methods: Clinically healthy women with normoevolutive pregnancy, umbilical cord blood and placenta of term newborns (n = 33) were included, and were classified according to birth weight in small (SGA, n = 11), adequate (AGA, n = 10) and large (LGA, n = 12) for gestational age. The concentrations of vitamin B12, biotin, and folic acid in maternal serum, umbilical cord serum, and placental homogenates were determined by ELISA, and clinical and anthropometric data were recorded.

Resultados/Results: Average maternal age was 25.2 ± 4.4 years, pregestational BMI was 24.5 ± 4.0, maternal vitamin B12 concentrations were 2134.8 ± 1351.2 pg / mL, biotin 180.5 ± 131.6 ng / mL and folic acid 14.8 ± 10.4 umol / L. In the umbilical cord serum, vitamin B12 concentrations were 1697.9 ± 652.4 pg / mL, biotin 534.7 ± 195.1 ng / mL, and folic acid 3.2 ± 1.1 umol / L. Placenta concentrations of vitamin B12 were 118.0 ± 146.1 pg / mL / µg protein, biotin 88.7 ± 32.2 ng / mL / µg protein, and folic acid 2.06 ± 3.4 ummol / L / µg protein. Maternal vitamin B12 concentrations were positively correlated with maternal folic acid levels ($r = 0.55$, $p = 0.005$) and with vitamin B12 levels in the umbilical cord ($r = 0.41$, $p = 0.031$). Maternal serum vitamin B12 levels were inversely associated with birth weight ($r = -0.59$, $p = 0.001$) and placental weight ($r = -0.43$, $p = 0.028$). Both the placental levels of folic acid and vitamin B12 were positively associated ($r = 0.99$, $p = 0.048$).

Conclusões/Conclusions: The association of maternal vitamin B12 concentrations with umbilical cord vitamin B12 concentrations and in turn with birth weight, highlights the importance of maternal nutrition in fetal development and its potential impact on future health. More studies are necessary to provide evidence of recommendations for the adequate intake and supplementation of these nutrients during pregnancy

Palavras Chave/Key-words: Vitamin B12; biotin; folic acid; birth weight.

ID: 3160

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Gestational Caloric Restriction Improves Redox Homeostasis Parameters in the Prefrontal Cortex of Wistar Rats.

Embasamento/Background: It is well established that the intrauterine life is a key period for proper brain development, in accordance to the Developmental Origins of Health and Disease (DOHaD) concept. There is plenty of evidence to state that caloric restriction (CR) has a role in modulating redox homeostasis, and has been shown to improve the antioxidant system through diverse mechanisms. However, the impacts of caloric restriction during pregnancy are poorly reported, especially when considering malnutrition prevention. Therefore, we aimed to evaluate the effects of 20% caloric restriction allied to micronutrient supplementation during pregnancy in redox homeostasis parameters in the prefrontal cortex of Wistar rats' offspring.

Métodos/Methods: Control group had free access to water and a 22% (w/w) protein commercial chow. CR group also had free access to water and the same commercial chow; however, the amount was reduced by 20% and it was adjusted daily by body weight. In addition, micronutrient supplementation was administered daily to the CR group, in order to equalize micronutrient consumption between groups. CR dams were submitted to the caloric restriction protocol during the entire course of pregnancy. On postnatal day (PND) 0, PND7, PND21 and PND60 the prefrontal cortex was dissected and rapidly isolated in a Petry plate on ice and stored at −80 °C until utilization. We evaluated oxidants content through the dichlorofluoresceine (DCFH) oxidation. Enzymatic antioxidant defenses activity was also evaluated. The concentration of indicators of oxidative damage to biomolecules such as malondialdehyde (MDA), sulfhydryl and carbonyl was also evaluated. The experiments were approved by local Ethics Commission (Comissão de Ética no Uso de Animais/Universidade Federal do Rio Grande do Sul) under the number 30044.

Resultados/Results: The total amount of oxidants quantified by DCFH oxidation was significantly increased on PND0, and on PND7 it dropped below control levels. Superoxide dismutase activity was higher on PND60. On PND7 and PND60 catalase activity was increased. We noticed a decrease in glutaredoxin activity on PND0, followed by its activation on PND60. Thioredoxin reductase had its activity increased on PND0, and it was activated once again on PN60. It was verified a reduction in the levels of GSH on PN0, and on PND60, GSH content was increased. Vitamin C also had lower concentrations on PND0, with an increase in its concentration on PND60. It was found a significant decrease in the levels of lipid peroxidation by the measurement of MDA concentration, which showed decreased levels on PND7, 21 and 60.

Conclusões/Conclusions: Our data shows that a low intensity CR associated to responsible malnutrition prevention improves redox homeostasis parameters. In a general way CR appears to increase antioxidant profiles and may boost antioxidant defenses. Results suggests that the increased oxidants production during the early stages of development might lead to hormetic adaptions by the antioxidant system. Financial support: this study was funded by CNPq (PQ nº: 304293/2018-0 and INCT 465671/2014–4), CAPES and PROPESQ-UFRGS.

Palavras Chave/Key-words: Dietary restriction; Intrauterine environment; Redox status; Metabolic programming; Pregnancy.

ID: 3419

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Exposure to Trans Fat During Development Decreases Life Expectancy and Increases Aggressive Behavior in Drosophila melanogaster

Embasamento/Background: The health and composition of the maternal diet greatly influence the development of offspring. Studies show that early exposure to trans-fat can influence the neurophysiological development of the offspring, making individuals more susceptible to developing long-term behavioral and mood disorders, in addition to negatively affecting their growth and development. Therefore, it is important to use alternative models that help to understand such disorders. Drosophila melanogaster has emerged as a promising organism for behavioral and neuroscience-related studies. Unlike mammals, the developmental phase of the fly occurs outside the maternal body, that is, in the environment in which they are subjected. In addition, this model allows studying changes transmitted from different generations, where the impact of the parents' diet on the health of the offspring can be determined by changing the diet of their progenitors. The objective of the work is to evaluate exposure to trans-fat during development on life expectancy and aggressive behavior in Drosophila melanogaster.

Métodos/Methods: Parents were divided into 4 groups, containing 50 flies of both sexes in each: (1) RD (corn flour, sugar, wheat germ, salt, powdered milk, and agar), (2) SHVF (HVF replaced fat values of RD in the same proportion), (3) HVF 10% (RD with 10% HVF) and (4) HVF 20% (RD with 20% HVF). After 7 days of exposure, the parents were removed from the medium, leaving the larvae and eggs. Larval food consumption was evaluated to analyze the acceptability of the larvae to the diet, through the use of a blue dye added to the diet. The total hatch rate of the flies was assessed by counting the total number of flies born alive in each group (first day = 0 flies) after removing the progenitors from the medium until there were no more viable eggs. The offspring were removed daily at the same time each day. Longevity rate was evaluated by a daily count of the number of living flies until there were no more live flies. Aggressive behavior was assessed after 1-3 days of hatching. Statistics: For the normality of data, the Shapiro – Wilk test was used, for homogeneity, Bartlett's test. Normal and homogeneous data were assessed by one-way ANOVA, followed by Tukey. The longevity was determined using the Mantel-Cox log-rank test. It was considered significant when $p < 0.05$.

Resultados/Results: Food consumption was similar among the larvae of all experimental groups (One-way ANOVA, $F3, 36 = 0.33$, $p = 0.79$). There was a reduction in the total hatching rate and life expectancy of flies exposed to HVF in all concentrations, compared to RD ($p < 0.05$). There was an increase in the number of aggressive episodes in flies exposed to HVF in all concentrations compared to RD. In addition, flies exposed to HVF 20% had more aggression episodes than flies exposed to concentrations of SHVF and HVF 10% (One-way ANOVA, $F3, 12 = 375.6$, $p < 0.0001$).

Conclusões/Conclusions: Exposure to trans fatty acid during the development period can decrease the hatching rate and reduce life expectancy of flies. It is also responsible for increasing aggressive behavior in the Drosophila melanogaster model.

Palavras Chave/Key-words: dietary composition, aggression, humor

ID: 3167

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: ORAL

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Título/Title: Can Exposure to Topiramate During Adolescence Program Permanent Vascular Dysfunction in Rats?

Embasamento/Background: The Developmental Origins of Health and Disease (DOHaD) describe that adaptations to environmental disturbances, during periods of developmental plasticity, can have a long-term impact on an individual's health. Adolescence has been described among periods of developmental plasticity. Topiramate (TOP) is a Food and Drug Administration (FDA) approved drug for migraine prophylaxis in adolescents and this drug has been reported to increase the risk of vascular disease in humans. The vascular endothelium plays an important role in the maintenance of cardiovascular homeostasis. Studies have shown that endothelial cell dysfunction may favor the development of the cardiovascular disease. However, the effect of TOP treatment during adolescence on vascular function has not been investigated. Thus, the present study aimed to evaluate the vascular function of adolescent and adult rats after TOP treatment during adolescence.

Métodos/Methods: For this, Wistar rats were treated with TOP (41 mg/kg/day) or vehicle (CTR group) by postnatal day gavage (PND) 28 to 50, adolescence period. During treatment, body mass gain and food intake (at last week of treatment) were followed. After the treatment, both groups were evaluated at PND 51 and PND 120. The indirect blood pressure and heart rate was measured by a tail-cuff blood pressure system in conscious rats. In vitro thoracic aorta reactivity to the vasoconstrictor phenylephrine in the presence (E+) or absence of endothelium (E-), and to vasodilators acetylcholine (Ach) and sodium nitroprusside (SNP) was evaluated. The aorta thickness was evaluated through hematoxylin-eosin histological technique. For statistical analysis, were used One-way ANOVA followed by the Tukey test (aortic reactivity to phenyl); T-Student test (aortic reactivity to ACh and SNP, blood pressure, heart rate and histology) and multiple T-tests to assess point-to-point weight gain and food intake. Data were expressed as mean ± standard error of the mean (SEM). Differences were considered statistically significant when $p < 0.050$ (CEUA: 9379.2018.26).

Resultados/Results: It was observed that there was no difference between the CTR and TOP groups for food intake, body mass gain, blood pressure and heart rate. In the presence of endothelium, at PND 51, the aortic Rmax to the phenylephrine was higher in TOP group compared to CTR Rmax [CTR E+: 1.98 ± 0.06g (n=10) vs TOP E+ 2.51±0.05g (n=10)] and endothelium removal abolished this difference. The response to the vasodilators was similar between the TOP and CTR groups at PND 51. At PND 120, the aortic rings of TOP and CTR rats, in the presence or absence of the endothelium, showed similar response to phenylephrine. Regarding vasodilation at PDN 120, the aortic rings of TOP group presented a decrease in pD2 for ACh [CTR: 7.48 ± 0.07 (n=9) vs TOP: 7.11 ± 0.11 n=9)] without alteration of Rmax. Also, the aortic thickness was similar between the groups at PND 51 [CTR: 60.76 ± 1.67µm (n=9) vs TOP 60,60 ± 2.77 µm (n=6)] and at PND 120 [ CTR: 73.69 ± 3.14 µm (n=6) vs TOP 67.01 ± 1.51 µm (n=7)].

Conclusões/Conclusions: Our data demonstrated that treatment of rats with TOP during adolescence, using 41 mg/kg/day, promotes permanent impairment of endothelial function. Suggesting that this exposure during adolescence may program vascular disease in adulthood.

Palavras Chave/Key-words: topiramate; adolescence; vascular; endothelium.

ID: 3170

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Low-Protein Diet in Puberty Impairs Endothelial Dysfunction in Adult Male Rats

Embasamento/Background: Protein restriction during puberty malprograms rats to exhibit metabolic and cardiovascular disorders. The vascular system and endothelial function have central role in the establishment of cardiometabolic disorders. However, as far as we know, the consequence of protein restriction during puberty upon endothelial function of adult rats has not been evaluated. Thus, our study aimed to evaluate the mechanism involved with endothelial dysfunction in adult rats feed with low-protein diet during puberty.

Métodos/Methods: The study was approved by the Ethics Committee of UEL (13068.2019.60). Wistar male rats at postnatal day (PDN) 30 were distributed in two groups: LP group that received a low-protein diet (4% protein) and CTR group that received normoprotein diet (23% protein) during adolescence (PND30-60). After PDN 60 the rats from both groups received normoprotein diet. At adulthood (PND120), the thoracic aorta reactivity to phenylephrine (phenyl), acetylcholine (ACh) and sodium nitroprusside (NPS) was evaluated in the presence (E+) or absence (E-) of endothelium. The comparison between the groups was made using the maximum response (Rmax) for the drugs. Mechanisms involved with phenyl response were investigated using indomethacin, apocinin and tempol. The variables were analyzed with ANOVA and independent test t; the results expressed as mean ± mean standard error, differences were considered statistically significant if *$p<0.05$.

Resultados/Results: Regarding the vasodilation, the Rmax to ACh was reduced in aortic rings E+ from LP group when compared with CTR [CTR 2.618 ± 0.3466 (n=8) vs LP 1.849 ± 0.2286 (n=8), $p<0.05$]. On the other hand, the Rmax to NPS in aortic rings E- was similar between CTR e LP groups. The Rmax to the vasoconstrictor phenyl was increased in aortic rings E+ from LP group when compared with aortic rings E+ from CTR group [CTR 1.513 ± 0.08765 (n=10) vs LP 2,495 ± 0.1300 (n=9); $p<0.05$]. The Rmax to phenyl was similar between CTR e LP in aortic rings E-. Thus, in another series of experiments, the mechanisms involved with the increased response to phenyl observed in LP`s aortic rings in the presence of endothelium was evaluated. The aortic rings E+ incubation with apocynin, a NAPH oxidase inhibitor, reduced the Rmax to phenyl in LP group [LP E+ without blocker 2,480±0,2414 (n=13) vs LP E+ apocynin 1.849 ± 0.2286; (n=8); $p<0.05$], but did not interfere with the Rmax to phenyl in CTR group. The E+ aortic rings incubation with indomethacin, a cyclooxygenase inhibitor, or tempol, a reactive oxygen species scavenger, did not interfere with the phenyl response in LP and CTR groups.

Conclusões/Conclusions: Protein restriction in adolescent rats induced endothelial dysfunction in aorta during adulthood, probably through a mechanism involving reactive oxygen species generated by NAPH oxidase. Our results suggest that puberty is an important window to program vascular disease later in life.

Palavras Chave/Key-words: developmental concept of health and disease, low protein diet, vascular reactivity, adolescence

ID: 3429

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Administration of Sodium Butyrate Prevents Macrosomia and Liver Lipid Overaccumulation in Fetuses from Overweight Rats - Florencia Heinecke*, Daiana Fornes*, Evangelina Capobianco*, Alicia Jawerbaum*, Verónica White* - *CONICET-UBA, Center of ph

Embasamento/Background: Maternal programming of metabolic alterations is considered a cause for the worldwide increase in obesity. Maternal obesity induces anomalies in fetuses and placentas that precede the programming of metabolic derangements in the offspring. Moreover, fetal liver lipid overaccumulation is a clear predictor of fatty liver later in life. Butyrate is a short chain fatty acid (SCFA) product of fiber metabolism from the intestinal microbiota. This SCFA improves lipid and glucose homeostasis and protects gut barrier function. Our aim was to evaluate whether maternal administration of butyrate during gestation prevents the development of macrosomia and liver lipid overaccumulation in fetuses from overweight rats.

Métodos/Methods: Female Wistar rats were fed with standard (CT rats) or standard supplemented with saturated fat diet (28% fat) since they were 6 week-old (FD rats). After 8 weeks, they were mated with control males. Sodium butyrate (3%) or vehicle, was orally delivered daily during gestation (FDB rats). Control, FDB, and FD rats were euthanized at 21 days of gestation, fetuses, maternal and fetal livers and placentas were explanted and weighed. Maternal and fetal plasma was obtained by decapitation. Plasma glucose, triglycerides (TG) and cholesterol levels were assessed by colorimetric assays. Maternal and fetal liver lipid levels (Phospholipids (PL), Free fatty acids (FFA), Cholesterol (Ch), TG and Cholesterol Esters (Ch E)) were assessed by thin layer chromatography (TLC) and maternal hepatic mRNA levels of genes involved in lipid metabolism were assessed by RT-qPCR.

Resultados/Results: Maternal TG were increased in plasma from FD rats (36% $p<0.05$ vs CT) whereas the administration of butyrate restored the control values (31% $p<0.05$ vs FD). Maternal livers showed lipid overaccumulation in FD rats (TG: 301% and Ch E: 150% $p<0.001$ vs CT) that persisted in FDB rats (TG: 443% and Ch E: 204% $p<0.001$ vs CT). Maternal hepatic mRNA levels of Cd36, Fas and Acc1 were decreased in FD rats (49%, 62% and 39% $p<0.01$ vs CT). The administration of butyrate maintained the decrease in the mRNA levels of Cd36, Fas and Acc1 (50%, 64% and 52% $p<0.01$ vs CT), while increased the mRNA levels of Srebp-1c (41% $p<0.05$ vs CT). Fetuses from FD rats were heavier than controls (7% $p<0.05$ vs CT) and their livers showed lipid overaccumulation (TG: 140% and Ch E: 144% $p<0.05$ vs CT). The administration of butyrate was able to prevented fetal macrosomia (7% $p<0.05$ vs FD) and liver lipid overaccumulation (TG: 48% and Ch E: 47% $p<0.05$ vs FD).

Conclusões/Conclusions: Maternal oral administration of butyrate prevents the increase in maternal triglyceridemia, fetal macrosomia and liver lipid overaccumulation, clear markers of fetal fatty liver programming. The prevention of these alterations will probably influence the metabolic health of the offspring in later stages of their life. Financial Support: Agencia de Promoción Científico y Técnica, Ministerio de Ciencia y Técnica de la República Argentina PICT 2015 750.

Palavras Chave/Key-words: Maternal overweight, Intrauterine programming, Liver, Butyrate

ID: 3695

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Effects of (-)-Epicatechin Intervention on the Reproductive Function of Male Rats Fed a High Fat Diet and Born to Obese Mothers

Embasamento/Background: Obesity during pregnancy and lactation predisposes male offspring to a deterioration in fertility and premature aging of reproductive function; in addition, this the negative factors of postnatal life such as continuing with the consumption of a high fat diet, are a “second hit” that can accentuate negative programming and phenotype. Epicatechin is a polyphenolic antioxidant that comes from cocoa that has shown benefits for metabolic and cardiovascular health, however, little is known about the effects on male reproductive function. We hypothesize that epicatechin intervention attenuates the adverse effects in male offspring on reproductive function caused by maternal obesity and a high fat diet postnatal consumption.

Métodos/Methods: Female rats (F0) rats were fed either a control (5% fat) or a high-fat diet (25% fat) from weaning and througouth pregnancy and lactation. At postnatal day (PND) 21 male offspring (F1) were weaned and fed a control or high fat diet and were divided into four experimental groups (according to the maternal they came from and offspring diet) : control group (C), maternal obesity (MO), maternal obesity + F1 fed with a high-fat diet (MOHF) and maternal obesity + F1 fed with a high fat and epicatechin intervention (MOHFEpi) to which 1mg / kg of epicatechin was given twice a day orally from PND 21 to 110.At PND 110 male F1 were euthanized. Epididymal fat was measured, sperms from the epididymal head and vas deferens were obtained to measure 1) sperm concentration and 2) reactive oxygen species (by fluorescence), and reproductive capacity that was evaluated as fertility rate.

Resultados/Results: At PND 110 , epididymal fat was similar in C and MO, and increased in MOHF with respect to MO, while in the MOHFEpi group it was reduced with respect to MOHF but remained higher than C and MO. The reactive oxygen species were similar in C, MO and MOHFEpi and increased in MOHF with respect to MO. Sperm concentration was lower in MO, MOHF and MOHFEpi with respect to C, however, MOHF had a lower concentration as compared to MO and MOHFEpi. The fertility rate was expressed as a percentage of fertile males; was similar between in C and MO, but in MOHF it decreased more than 50% with respect to MO. The fertility rate was improved in MOHFepi without being similar to C.

Conclusões/Conclusions: The high fat diet is a second hit that accentuates the adverse programming of maternal obesity in the male offspring reproductive function. The epicatechin intervention attenuates the adverse effects in offspring on male reproductive function caused by maternal obesity and the consumption of a high fat diet postnatal.

Palavras Chave/Key-words: Developmental Programming, Male Fertility, Epicatechin Intervention

ID: 3192

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: ORAL

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Título/Title: The Influence of Estrogen in Vascular Reactivity of Female Progeny Exposed to Fluoxetine in Utero and Through Lactation

Embasamento/Background: Selective serotonin reuptake inhibitors (SSRIs) have been widely indicated for the treatment of affective disorders, covering populations such as pregnant women, due to greater safety and less toxicity compared to the classes of tricyclics and monoamine oxidase inhibitors. Treatment with fluoxetine (FLX), the main SSRI representant, during pregnancy can expose fetuses in critical stages of development, since FLX can cross the placental barrier reaching fetal plasma. Recently, it has been described that early exposure to FLX can blunt aortic contractile response in female progeny, but not in male. The mechanism by which this alteration occurs has not been completely elucidated. Therefore, this study aimed to comprehend how FLX-induced endothelium-dependent hyporeactivity in aorta occurs and its relationship with the female gender.

Métodos/Methods: Female Wistar rats, whose mothers received FLX (5 mg/kg) or tap water (control [CTR]) during the whole pregnancy and lactation were evaluated at PND28, before vaginal opening, for vascular reactivity (prepubertal phase). Siblings at the same age were submitted to bilateral ovariectomy (OVX) or sham surgery. Pre-pubertal, adult sham and OVX from CTR and FLX groups were anaesthetized, had aorta removed and cut into two rings, one with (E+) and one without (E-) endothelium. Concentration-effect curves for phenylephrine (Phe), acetylcholine (ACh) and sodium nitroprusside (SNP) were performed. In order to evaluate the role of ovarian hormones on Phe-induced vasoconstriction, E+ aortic rings from CTR and FLX rats were incubated with MPP, Estrogen Receptor (ER) α inhibitor or PHTPP, ER β inhibitor. The mean of lumen diameter and of middle layer thickness were assayed through hematoxylin-eosin stained aortic sections. Mean arterial blood pressure (MAP) was measured by CODA tail-cuff blood pressure system and plasmatic estradiol levels were assayed by immunoassay with chemiluminescent particles (Kit 7K72-Architect-estradiol® Abbott Laboratories) in CTR sham, FLX sham, CTR OVX and FLX OVX groups.

Resultados/Results: There was no difference in aortic contractile response between exposed and non-exposed prepubertal female rats in the presence neither in the absence of endothelium. The relaxation responses to ACh and SNP were similar between prepubertal female groups. In adult progeny, FLX sham group presented reduced vasoconstriction when compared to CTR sham in the presence of endothelium (CTR: 2.37 ± 0.12 [n=14] vs FLX: 1.15 ± 0.10 [n=10], $p<0.05$), but no differences between CTR OVX and FLX OVX E+ aortic rings (CTR OVX: 2.39 ± 0.07 [n=13] vs FLX OVX: 2.17 ± 0.12 [n=14]). In the E+ vasodilatation response, there was no difference to ACh among the groups. The absence of endothelium led to similar contractile response to Phe between CTR sham and FLX sham groups, and between CTR OVX and FLX OVX groups. There was no difference in relaxation response to SNP among groups. The ERβ incubation increased the Phe induced contraction in FLX sham group (2.01 ± 0.14 [n=10]) equaling to CTR sham group (2.42 ± 0.15 [n=9]). There was no difference in the mean diameter of the lumen nor in the middle layer thickness of aortic slices from CTR sham, FLX sham, CTR OVX and FLX OVX groups. Also, the blood pressure was similar between CTR sham, FLX sham, CTR OVX and FLX OVX rats. Bilateral ovariectomy performed at prepubertal age reduced plasmatic estradiol concentrations in adult female rats from CTR groups (OVX: 32.09 ± 1.20 pg/ml [n=11] vs sham: 46.58 ± 2.00 pg/ml [n=12], $p<0.05$) and FLX groups (OVX: 30.91 ± 0.99 pg/ml [n=11] vs sham: 50.27 ± 3.85 pg/ml [n=11], $p<0.05$).

Conclusões/Conclusions: As previously demonstrated intrauterine and lactational exposure to FLX reduced the aortic contraction. Here we add that vascular dysfunction observed in female adult offspring is probably related to ovarian hormones acting through endothelial ERβ, highlighting the susceptibility on the vascular system of female offspring to FLX early exposure.

Palavras Chave/Key-words: Fetal programming; ovarian hormones; pregnancy

ID: 3213

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Maternal Vitamin D Deficiency Selectively Induces Hypertrophy and Strength Gain in Glycolytic Muscles in Male Adult Offspring Rats

Embasamento/Background: Fetal stage is a developmental critical window for the skeletal muscle, but little information is available about the impact of maternal vitamin D deficiency (VDD) during pregnancy on offspring skeletal muscle development. Therefore, we analyze the effects of maternal VDD in utero and early postnatal life on muscle development in adulthood of male and female rats.

Métodos/Methods: Twelve 5-week-old female Wistar Hannover rats were fed either a control diet (Vit. D3+ diet; AIN93G with 1000 IU vitamin D3/kg diet) or Vit. D3- diet (AIN93G without vitamin D3) for six weeks and then bred to male rats. Females were maintained on the diets throughout gestation and lactation. At weaning, male and female offspring were separated into four groups: male and female offspring control (M-CTRL and F-CTRL, respectively) from dams with Vit. D3+ diet and male and female offspring VDD (M-VDD and F-VDD, respectively) from dams with Vit. D3- diet. Offspring received a standard diet (Nuvilab) until 180 days of age, at which point tissues were

harvested for analysis. *P≤0.05 (CEUA 052/2018).

Resultados/Results: Both male and female VDD groups showed a reduction in the calcidiol serum concentration (23±1 vs 40±2 ng/ml in M-CTRL and 23±2.2 ng/ml vs 36.6±0.9 ng/ml in F-CTRL) without affecting Ca+2 serum. In the first month, male and female VDD weighed less than their respective controls (69±2 vs 78±2 g in M-CTRL and 66±2 vs 76±1 g in F-CTRL) showing a delay in the development, but they recovered weight in the 60 days post-weaning. At 180 days, Extensor digitorum longus (EDL) muscle from the M-VDD showed a decrease (20 %; $p<0.05$) in the number of total fibers but an increase in the cross-sectional area of IIB (17 %; $p<0.05$), IIA (19 %; $p<0.05$) and IIAX (21%; $p<0.05$) fibers. The fiber hypertrophy was accompanied by the activation of the myogenic program as indicated by the higher protein levels of MyoD (43%; $p<0.05$) and Myogenin (160%; $p<0.05$) and in the number of satellite cells (128.8±14 vs 91±7.6 nuclei Pax7+ in the M-CTRL ). Moreover, M-VDD showed an increase in the levels of serum insulin (INS), mRNA IGF-I, and Glut4 protein, as well as in the phosphorylation levels of IGF-1/INS receptor and different INS downstream targets related to protein synthesis including Ser 473 Akt and Ser 21/9 GSK-3β. These changes were not found in Soleus from the M-VDD group and in both EDL and Soleus from the female offspring. Consistently with muscle hypertrophy, EDL from M-VDD showed attenuation in the decline of post-fatigue specific force (FSF) (78%) and specific tetanic force during the fatigue protocol (66% ) indicating fatigue resistance. On the other hand, Soleus showed lower FSF in the pre and post-fatigue conditions (39% and 62% respectively) as well as a decrease in force production (~45%) during fatigue induction indicating a functional impairment.

Conclusões/Conclusions: Maternal VDD differentially affects the development and function of male offspring rat skeletal muscles. While EDL develops type-II muscle fiber hypertrophy, activation of myogenesis, and attenuation in the decrease of FSF and fatigue resistance, Soleus shows impairment in these functional parameters. The muscle protein accretion and myogenesis are probably due to the activation of the INS/PI3K/Akt signaling pathway, which leads to the inactivation of GSK-3β. Muscles from female offspring seem to be protected from this metabolic disturbance showing a clear sex-specific effect induced by maternal VDD. Support: FAPESP (19/06517-1; 18/10089-2).

Palavras Chave/Key-words: VITAMIN D DEFICIENCY; SKELETAL MUSCLE DEVELOPMENT; PROGRAMMING

ID: 3738

Área: DOHaD and abuse drugs

Forma de Apresentação: ORAL

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Direct calorimetry is widely used to study molecular interactions of bio-molecules, to elucidate the thermodynamics of physiological processes, or direct calorimetry is simply used as an analytical tool for the determination of bacterial contaminations and the investigation of drug effects in single cells, isolated tissues, mini-organs, and small multicellular organisms.

Here, a miniaturized calorimeter will be presented, which allows the determination of the heat dissipation of tissue samples in a very simple manner. The heat measurement is based on a silicon thermopile chip with a heat power resolution of less than 20 nW. Practically any kind of sample can be investigated: high- density cell suspensions, small pieces of tissue, mini-organs, and small animals. A special facility allows the monitoring of drug treatment effects.

ID: 3485

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: FECAL SHORT-CHAIN FATTY ACIDS IN ADULTHOOD: ASSOCIATIONS OF EARLY LIFE EVENTS AND DIETARY CONSUMPTION IN THE NUTRITIONIST'S HEALTHY STUDY

Embasamento/Background: Environmental factors in early life years such as type of delivery and breastfeeding, modulate, at least partially, the development of early human gut microbiota composition, which is formed until the first three years of life. The period of food introduction is an opportunity to start good eating habits. Consumption of different types and proportions of foods and/or nutrients also strongly influences the development of gut microbiota. The short-chain fatty acids (SCFA) are produced by gut microbiota fermentation of dietary fiber and exert favorable systemic effects in metabolic homeostasis. The aim was to investigate associations between fecal SCFA in adulthood with type of delivery, duration of breastfeeding, food preferences in the first two years of life, and actual dietary consumption.

Métodos/Methods: Cross-sectional study approved by the Ethical Committee of UNICAMP CAAE 79775817.4.1001.5404 conducted with 111 young women, undergraduates or nutrition graduates. Early life events (type of delivery, breastfeeding duration, and food preferences in the 1st and 2nd years of life) were recalled. The usual food intake in adulthood was assessed by a food frequency questionnaire previously validated. Daily energy and nutrient intakes (total carbohydrate, fructose, sucrose, glucose, total fat, saturated/monounsaturated/polyunsaturated/trans fatty acids, protein, sodium and total/soluble/insoluble fiber were estimated considering the USDA National Nutrient Database for Standard Reference. Fecal concentration of SCFA was quantified using gas chromatography coupled with mass spectrometry. Spearman's rank correlation coefficient test and Mann-Whitney U test were applied.

Resultados/Results: Median age was 28 (IQR 24;31) and BMI was 24 (IQR 18;30). The delivery by cesarean was 62% and the median duration of breastfeeding was 9.5 months (IQR 3;11), which were not associated with fecal SCFA in adulthood (p>0.05). Concerning food preferences, participants who reported preference, in the 1st year of life, for candy (p=0.007) had lower fecal concentrations of acetate and for salty cracker (p=0.031) and porridge with sugar (p=0.047) for propionate. In the 2nd year of life, the preference for fruits was positively associated with butyrate (p=0.021); while negative associations were found by the preferences for: salty cracker with propionate (p=0.003), chocolate milk with propionate (p=0.032) and butyrate (p=0.039), and cheese with acetate (p=0.046). Participants with preference for candy in early-life had current higher consumption of energy (p=0.027), sodium (p=0.011), total fat (p=0.016), protein (p=0.045), saturated (p=0.005), monounsaturated (p=0.027), polyunsaturated (p=0.046) and trans fatty acids (p=0.008). Preference for porridge with sugar was positively associated with current consumption of total fat (p=0.016), saturated (p=0.005), monounsaturated (p=0.027) and polyunsaturated fatty acids (p=0.046).

Conclusões/Conclusions: Type of delivery and duration of breastfeeding were not associated with fecal SCFA in adulthood. Early-life preference for foods rich in sugar, fat and sodium were negatively associated with fecal SCFA; and preference for fruits was positively associated with SCFA. The results reinforce the importance of food introduction in the modulation of gut microbiota, its metabolites and food habit in adulthood.

Palavras Chave/Key-words: gut microbiota; short-chain fatty acids; first 1000 days of life

ID: 2981

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: A Maternal Diet Enriched In Extra Virgin Olive Oil Prevents Alterations In Placental Morphology And Overactivity Of Matrix Metalloproteinases In Maternal Blood In Gestational Diabetes Mellitus Pregnancies.

Embasamento/Background: Gestational diabetes mellitus (GDM) is a prevalent disease that increases the risks of maternal, fetal and placental complications and leads to the programming of metabolic and cardiovascular diseases in the offspring. The placenta is relevant in fetal programming and changes in its morphology are associated to an adverse programming in different maternal diseases. Matrix metalloproteinases (MMPs) are proteolytic enzymes highly relevant in development, but markers of a pro-inflammatory state when produced in excess. GDM is associated to an intrauterine proinflammatory environment. At term, GDM pregnancies show increased MMPs activity in the placenta, an alteration that may also occur in maternal blood. Our recent studies have shown that a dietary supplementation with extra virgin olive oil (EVOO) is capable of preventing increased maternal weight gain and circulating triglycerides, as well as modulating MMPs overactivity in the placenta. In this work, we hypothesized that a maternal diet enriched in EVOO modulates placental macroscopic morphology, circulating total and HDL-cholesterol levels and maternal blood MMPs activity in women with GDM.

Métodos/Methods: Fifty heathy (Control) and GDM patients were enrolled after signing an informed consent (protocol approved by the Ethics Committee of Hospital General de Agudos Dr. Ignacio Pirovano, Buenos Aires), and all of them were advised to follow the WHO diet for pregnancy. GDM patients were randomized to receive or not a daily dietary supplementation of EVOO (three tablespoons) from diagnosis (week 24-28 of gestation) until delivery. Blood from the mothers was obtained at diagnosis and at term (weeks 37 of gestation). Cholesterol levels (colorimetric assay) were evaluated at term, and the gelatinolytic activity of MMPs was evaluated both at enrollment and at term (zymography analysis). At delivery, placental morphology was evaluated.

Resultados/Results: Although the placenta diameter and perimeter were similar in the three evaluated groups (Control, GDM and GDM-EVOO groups), the placentas from the GDM group were thicker compared to the Control group (15%, p<0.05), an alteration prevented by the EVOO-enriched diet (p<0.05, GDM-EVOO vs. GDM). Total cholesterol and HDL-cholesterol in maternal blood showed no changes in the three experimental groups evaluated. The activity of MMP-2 showed no changes in the three experimental groups evaluated both at GDM diagnosis and at term. MMP-9 activity was unchanged at enrollment but increased in maternal blood of the GDM group at term (81%, p<0.01 vs. Control group), an alteration prevented by the diet enriched in EVOO (p<0.05 vs. GDM).

Conclusões/Conclusions: Maternal GDM led to increased placental thickness, an alteration that may impair the placenta transport function and may cause programming effects. The maternal dietary treatment enriched in EVOO was able to prevent this placental alteration in GDM patients. The increase in MMPs activity observed in maternal blood in GDM pregnancies is similar to that previously observed in GDM placentas. The capacity of EVOO dietary treatment to prevent MMP overactivity in maternal blood evidences its beneficial effects in the mother, and identifies MMP activity as a putative biomarker of EVOO maternal consumption.

Palavras Chave/Key-words: MATERNAL DIET, GESTATIONAL DIABETES, PLACENTA, OLIVE OIL

ID: 3501

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal High-fat diet during periconceptional period and gestation-lactation, alters body weight and glucose tolerance.

Embasamento/Background: Obesity currently causes around 34 million deaths worldwide. One of the origins of obesity can be through maternal effects. Previous studies have suggested that maternal high fat diet (HFD) can affect the normal development making the offspring prone to diseases such as diabetes, cardiovascular diseases, and obesity. Here, we propose that maternal HFD during gestation and lactation, or just during the periconceptional period, in the absence of obesity, affects the metabolism in the adult offspring mice.

Métodos/Methods: MF1 female mice were divided into three different diet groups from conception: Control Fat Diet group (CFD, females were fed with a chow diet from SDS-UK-801151), Embryonic HFD group (EmbHFD, females were fed with HFD between day 0.5 to 3.5 of pregnancy, HFD from SDS-UK-824053), and HFD group (females were fed with HFD from conception until end of lactation). The chow diet contained Fat:7.5%Kcal, Protein:17.5%Kcal, and Carbohydrates: 75%Kcal. The HFD contained Fat:45%Kcal, Protein:20%Kcal, Carbohydates:35%Kcal. After weaning, all the offspring were fed with the CFD until 15 weeks of age. The offspring phenotype was analyzed through weekly bodyweight measurements and the glucose tolerance testing (GTT), at 9 and 13 weeks of age. The groups were compared by one-way ANOVA or two-way ANOVA followed a posthoc Tukey test, and for GTT analysis the area under the curve (AUC) was used for the analysis.

Resultados/Results: Maternal HFD leads to significant differences in bodyweight in the offspring. EmbHFD males had decreased body weight ($n=9$, week 2 and 9 $p<0.01$, and weeks 7 and 8 $p<0.001$) and HFD males had increased body weight ($n=6$, weeks 2 and 3 $p<0.0001$) compared to the CFD ($n=9$) males. Also, the EmbHFD gain less weight than HFD (weeks 2 and 3 $p<0.0001$, week 4p $p<0.01$, weeks 6, 7, 8 and 9 $p<0.05$). In females, the EmbHFD group showed a decreased body weight ($n=8$, week 1 $p<0.05$, weeks 2 and 3 $p<0.0001$, weeks 4, 5, 6, 7, 8 and 9 $p<0.01$) and HFD group showed body weight increased ($n=6$, weeks 2 and 4 $p<0.05$, week 3 $p<0.01$) compared to the CFD ($n=7$) group. There were differences between EmbHFD and HFD females (weeks 2 and 3 $p<0.001$, weeks 4, 5, 6, 7 and 8 $p<0.01$ and week 9 $p<0.05$). We observed that males gained more weight than females from the 4th to 9th weeks ($p<0.01$). GTT data were analyzed in the offspring at 9 and 13 weeks of age. A significant decrease in the AUC was found in the EmbHFD group compared to the CFD group (males $n=9$, $p<0.01$, females $n=8$,$p<0.05$). In the 13th week, the AUC was reduced in HFD females compared to the CFD females ($p<0.05$).There was a significant decrease in females compared to males in the HFD group ($p<0.05$). We observed lower AUC values in EmbHFD and HFD females compared to EmbHFD and HFD males ($p<0.01$, and $p<0.05$ respectively).

Conclusões/Conclusions: Our preliminary data showed that maternal HFD without obesity affected the offspring's physiology. EmbHFD showed lower body weight from the 7th week compare to CFD, which may support the idea that the HFD during the periconceptional period is critical for the offspring growth. Despite some studies highlighting an increased body weight after HFD during gestation and lactation, here we did not observe any difference between the CFD and HFD group from the 5th week. At 13 weeks old, we observed significant differences in GTT between males and females in the HFD and EmbHFD suggesting a sex-specific response. These results indicate that not only the maternal diet is affecting the physiology of the offspring but also the sex and time of diet exposure. Funding: The project has received funded from EU's HORIZON2020 MARIE SKŁODOWSKA CURIE ACTIONS–ITN-DohART-NET Periconceptional Programming of Health Training Network, under grant agreement 812660.

Palavras Chave/Key-words: Maternal diet, High-Fat diet, periconceptional period.

ID: 3249

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: TREATMENT WITH FIBROBLAST GROWTH FACTOR 19 (FGF-19) ATTENUATES THE DAMAGE TO MUSCLE FIBERS IN MODEL OF CEREBRAL PALSY

Embasamento/Background: Despite the known neuromotor impairments of Cerebral Palsy (CP) as a delay in the acquisition of motor skills and muscular atrophy, the current treatment is to assist the sequelae, being unable to reverse the primary musculoskeletal damages. Recently, it was demonstrated that musculoskeletal is a direct target for the Fibroblast Growth Factor 19 (FGF-19) which has a therapeutic potential to restore muscle structure in models of muscle atrophy. Although the result is promising, the literature is scarce regarding its effects on models of neurological diseases such as CP. Thus, the aim of the present study was to evaluate the effects of treatment with FGF-19 on the musculoskeletal of rats submitted to experimental CP.

Métodos/Methods: This is an experimental study approved by the ethics committee on animal experimentation at the Center for Biological Sciences at the Federal University of Pernambuco campus Recife - PE, Brazil (CEUA: 0011/2017). Male Wistar rat pups were used, divided into the experimental groups: Vehicle (V, n = 11), Vehicle + FGF19 (F, n = 10), PC + Vehicle (PCV, n = 12) and PC + FGF19 (PCF, n = 13). The experimental PC model performed associated perinatal anoxia, on the day of birth and on the 1st day of postnatal life (P0 and P1), the sensory motor restriction of the hind legs, for 16h per day from P2 to P28. The pharmacological manipulation occurred daily from P22 to P28 who the animals received the vehicle solution (PBS / 0.1% BSA) or FGF19 (0.1 mg / kg in vehicle solution) subcutaneously on the back. At P29, the animals were euthanized to collect the soleus and long finger extensor (EDL) muscles, in which their absolute and relative weight were obtained. Afterwards, the muscles were frozen and through transversal cryosection (8um), the cuts were fixed on slides and stained using the myofibrillar ATPase technique. The sections were photographed under an optical microscope and analyzed using the Image J software. Thus, data were obtained regarding the area, perimeter and type of muscle fibers - type I (darker), type IIa (pale) and type IIb (gray). The data were analyzed using the Kolmogorov Smirnov normality test, the ANOVA Two Way test followed by the Tukey post-test, considering $p < 0.05$

Resultados/Results: The PC vehicle animals showed characteristics of muscular atrophy observed through the lower absolute and relative weight of the soleus and EDL muscles ($p < 0.05$) and smaller area and perimeter of both muscles ($p < 0.05$) compared to the group control. Treatment with FGF-19 was able to reduce muscle loss resulting from the CP model, promoting an increase in the absolute weight of the soleus and EDL muscles ($p < 0.05$), as well as an increase in the relative weight of the EDL muscle ($p < 0,05$), in addition to promoting an increase in the area and perimeter of the muscle fibers of both muscles ($p < 0.05$). As for the proportion of types of muscle fibers, experimental CP resulted in an increase in type I fibers in the soleus muscle ($p < 0.05$) and type IIb fibers in the EDL ($p < 0.05$), and reduced type IIa fibers in EDL ($p < 0.05$). Treatment with FGF-19 reversed the effect of this model on the EDL muscle, reducing type IIb fibers and increasing type Iia fibers ($p < 0.05$).

Conclusões/Conclusions: The CP model was able to promote long-term musculoskeletal damage similar to CP in humans, being evidenced in this study through muscle atrophy and changes in the types of muscle fibers in the soleus and EDL. And the treatment with FGF19 reduced the damages resulting from the experimental CP, attenuating the muscular atrophy in both muscles and reversing the changes in the type II fibers of the EDL muscle.

Palavras Chave/Key-words: Animal models, skeletal muscle, atrophy, phenotypic plasticity.

ID: 3253

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal diets enriched in sunflower and chia oil administrated during early postimplantation prevent morphological anomalies in the fetus, decidua and placenta of diabetic rats at day 14 of pregnancy

Embasamento/Background: The postimplantation period is crucial for the embryo development and the correct establishment of the future placenta. The decidua plays an essential role in this process and its impaired function may lead to embryo resorption. Diabetes mellitus is a metabolic pathology that affects decidual, embryo and placental development. In the rat, the decidua from day-9-pregnant rats showed alterations in both PPAR and mTOR pathways. PPARs are involved in lipid metabolism, development and antioxidant pathways whereas mTOR is a nutritional sensor involved in cell growth, proliferation and migration. We previously found that decidual PPAR and mTOR pathways are regulated by diets enriched in sunflower oil (rich in PUFAs n-6) or chia oil (rich in PUFAs n-3) in 9-day-pregnant diabetic rats. Here, we hypothesized that maternal diets enriched with sunflower and chia oil, administrated from days 7 to 9 of pregnancy, can improve fetal, decidual and placental growth in 14-day-pregnant diabetic rats.

Métodos/Methods: Diabetes was induced in female rats by streptozotocin administration (50 mg/kg) two weeks before mating. Diabetic rats received a standard diet or a diet enriched either in 6% sunflower oil or 6% chia oil from days 7 to 9 of pregnancy. On day 14 of pregnancy, the fetus, decidua and placenta were explanted. The cephalic length was measured in the fetuses and the placenta and decidua were weighed. The resorption rate was registered.

Resultados/Results: We found an increase in the resorption rate in the diabetic group (120%, $p<0.01$ vs control group), which was not prevented by the maternal diets enriched in PUFAs. The cephalic length was decreased in fetuses of the diabetic group (7.5%, $p<0.05$ vs control group), an alteration prevented by the diet enriched in sunflower oil (7.5%, $p<0.05$ vs diabetic group) but not by the diet enriched in chia oil. Both the decidua (18.3%, $p<0.05$) and the placenta (12.4%, $p<0.05$) weights were decreased in the diabetic group. The diet enriched in sunflower oil increased the decidua weight (20.8%, $p<0.05$ vs diabetic group) to control values, whereas the diet enriched in chia oil increased the placenta weight (42.5%, $p<0.001$ vs diabetic group) to control values.

Conclusões/Conclusions: Diets enriched in PUFAs administered only on days 7 to 9 of pregnancy could not reverse the increased resorption rate in the diabetic group, but were able to prevent impaired fetal growth, measured on day 14 of pregnancy by the cephalic length. Differentially, diets enriched in n-6 and n-3 PUFAs regulate decidual and placental weight in diabetic rats. Further studies will analyze the putative mechanisms involved.

Palavras Chave/Key-words: DIABETES PREGNANCY PUFAs-DIET POSTIMPLANTATION

ID: 3518

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Effect of Long-term Nutritional Supplementation of Bulls with Polyunsaturated Fatty Acids on In Vitro Sperm Fertilizing Ability and Intracytoplasmic Lipid Content in Descendant Embryos.

Embasamento/Background: Dietary supplementation of ruminants with polyunsaturated fatty acids (PUFA) has been carried out both with the aim of increasing the energy density of the diet and also to improve reproductive performance. In males, ingested PUFA are metabolized

and then transferred to different tissues and cells, including sperm membranes where they will affect fluidity and, consequently, the in vitro sperm fertilizing ability. More recently, studies carried out in humans and rodents have shown that the paternal diet during spermatogenesis affects not only sperm, but also the metabolic state of the offspring. However, few studies have been carried out in livestock. In addition, most studies conducted to date have investigated the effects of the paternal diet on living offspring, but the evaluation of pre-implantation bovine embryos is still scarce.Thus, the aim of this study was to examine the effects of long-term dietary supplementation of young Nellore bulls (B. taurus indicus) with rumen-protected PUFA on in vitro sperm fertilizing ability and intracytoplasmic lipid content in descendant embryos.

Métodos/Methods: Twelve Nellore bulls were supplemented with rumen-protected PUFA (PUFA group; n = 6) or with base diet (control; n = 6) from 14 to 24 months of age. The semen was collected and cryopreserved when animals reached 24 months of age. The frozen/thawed semen was then used for in vitro production of embryos (IVP). Cumulus-oocyte complexes (COC) were obtained from bovine ovaries collected at a local abattoir by puncturing follicles measuring 3 to 8 mm with a 10 mL syringe coupled to an 18-G needle. Selected COCs were in vitro-matured (IVM) for 22h in IVM medium (TCM-199 with bicarbonate, 0.5 mg/mL FSH, 100 IU/mL hCG, 10% FCS and hormones) and then fertilized in vitro (IVF) using the semen of each bull belonging to each treatment. Presumptive zygotes were cultured until day 7 to evaluate the embryonic development to the blastocyst stage. The blastocysts produced with the semen of the bulls belonging to the same treatment were pooled and stained with 1% of the lipophilic dye Sudan Black B for determination of the intracytoplasmic lipid content. Stained embryos were evaluated under light microscopy. Images were analyzed using the Image J 1.50b software (National Institutes of Health, Bethesda, MD, USA) to determine the area and mean gray intensity (expressed in arbitrary units - AU) of the delimited area of each embryo. Data were analyzed by ANOVA, followed by Tukey's test ($P<0.05$).

Resultados/Results: There was no effect ($P > 0.05$) of dietary supplementation on the rates of cleavage (70.3% ± 4.4 vs 70.8% ± 4.4) or embryonic development to the blastocyst stage (37.2% ± 4.1 vs 37.9% ± 4.1) for control and PUFA groups, respectively. However, embryos produced with semen of bulls supplemented with PUFA exhibited higher ($P < 0.05$) intracytoplasmic lipid accumulation (0,340 ± 0.006 AU) than embryos descendants from bulls fed control supplement (0.324 ± 0.006 AU).

Conclusões/Conclusions: In conclusion, supplementation of bulls with PUFA did not improve the in vitro sperm fertilizing ability, but it did increase the intracytoplasmic lipid content of descendant embryos in the pre-implantation phase. Our data reveal an interesting effect of the paternal diet on an important phenotypic characteristic of the bovine embryo, considering that the increase in the intracytoplasmic lipid content negatively impacts its cryotolerance. Financial support: CNPq (#307416/2015-1), CAPES (001) and FAPESP (#2013/13696-3, #2015/06733-5 and #2019/11174-6).

Palavras Chave/Key-words: Cattle; Nongenetic inheritance; Paternal effect; Lipid.

ID: 3265

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Is Paternal Nutritional Status Associated With Birth Weight, Besides The Presence of Maternal Excessive Weight and Gestational Diabetes? Caio Bedani1, Camila Rodrigues de Souza Carvalho1, Patricia Dualib1, Rosiane Mattar1,2, Bianca de Almeida Pittito1,3.

Embasamento/Background: In Brazil and in the whole world, noncommunicable chronic diseases (NCD) are the leading causes of morbimortality, justifying the identification of and the fight against their risk factors. Nutritional status in different life stages has been shown as determinants of NCD in adulthood. There is consistent evidence that relates small and large babies for their gestational age (LGA) with child obesity and NCD in adult life. The influence of maternal nutritional status and gestational diabetes (GDM) for birth weight, specially LGA, are well established. However, it is not totally clear the role of paternal nutritional status in influencing child's birth. The objective of this study was evaluate the relationship between paternal nutritional status and the occurrence of LGA, considering the maternal nutritional status with or without gestational diabetes.

Métodos/Methods: This longitudinal study included 74 pregnant women (BMI>25kg/m2) with and without GDM (according to the IADPSG criteria), their babies (gestational birth age between 36 and 42 weeks) and the related fathers. Data from the women and babies were collected during the prenatal assistance at the Obstretic and Diabetes & Gestation outpatient clinic (2018-2020). Fathers' anthropometric data were collected by standardized questionnaire and checked twice. Parents were classified based on the BMI values as normal (18,5-24,9 kg/m2), overweight (25-29,9 kg/m2) or obese (≥30 kg/m2). The babies were classified according to birth weight as Small for Gestational Age (SGA, birth weight <10th percentile), Adequate for Gestational Age (AGA, from 10th to 90th) or Large for Gestational Age (LGA, >90th). Variables of interest were compared according to parent's nutritional status and birth weight categories.

Resultados/Results: The fathers had an average (SD) age of 34(8) years and BMI of 28(5) kg/m2, being 23(31%) obese and 10(13%) with higher education, while the mothers had age of 30(6) years, BMI of 30(4) kg/m2, being 29(39%) obese, 38(51%) with GDM and 21(28%) with higher education. Obese fathers did not show a significant difference in the frequency of obese mothers (39% vs 39%, p=0,99) or GDM (60% vs 47%, p=0,27) when compared to non-obese fathers. The birth weight average was 3,3(0,5) Kg, being 4(5%) classified as SGA and 15(20%) as LGA. The LGA group presented higher pre-pregnancy maternal (84,7(12,4) vs 75,2(11,2)Kg, p=0,006) and paternal weight (95,0(30,7) vs 84,8(14,2)kg, p=0,067) when compared to the AGA group; within results without statistic significance, we observed lower frequencies of paternal (7,1 vs 14,5%, p=0,41) and maternal (20,0 vs 27,3%, p=0,41) higher education, and greater of paternal (14,5 vs 7,1%, p=0,41) and maternal (53,3 vs 32,7%, p=0,12) obesity and of GDM (60,0 vs 45,5%, p=0,24), in the LGA vs AGA groups, respectively. Gestational weight gain did not differ between babies' groups. The LGA prevalence was 20% when neither parents were obese, 12.5% when one of them was obese and 62.5% when both parents were obese.

Conclusões/Conclusions: The results show that not only mothers but also fathers of LGA babies had higher weight when compared to AGA parents. Most notably, we observed a greater prevalence of LGA babies when both parents were obese. It is important to emphasize that the group of obese fathers was not associated with higher frequencies of mothers with obesity or GDM. The father's nutritional status seems to influence the baby's birth weight. Paternal obesity contributed to a higher occurrence of large babies for gestational age, even considering

the mother's nutritional status and the status of gestational diabetes. This data corroborates with the hypothesis that, in addition to the pre-gestational weight and GDM status of the mother and weight gain during pregnancy, the father's weight must also be considered when thinking about LGA prevention strategies. Financial Support: Sponsorship provided by PIBIC-CNPq; FAPESP (project 2018/14795-9).

Palavras Chave/Key-words: paternal obesity, maternal obesity, gestational diabetes, birth weight, large for gestational age

ID: 3291

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Changes in Sperm Quality of the Offspring Caused by Diet-Induced Maternal Overweight Meneghini, María Agustina, Flores Quiroga, Jeremías Pablo, Cortez, Analía Elisabeth, Faletti, Alicia Graciela Centro de Estudios Farmacológicos y Botánicos (CEFYBO-

Embasamento/Background: Maternal obesity has become a stressor factor during the fetal programming that represents an important health determinant in the offspring during childhood and adult life. The risk of developing pathologies in the offspring has a direct relation to the degree of overweight or severity of maternal obesity. Previously, we demonstrated that male offspring from rats fed with a high-fat diet exhibited higher body and testis weight, greater ano-genital distance, altered puberty and a high level of testosterone with normal glycemia. Also, offspring from rats with different degree of obesity showed a lower number of germ and somatic cells, altered morphology in spermatozoa and motility, and abnormal spermatogenic process. Thus, the aim of the present study was to continue studying the effect of maternal overweight, induced by diet with high-fat content, on both the quality and function of sperm.

Métodos/Methods: To this end, at 22 days of age, female Sprague Dawley rats were fed with a standard (SD) or high-fat diet (cafeteria diet, CD) continuously until weaning of their offspring. All male offspring (OSD and OCD, respectively) were fed with SD, inspected periodically and euthanized at 60 days of age. Sperm capacitation by acrosomal reaction, the presence of the reactive oxygen species by flow cytometry in the germ cells using a fluorescent probe (2',7'-dichlorofluorescein diacetate), DNA fragmentation by Tunel kit, mitochondrial function using the probe 3.3'-diaminobenzidine, the membrane functional status by hypoosmotic swelling test, and the presence of abnormal chromosomes by cytogenetic assay (Evan test), were examined.

Resultados/Results: Compared with OSD rats and expressed as percentage, OCD group showed a decrease in the acrosome-reacted sperm (57+/-3 vs 69+/-2, $p<0.01$), hypoosmotic-reacted sperm (15+/-1 vs 23+/-2, $p<0.01$), and an increase in the abnormal metaphases (6+/-1 vs 2.1+/-0.7, $p<0.001$). Likewise, OCD rats exhibited a reduction in the testis and epididymal index (x 1000) (4.1+/-0.1 and 0.90+/-0.02, respectively, $p<0.01$) compared with OSD (4.5+/-0.1 and 1.04+/-0.03, respectively).No differences were found in the Tunel positive cells, but OCD exhibited higher fluorescein intensity expressed as relative units (577+/-74, $p<0.01$) compared with OSD (233+/-27). Finally, 50% of OCD rats displayed a lower mitochondrial activity, expressed as percentage (94.8+/-4 vs 97.7+/-0.4 from OSD, $p<0.01$).

Conclusões/Conclusions: These results indicate that diet-induced maternal overweight affect the sperm quality of the offspring, likely leading to a decrease in the reproductive capacity. Financial support: PICT 2015-0588, Fondo para la investigación Científica y Tecnológica (FONCYT) and UBACYT 20020170100130BA, Universidad de Buenos Aires.

Palavras Chave/Key-words: Maternal overweight, Offspring, Sperm quality.

ID: 3039

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Developmental Programming: Intrauterine Caloric Restriction Promotes Upregulation Of Mitochondrial Sirtuin With Mild Effects On Oxidative Parameters In The Ovaries And Testes Of Offspring

Embasamento/Background: According to the developmental origins of health and disease (DOHaD) hypothesis, the maternal environment can influence early embryo and fetal development, modulating the offspring's lifelong health, even conferring resistance to diseases. In Western society, most of the population has a sedentary lifestyle, with a diet that consists of a high intake of low-quality food, leading to growing obesity ratios. In this context, increasing number of studies have demonstrated the biological advantages of caloric restriction (CR). Despite this, little is known about the effects of gestational CR in the offspring. We evaluated some antioxidant parameters and molecular mechanisms of action on the reproductive organs of offspring, delivered to gestational CR dams.

Métodos/Methods: This study assessed the effects of moderate intrauterine (20%) CR on reproductive organs of the adult offspring. Pregnant Wistar rats were divided into two groups: control, that received water and chow ad libitum, and CR group, that received 20% less commercial chow than the control group. To ensure similar micronutrient consumption between groups, CR dams were supplemented daily with a multivitamin and mineral mix via oral gavage. To ensure the 20% CR protocol was maintained correctly, all rats from both groups

were weighed daily throughout pregnancy, and their diet was adjusted according to body weight using the consumption of the control group as a standard for the chow given to the CR group. On postnatal day 60 (PND 60), female and male littermates were euthanized, the ovaries and testes dissected out in a Petri dish for the analysis of redox status parameters, molecular expression of sirtuin (SIRT) 1 and SIRT3 and histopathological markers. Maternal uteri was dissected on PND 0 (of non pregnant dams) and PND 21 (of pregnant dams, post-weaning) for implantation index analysis. The study procedures were approved by the local ethics committee (Comissão de Ética no Uso de Animais/ Universidade Federal do Rio Grande do Sul; Permit no. 34056) and the study was performed in accordance with national and international animal rights regulation. All efforts were made to minimize the suffering of the animals used.

Resultados/Results: Although antioxidant enzyme activity was increased, ovaries from female pups contained high levels of oxidants, as evidenced by augmented levels of DCFH and MitoSox. Conversely, testes from male pups had decreased antioxidant enzyme defenses, as evidenced by diminished glyoxalase I activity and reduced glutathione content. Expression of SIRT3, a deacetylase enzyme related to cellular bioenergetics, was increased in both ovaries and testes in the CR group. Previous studies have suggested that, in ovaries, diminished antioxidant network can lead to premature ovarian failure. Although testes' decreased antioxidant function, there is little information regarding the redox profile in the testis, according to the available studies from other groups.

Conclusões/Conclusions: This study is the first to assess the redox network in both ovaries and testes, suggesting that, although intrauterine CR improves molecular mechanisms, it has a negative effect on the antioxidant network and redox status of reproductive organs of young adult rats.

Palavras Chave/Key-words: nutrition, early development, pregnancy, reproduction.

ID: 3050

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: ORAL

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Título/Title: Antecipation Of Puberty in Bisphenol A Treated-Female Rats Is Related To Alterations In The Pattern Of Kisspeptin Expression

Embasamento/Background: Bisphenol A (BPA) is still widely used in the production of plastics and epoxy resins for the production of food and beverage packaging. BPA is classified as endocrine-disrupting chemical because of its weak action in estrogen receptors, anticipating the beginning of puberty in female rats. Peripubertal period is an important window of sensitivity due to the start of the GnRH pulses and activation of gonadal function. Disturbances in this phase may compromise the regulation of hypothalamic-pituitary-gonadal axis in adulthood. In this sense, this study aims to evaluate the status of hypothalamic activation in peripubertal period to verify the mechanisms underlying the anticipation of puberty in female rats.

Métodos/Methods: For this, sixty female Wistar rats recently weaned were divided into two groups and treated with 0 or 5 mg BPA/kg by gavage from Post Natal Day 22 (PND) to PND44 (CEUA 02/2019). Pubertal development was verified by the opening of the vaginal canal. Body growth was assessed by daily weighing. Hypothalamus was collected in three moments: pre-puberty, at puberty and after puberty detection; quickly excised, frozen in liquid nitrogen and stored in ultrafreezer. Total RNA from whole hypothalamus was extracted by guanidine-phenol-chloroform method and the relative expression of the genes in the hypothalamus (Gnrh1, Kiss) was performed by RT-qPCR. The relative expression was calculated by 2-ΔΔCt method using Rpl19 as internal control. Statistical analyzes were performed by planned comparisons between groups (0 and 5 mg BPA/kg) and developmental phase (pre-puberty, puberty and postpuberty), using two-way ANOVA and posthoc tests of Sidak and Dunnet ($p<0,05$) with resources of the software GraphPad Prism 6.0.

Resultados/Results: BPA did not alter growth during the evaluated period, but it anticipated age to puberty. In the control group, the transcript expression of the kisspeptin increased at puberty compared to pre-puberty and decreased again in the post-puberty period to the values observed in pre-puberty. Exposure to BPA affected its expression in the post-puberty period, maintaining high levels in comparison to both pre- and puberty. Regarding the expression of the Gnrh1 transcript, a decreasing abundance was observed in the control group between the three studied phases. The group treated with BPA showed an increase in its expression in post-puberty, without demonstrating the decreasing pattern of the control group.

Conclusões/Conclusions: The anticipation of puberty in female rats exposed to BPA is related to changes in the expression of kisspeptin which related to the triggering of Gnrh synthesis and secretion. Further studies are necessary to assess the impact of these changes across the hypothalamic-pituitary-gonadal axis.

Palavras Chave/Key-words: BPA, endocrine-disrupting chemicals, hypothalamic-pituitary-ovarian axis.

ID: 3065

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Diet Interventions Impact Gene Expression Of Prlr And Esr1 In The Adipose Tissue And Hypothalamus Of Mice Dams

Embasamento/Background: A growing number of studies are focusing on the repercussion of the maternal nutritional status, during pregnancy and lactation, in the offspring. They have demonstrated that early diet interventions can impact the physiological programming. These results contribute to the understanding of how the maternal diet can affect fetal programming, through epigenetic mechanisms that

modify the gene expression. Thus, our objective was to analyze the effects of a hypercaloric or restrictive diet on the gene expression of prolactin (Prlr) and estrogen alpha (Esr1) receptors, in the adipose tissue and hypothalamus, of mice dams.

Métodos/Methods: The Institutional Animal Care and Use Committee of UFCSPA (#388/15) approved this study. Thirty female BALB/c albino mice (60 days old) were separated in 3 different groups (n=10/group) and individually housed. To the control group (CONT) was administrated a standard mice chow ad libitum, with a total energy content of 3.4 kcal/g; the restrictive diet group (RD) had 30% reduction in the standard chow amount, compared according to the consumption of CONT group; and the hypercaloric diet group (HD) was fed with a special chow ad libitum, with total energy content of 4.9 kcal/g. Diet adaptation lasted 25 days, after they were housed with males for mating. When pregnant, they were housed in separate cages until delivery. On the first postpartum day, litters were standardized at 6 pups. After weaning, the dams were euthanized, and the tissues were collected for further analysis. Amplification products were analyzed using the SYBR™ Green method by Real-Time PCR, and the relative quantification analysis was performed according to the results of the amplification efficiency tests of the genes, by the 2-ΔΔCT method.

Resultados/Results: We did not found differences in gene expression of Prlr and Esr1 in the adipose tissue of the dams. Prlr gene expression in the hypothalamus was also evaluated, showing a decrease in RD and HD-fed dams, compared to CONT group [$F(2,16)=11.39$; $p<0.001$]. However, gene expression of Esr1 in the hypothalamus did not show any differences among the groups.

Conclusões/Conclusions: Gene expression of Prlr and Esr1 in the adipose tissue was not changed, regardless of diet received. However, it has to be taken into account that our study was performed during pregnancy and lactation, and the dams' tissue was collected right after lactation. Robust hormonal and metabolic changes occur naturally in lactating females and cause a striking raise in the blood levels of prolactin, which may be the reason we could not find changes in the gene expression of Prlr and Esr1 caused by nutritional interventions. Hypothalamus plays a central role in the regulation of energy homeostasis. Furthermore, early nutritional influences can impact the normal development and maturation of hypothalamic neuroendocrine network and physiological programming. Besides its peripheral actions to shift precursors to milk production during lactation, prolactin is also involved in hypothalamic signaling that regulates hepatic insulin sensitivity. In our analyses in the hypothalamus of the dams, we found a decrease of Prlr in RD and HD, compared to CONT. This result was different from what we showed in the adipose tissue, but it reinforces the impact of nutrition on the prolactin signaling. Financial Support: CAPES, CNPq, UFCSPA

Palavras Chave/Key-words: Restrictive Diet, Hypercaloric Diet, Prolactin Receptor, Estrogen Receptor

ID: 3067

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Naringin Supplementation During Pregnancy Alters Offspring's Redox Homeostasis and Mitochondrial Function in the Cerebellum and Striatum During Postnatal Development

Embasamento/Background: Naringin is a glycosylated flavonoid mainly found in citrus fruits. Studies using adult animal models of cognitive dysfunction have been demonstrating naringin's capacity to improve antioxidant defenses and reduce oxidative stress, thus, leading to neuroprotection. However, little is known if this supplementation might be detrimental if used during critical periods of development. The Developmental Origins of Health and Disease (DOHaD) concept postulates that interventions during the first one thousand days of life are critical to and individual's development. Thus, any interventions in the maternal diet composition, such as increased polyphenol intake or supplementation during pregnancy, can potentially modify offspring's development. Thereby, we aimed to evaluate the effects of naringin supplementation during pregnancy in the female offspring's redox homeostasis and mitochondrial function in the cerebellum.

Métodos/Methods: Pregnant Wistar rats were separated into two groups: control (vehicle) and naringin (100 mg/kg), by oral gavage during pregnancy. On postnatal day (PND) 1, 7, and 21, female pups were euthanized, and the cerebellum was dissected. Total oxidants content, mitochondrial superoxide levels, nitric oxide levels, reduced glutathione, total thiol, carbonyls, and the antioxidant enzymes activity were evaluated. We also measured mitochondrial mass and membrane potential along with mitochondrial complexes activity. Data was analyzed by Student's t test or Mann Whitney's U test and considered significant when $p < 0.05$. The research was approved by the local ethical commission (CEUA-UFRGS n° 31397).

Resultados/Results: On PND 1 we found that naringin supplementation increased reduced glutathione content but decreased complex IV activity and mitochondrial membrane potential. On PND 7, increased nitric oxide content and glutaredoxin activity were observed along with decreased mitochondrial membrane potential in female pups' cerebellum. On PND 21, naringin exposed pups showed increased reduced glutathione content, which was accompanied by decreased nitric oxide levels, catalase, and glutaredoxin activity. Also, decreased succinate dehydrogenase and complex IV activity were found on PND 21.

Conclusões/Conclusions: Our findings demonstrate that naringin supplementation to pregnant rats disrupted female offspring's redox homeostasis and mitochondrial function in the cerebellum. There were alterations detected up to PND 21, which indicates that the programming effects elicited by naringin during gestation are persistent even during postnatal development. Moreover, our results show that the effects of naringin supplementation can change according to the period of the development it is consumed, suggesting that the beneficial effects usually found in adult rodent models might actually turn to detrimental effects if the supplementation is applied during a critical period of development.

Palavras Chave/Key-words: flavonoids, pregnancy, mitochondrial function, antioxidant.

ID: 3645

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Impact of diabetes-induced fetal programming and post weaning feeding of high fat diet in adult rats– Preliminary results. Débora Cristina Damasceno1; Verônyca Gonçalves Paula1,2; Yuri Karen Sinzato1; Eduardo Kloppel1; Rafaianne Queiroz de Moraes-Sou

Embasamento/Background: There is evidence of the effects of maternal diabetes on the health of offspring. However, the influence of maternal intrauterine exposure, postnatal environment, genetic characteristics, and lifestyle in human populations is difficult to identify. Then, we aimed to create an unfavorable intrauterine environment in association with inadequate food intake (high-fat diet – HFD) to allow for studying the consequences in the metabolism of rats at adulthood. Objective: To evaluate the impact of diabetes-induced fetal programming and post-weaning consumption of high-fat diet in adult rats.

Métodos/Methods: Female rats received citrate buffer (C) or streptozotocin (D) on day 5 post-natal. In adulthood, these rats were mated to obtain female offspring, who were fed a standard diet (SD) or high-fat diet (HFD) from weaning to adulthood (n=7 rats/group): OC/SD and OC/HFD: female offspring of control mothers and received SD or HFD, respectively; OD/SD and OD/HFD: female offspring of diabetic mothers and received SD or HFD, respectively. At adulthood (day 115 of life), the oral glucose tolerance test (OGTT) was performed to evaluate fasting blood glucose and insulin levels. Next, the rats were anesthetized and sacrificed to withdraw visceral fat and obtain its relative weight. A P-value lower than 0.05 was considered a statistically significant limit.

Resultados/Results: The OC/HFD, OD/SD, and OD/HFD groups showed higher fasting glycemia compared with the OC/SD group. The OD/HFD rats had greater fasting glycemia than OD/SD group. During OGTT, serum insulin concentrations were determined, and at time 0 (fasting), the group OD/HFD presented lower insulin concentration compared with other groups. At time point 30 min, the insulin concentration was higher in the group OC/HFD than in the groups OC/SD and OD/HFD. At time-point 60 min, there is no difference between the groups. The group OD/HFD had lower insulin concentration compared with the OC/HFD and OD/SD rats at time-point 120 min. Homeostatic Model Assessment (HOMA) evaluation was performed to estimate pancreatic beta-cell function (HOMA-beta), and it was lower in both daughters of diabetic rats in relation to OC/SD and OC/HFD rats. Also, the HFD caused greater relative visceral fat weight compared with the OC/SD and OD/SD.

Conclusões/Conclusions: Conclusion: Our preliminary results showed that both the hyperglycemic intrauterine environment and the HFD consumption can damage glucose tolerance in adult offspring. In addition, the high-fat diet consumption increased visceral fat, leading to insulin alterations and lower beta-cell function. These findings suggest that an unfavorable maternal environment and inadequate feeding after weaning contributes to damage metabolism at adulthood. Financial Support: FAPESP (Process number 2016/25207-5), and CNPq Research Fellowship (coordination of Prof. Dr. Débora Cristina Damasceno), and grant of the Ph.D. scholarship by the Coordination for the Improvement of Higher Education Personnel (CAPES).

Palavras Chave/Key-words: diabetes; fetal programming, high-fat diet; insulin

ID: 3646

Área: DOHaD and exercise

Forma de Apresentação: Ê-POSTER

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Título/Title: Resistance Training with or without Blood Flow Restriction Improves Short-Term Memory in Rats Macário Aosti Rebelo, Nádia Fagundes Garcia, Enrico Fuini Puggina, Camila de Moraes, University of São Paulo, Ribeirão Preto, Brazil.

Embasamento/Background: Low load resistance training with blood flow restriction is usually used for improvements in muscle strength in special care conditions. However, there is limited information regarding the effects of this exercise approach on memory function. The aim of this study was to investigate the effect of resistance training with or without blood flow restriction, carried out three times a week, on short-term memory.

Métodos/Methods: Male Wistar Hannover rats (70 days old) were divided into four groups: Sedentary Sham (S/S, n=10), Trained Sham (T/S, n=10), Sedentary with blood flow restriction (S/BFR, n=11), Trained with blood flow restriction (T/BFR, n=9). Animals from the S/BFR and T/BFR had their right femoral artery flow restricted (blood arrival and venous return) about 36-38% and animals from sham groups were submitted to the same surgical procedures except blood restriction. Experimental protocol was approved by local ethic committee (protocol: 2016.5.80.90.4). Exercise training began two weeks after surgery procedures. The exercise sessions were carried out three times a week and consisted of climb a vertical ladder (110 cm high, 18 cm wide, 2 cm grid, 80º inclination), carrying a load (50% of 1 Maximum Repetition) for 6 sets of 10 repetitions with 1-minute rest between sets. After four weeks of exercise training, memory performance was assessed using the Object Recognition Test and the discrimination index (dI) was calculated (dI= [(time spent exploring the novel object minus time spent exploring the familiar object)/ total exploration time]).

Resultados/Results: The interval between testing sessions 1 and 2 was 30 minutes. Femoral blood flow restriction did not cause impairment on memory performance (S/SdI=0.33±0.08 vs S/BFRdI=0.37±0.03). On the other hand, exercise training improved memory performance in both groups (T/SdI=0.76±0.07 vs T/BFRdI=0.59±0.04). A weak correlation was observed between the short-term memory performance and epididymal fat mass (r=0.046, p=0.768). However result was verified between short-term memory performance and handgrip test for strength show a moderate correlation (r=-0.490 p=0.000).

Conclusões/Conclusions: The resistance training, carried out 3 times a week, was effective to improve short-term memory either with or without peripheral blood flow restriction.

Palavras Chave/Key-words: Blood Flow Restriction, Resistance Training , Short-Term Memory

ID: 3647

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Glycemic and Reproductive Profiles of Adult Female Offspring from Diabetic Rats: Preliminary Results

Embasamento/Background: During the intrauterine life, several alterations may influence both the embryofetal development and adult life of the offspring, leading to a higher risk for the appearance of diseases. The epidemiological and experimental studies show that maternal chronic diseases cause consequences in their offspring. Objective: To determine and analyze the glycemia obtained by the area under the curve (AUC) of adult offspring of rats with diabetes and the repercussions on their reproductive performance.

Métodos/Methods: Mild diabetes was induced in female Sprague Dawley rats by streptozotocin (beta cytotoxic drug) at the neonatal period. The non-diabetic females received the citrate buffer (vehicle). At adulthood, the control and streptozotocin-induced rats were submitted to an oral glucose tolerance test (OGTT) and included as mildly diabetic. Following, the rats were mated to obtain their female offspring. At adulthood, the adult offspring from control (OC) and diabetic (OD) dams were also submitted to OGTT, and next mated to obtain granddaughters from diabetic rats (GDD). The adult GDD rats were submitted to OGTT and mated with healthy male rats. The OC, OD, and GDD rats were anesthetized and sacrificed at the end of pregnancy to evaluate embryonic losses and fetal viability. For comparative analysis of the data, Tukey´s Multiple Comparison Test was used for glycemia of AUC, and Fisher´s Exact Test for proportion of variables was employed. For all statistical comparisons, a minimum confidence limit of 95% ($p<0.05$) was considered.

Resultados/Results: The rats of the experimental groups were submitted to OGTT (n=10 animals/group), resulting in greater areas under the curve (AUC) in the OD group compared with the OC and GDD rats. Then, the circulating blood glucose levels in 120 minutes of the OGTT were higher in OD rats (152 mg/dL/min) in relation to OC (110 mg/dL/min) and GDD (121 mg/dL/min). The embryonic losses before implantation were increased in OD and GDD compared with the OC rats, and fetal viability was reduced in OD relation to the OC and GDD groups.

Conclusões/Conclusions: According to the preliminary results, the adult female offspring of mildly diabetic had glucose intolerance, leading to an unfavorable intrauterine environment, which impairs embryo and fetal development. The granddaughters of mildly diabetic rats presented embryonic losses before implantation even not being characterized as glucose intolerant or diabetic. These findings show changes in the glycemic profile and maternal reproductive outcomes in adult offspring from diabetic rats, suggesting that diabetes is a chronic metabolic disease that causes transgenerational effects.

Palavras Chave/Key-words: diabetes; fetal programming; offspring; rats

ID: 3648

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Early Exposure to High-Sucrose Diet Increases Cardiovascular Lysine Acetylation and Short Chain Fatty Acids Production by Gut Microbiota in Weaned Male Rats.

Embasamento/Background: Western hypercaloric diets are known to cause important metabolic disorders mainly for its higher sugar and fat content, although some relating molecular mechanisms remain unclear. Recently, the role of post-translational protein modification, such as acetylation, has been considered as a possible mechanism by which dietary insults modulate the metabolism. Metabolites produced by intestinal microbiota, known as short chain fatty acids (SCFA), i.e. acetate, propionate and butyrate, may play a role in these alterations by acting as substrate for lysine residues acetylation. To assess the effects of post-weaning exposure to excess table sugar on the production of SCFA by the gut microbiota and its correlation with total lysine acetylation in cardiometabolic organs.

Métodos/Methods: Weaned Wistar rats were fed for 22 weeks with a high-sucrose diet (HSD, 25% sucrose, n = 7) or standard chow (CTR, n = 6). For SCFA data, fecal samples were analyzed using gas chromatography with flame ionization detection. The total protein acetylation was evaluated by SDS-PAGE of samples from liver, heart and aorta.

Resultados/Results: HSD rats showed three-fold higher levels of faecal acetate (HSD = 1524 ± 151.2 μg/g vs. CTR = 595.3 ± 67.15 μg/g) and 69.3% of faecal propionate (HSD = 398.8 ± 53.44 μg/g vs. CTR = 235.5 ± 23.14 μg/g), but decreased faecal butyrate relative percent

(HSD = 30.15 ± 4.3 µg/g vs. CTR = 55.01 ± 7.37 µg/g). Higher acetate production in HSD rats was correlated with a marginal increase of total lysine acetylation in the liver (~ 20%), but strong increase in ventricular muscle (92%) and aorta (300%).

Conclusões/Conclusions: Higher concentrations of dietary sucrose changes SCFA production profile of the gut microbiota. In addition, HSD increased total lysine acetylation in heart and aorta showing that cardiovascular alterations may be ascribed to high-sucrose-induced dysbiosis. All together, these results indicate a potential role for added sugars in the development of cardiometabolic disorders, particular if precociously introduced since childhood.

Palavras Chave/Key-words: High-Sucrose Diet, lysine acetylation and short chain fatty acids.

ID: 3651

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Post-Weaning Exposure to High-Sucrose Diet Induces Metabolic Disorders Associated to the Disruption of Gut Microbiota Homeostasis in Male Wistar Rats.

Embasamento/Background: Metabolic syndrome (MetS) is reaching epidemic incidence worldwide in parallel with the increasing prevalence of its main comorbidities, namely obesity, dyslipidemia and type 2 diabetes mellitus. In addition, changes in the gut microbiota have emerged as one of the main mechanisms responsible for these disorders, which seem to be related with environmental insults during early stages of life, such as childhood. Thus, this study aimed to investigate the effects of precocious introduction of a high-sucrose diet, following breastfeeding cessation, on glycolipid metabolism and intestinal microbiota of weaned male rats.

Métodos/Methods: Wistar rats were fed a 25% sucrose-rich (HSD; n=8) or regular chow (CTR; n=6) for 22 weeks. Body weight and energy intake were measured throughout the nutritional challenge period. At its end, glucose (GTT) and insulin (ITT) tolerance tests were performed. Blood samples were collected for determination of glucose, triglycerides, total cholesterol, free fatty acids and insulin serum levels. Insulin resistance was estimated by TyG index calculation. Liver samples were collected for histological analysis using oil red staining and determination of glycogen content. Stool samples were collected and stored at -80 ºC for ulterior extraction of genomic DNA, amplification and sequencing of the 16S rRNA gene.

Resultados/Results: No differences were observed between groups regarding body weight, Lee Index and energy intake. However, HSD rats showed fasting and fed glucose levels augmented in 24.5 and 20.3%, respectively. This data was corroborated by the increase of serum triglycerides (134.9%), FFA (42%) and serum insulin (180%) levels, as well as TyG Index (13.2%) in HSD animals, as compared to CTR. In addition, HSD rats also showed glucose intolerance, insulin resistance, hepatic steatosis, and reduction of 47% in hepatic glycogen content. The dysfunctional metabolic profile found in HSD rats was correlated with microbiota sequencing data, which showed that excess sucrose intake modified the composition of feacal microbiota associated with increased proportions of genera from Firmicutes phylum (Blautia, Fusicatenibacter and Acetitomaculum), and decreased proportions of species from Romboutsia and Lactobacillus genera.

Conclusões/Conclusions: Therefore, the early introduction of sucrose in the diet of rats favors the development of metabolic disorders associated with MetS, such as hypertriglyceridemia, insulin resistance and hepatic steatosis. In addition, this nutritional perturbation, at early stages of development, was able to modify the gut microbiota, which may be related to the metabolic changes observed in these animals.

Palavras Chave/Key-words: metabolic syndrome, high-sucrose diet, insulin resistance, gut microbiota.

ID: 3652

Área: DOHaD and stress

Forma de Apresentação: Ê-POSTER

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Título/Title: Effects of Maternal Deprivation by Early Weaning on Feeding Behavior of Female Juvenile Wistar Rats

Embasamento/Background: Early life stress (ELS) is known to modulate the neurodevelopment of the individuals. Early weaning (EW) is a model of ELS that consists in precociously depriving pups from maternal care and breastfeeding, two important factors for a proper development. The feeding behavior is particularly sensible to early life environment, thereby we aim to investigates the effects of maternal deprivation by EW on the feeding behavior of female juvenile rats.

Métodos/Methods: This work was approved by the Animal Ethical Committee of the Federal University of Pernambuco (n. 0020/2018). Rats undergone Natural Weaning (NW) (PND30) or EW (PND15). Between PND45 and 50, female rats were food deprived for four hours and submitted to an acute injection of saline (NaCl 0.9%) or fenfluramine (10mg/kg), and the food intake was measured for a period of 1h after the injections. The same animals were tested with saline or fenfluramine, first with saline, and 72h later with fenfluramine. 72h after

the behavioral test, the animals were euthanized by decapitation and the hypothalamus was collected. RT-PCR was performed to measure the mRNA expression of Neuropeptide Y (NPY) and Protein related to gene Agouti (AgRP). Two-way Anova with tukey post-hoc was performed to analyze the food intake with and T-test to compare the effects of early weaning on the gene expression.

Resultados/Results: Fenfluramine administration decreased food intake ($P<0.01$) in EW (2,23g ± 0,47, n=10) and NW (1,42g ± 0,91, n=05), when compared to EW (3,52g ± 0,79, n=9) and NW (2,65g ± 0,58, n=06) which received saline treatment, respectively. No effects of EW were observed on saline group (NW 2,65 ± 0,58, n=06; EW 3,52± 0,79, n=9) or fenfluramine group (NW 1,42 ± 0,91, n=05; EW 2,23 ± 0,47, n=10), despite there was tendency of increased food intake in EW animals in both groups. Real time PCR demonstrated decreased mRNA expression ($2\Delta\Delta CT$) of NPY (NW, 1,0 ± 0,22, n=06; EW 0,26 ± 0,17, n=04, $p<0.001$) and AgRP (NW 1,0 ± 0,08, n=06; EW 0,28 ± 0,17, n=06, $p<0.001$).

Conclusões/Conclusions: Despite the EW modulates the gene expression of neuropeptides associated to the control of the feeding behavior, there was no statistic differences on food intake in early weaned animals, but only a tendency of increased food intake. The anorectic action of fenfluramine was effective in both NW and EW group, showing that the anorectic action of fenfluramine on food intake is not affected by early weaning in female juvenile rats. Financial support: CAPES - Finance Code 001 and PROEX 1734-2015; CNPq Universal 421752/2016-5.

Palavras Chave/Key-words: early life stress; early weaning; feeding behavior.

ID: 3653

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Okra (Abelmoschus esculentus) as Bioactive Food Attenuating Metabolic Derangements in Early Overfeeding Rats

Embasamento/Background: Obesity, characterized by the accumulation of adipose tissue, is considered as one of the major health problem around the word, burdening, herein Brazil, the Sistema Único de Saúde (SUS) due to its associated comorbidities that are a great risk factor, especially when affects people in childhood. In this study, our aim was to evaluate the effects of diet supplemented with okra (Abelmoschus esculentus, AE) on dietary behavior, body composition and biochemical parameter in adult rat offspring early overfeed.

Métodos/Methods: On the third day after birth, litter size was adjusted for 8 (control group, CONT) or 3 rats per nursing mother (small litter group, SL). At 22 days-old, rat offspring was weaned and groups subdivided into two subgroups: CONT-SD and SL-SD (rats fed a standard rodent diet) and CONT-AE and SL-AE (rats fed a standard rodent diet supplemented with 1.5% AE). Body weight and feeding behavior were accessed every two days throughout experimental period and the food intake at dark cycle assessed at 90 days-old, during the first 4 hours of dark cycle and overnight. At 100 days-old, euthanasia was performed, where blood and white adipose tissue stores collected to further biochemical and biometrical evaluation adiposity index of the animal. The Ethics Committee of the Federal University of Mato Grosso approved the experimental procedures.

Resultados/Results: SL rats were hyperphagic and 11.28% heavier than CONT rats throughout experimental period ($P>0.05$). At dark cycle, when compared to CONT-SD, CONT-AE rats ate 17.90% less in the first 4 hours ($P<0.05$). In turn, SL-AE rats ate 28.10% less than SL-SD ($P<0.05$). After 12 hours of food intake, the CONT-AE group ingested 46.20% less than the CONT-SD, while the SL-AE group ate 10.81% less than the SL-SD ($P<0.05$). The adiposity index of the SL-SD group was 19.32% higher than the CONT-SD rats ($P<0.05$). On the other hand, no statistical difference was observed in these parameters in the rats supplemented with AE diet, compared to their respective controls ($P>0.05$). AE supplementation reduced the glucose of SL rats by 22.49% compared to the SL-SD group ($P<0.05$).

Conclusões/Conclusions: Dietary supplementation with AE decreased hyperphagia and consequently fat mass index, as well as reduced blood glucose in obese rats.

Palavras Chave/Key-words: Childhood obesity; hyperfagia; metabolic programming.

ID: 3654

Forma de Apresentação: Ê-POSTER

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Título/Title: Carcinogenesis in the ventral prostate of offspring older rats exposed to maternal low protein diet. Role of microRNAs

Embasamento/Background: In the last decades, it has been observed an increase in the incidence of metabolic disorders, such as obesity, diabetes and even some types of cancer. Epidemiological evidence show that these diseases can originate from insults suffered by individuals during the intrauterine life, a condition known as Fetal Programming (FP). In this context, the increase of large-scale sequencing technologies based on the combination of "omes" (transcriptome, MicroRNAome) using bioinformatics tools has enabled a global integrative view of

molecular mechanisms in normal and pathological conditions. Here we analyzed the global expression of microRNAs (microRNoma) in offspring rat prostate born from dams fed low protein diet during gestation and lactation, to identify molecular pathways involved in the development of prostatic lesions.

Métodos/Methods: For that, male offspring rat (540 days old) born from dams fed standard diet (17% protein) or with low protein diet (6% protein) during gestation and lactation will be used. After this period, the animals were euthanized, and the ventral prostate was collected. Global expression profiles of microRNAs were analyzed by next-generation sequencing (HigSeq-2500 Illumina). After this, we performed a comparative analysis of these data with databases between the experimental groups. Initially we filtered the miRNAs by enrichment in the KEGG database, after this, in order to select the most prostate cancer-related targets we identified differentially expressed genes between normal and cancer samples using Genotype-Tissue Expression (GTEx) with 221 patients/samples and PCa (Prostate Cancer) human samples extracted from RNA-seq data using Prostate Adenocarcinoma (TCGA, The Cancer Genome Atlas Program) with 488 patients/samples data analyzed using the GEPIA database.

Resultados/Results: From All small RNA sequences analyzed we identified 452 miRNAs expressed in the prostate of both groups. We performed a differential expression analysis with a cut-off of adjusted p value < 0.05 and identified 57 miRNAs differentially expressed, the miRNAs were downregulated in the GLLP group, In order to optimize the results sought by the ortholog genes of rats in human, since a library of data validated in humans is wider. We were able to observe the correspondence of 43 human orthologous miRNAs. These 43 miRNAs were analysed in the enrichr tool, where 20 of them enriched for cancer-related processes. since this work aims to evaluate targets related to prostate cancer that developed in old animals of the GLLP group, we find it convenient to select these miRNAs to proceed with the analyses. After select these 20 miRNAs, we use the mirwalk tool to analyze the targets already validated for these miRNAs, thus 6,344 targets were observed. The End to refine the search for interesting targets, these targets were validated crossed with PCA databases of TCGA. From this match it is possible to observe the intersection between the two data sets, where 643 genes are common. From these, we use the enrichr tool to perform the ontological enrichment analysis, among the most enriched terms we focus on the terms “prostate” and “carcinoma” that were enriched respectively in the Human Gene Atlas and Jensen DISEASES databases. From these two term enrichments, we reached 22 genes that enriched both terms at the same time. Thus, we managed 22 validated target genes (ABCC4, ABHD2, ALDH1A3, CRISPLD2, DEGS1, EDNRA, FLNA, IDH1, JAG2, LAMP2, MYH11, MYLK, NKX3-1, PDLIM5, PMEPA1, POGZ, RAB3B, RDH11, SLC16A5, SLC39A6, SLC45A3 and SMTN) that were observed in enrichment analysis, we believe that these molecules may be important inducers of prostate cancer in these animals subjected to maternal protein restriction.

Conclusões/Conclusions: Validation analyzes using RNA samples from these same animals may point to this real change, which may generate interesting results for the detection of possible therapeutic targets for prostate cancer.

Palavras Chave/Key-words: DOHaD, maternal low protein, microRNAs, ventral prostate.

ID: 3655

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Gestational or gestational/lactational hypothyroidism and its renal effects to the young and adult offspring from wistar rats

Embasamento/Background: When the intrauterine environment is perturbed by adverse stimuli such as smoking, drugs, stress, infections, endocrine diseases, among others, the offspring may have its development compromised and present diseases in adulthood. Thus, the objective of this study was to evaluate renal functional and structural changes in young and adult offspring from Wistar rats exposed to hypothyroidism only during pregnancy or during pregnancy and lactation.

Métodos/Methods: For this, the 30 and 90 days-old (D) female pups were divided into 3 groups: CONTROL (C) - pups from dams exposed to euthyroidism during pregnancy and lactation; EXPERIMENTAL 1 (E1) – pups from dams exposed to gestational hypothyroidism and EXPERIMENTAL 2 (E2) – pups from dams exposed to gestational and lactational hypothyroidism. The thyroid disturb (hypothyroidism) was induced by methimazole 0.02% diluted in drinking water. Maternal liquid and food intake, as well as bodyweight were evaluated during pregnancy, while the thyroid hormone measurements were performed on the 5th day of lactation. Functional parameters such total cholesterol (TC), triglycerides (TG), T3 and T4 plasmatic levels, glomerular filtration rate (GFR), Urinary Protein Excretion (UPE), Systolic Blood Pressure (SBP) and Heart Rate (HR) were evaluated in the 90D female pups and parameters such bodyweight, renal relative weight, alpha-actin expression, number of proliferating cells and renal corpuscle, glomerular tuft and capsular space areas were evaluated in the 30 and 90D female pups. The one-way ANOVA with Tukey`s post-test was used for statistical analysis of maternal data and T3/T4, renal relative weight, TC, SBP, HR, GFR, corpuscle and glomerular tuft areas, number of proliferating cells and alpha-actin expression of offspring. Kruskall-Wallis with Dunn´s post-test was used for bodyweight, TG, UPE and capsular space area of offspring. The significance level adopted was $p<0.05$.

Resultados/Results: There were no differences between groups for maternal parameters such as water and food intake and weight gain during pregnancy, but dams from E2 had lower T3 and T4 levels, compared to C and E1 groups. The 30D pups from the experimental groups had lower bodyweight, while only the pups from E2 had lower renal relative weight. Data such as TC, TG, SBP and HR were not different between groups, but GFR and UPE were lower in E2, when compared to controls. The 30D experimental animals presented smaller renal corpuscle and glomerular tuft areas, but this last change was only maintained in the 90D animals from E2, as well as an increase in capsular space. The number of proliferating cells was higher in the tubulointerstitial (TBI) compartment from 30D experimental animals, as well as an increase in the expression of TBI alpha actin, but only in E2. T3 levels were only reduced in 90D animals from E2, while the T4 levels were not different.

Conclusões/Conclusions: Maternal hypothyroidism is capable of programming important renal structural changes in the young offspring from Wistar rats, which can result in impaired kidney function in adulthood. These changes are more evident when maternal hypothyroidism is maintained from pregnancy to lactation.

Palavras Chave/Key-words: maternal hypothyroidism, renal function, offspring, Wistar rats.

ID: 3656

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: The intrauterine and postnatal conditions like maternal low protein diet and postnatal sugar consumption by male offspring can alter the ventral prostate and cause the development of carcinoma in situ

Embasamento/Background: Maternal insults during intrauterine and postnatal life can alter offspring the morphology of organs, including the male genital system. Female rats that received low protein diet (LPD) during gestational and lactation periods can impair the prostate morphogenesis and causes an increased incidence of prostatic disorders in aging animals. Besides, the LPD is associate with the increasing of metabolic syndromes and these effects can be enhanced by sedentary life and an increase of postnatal sugar consumption. The aim of this study was to evaluate the effects of LPD and postnatal sugar consumption on the morphophysiology of ventral prostate (VP) of rats in adulthood (post-natal day - PND 90) and aging (PND 540).

Métodos/Methods: Male Sprague Dawley rats born from dams fed a control diet (17% protein) or hypoprotein diet (6% protein) during gestation and lactation periods, on PND 21 were divided into 4 groups and all started to receive the control diet: Control (CTR): born from CTR dams who consumed normal water ad libitum; Control+sugar (CTR+SUG): consumed 10% sugar solution diluted in water from PND 21 to PND 90; GLLP: born from GLLP dams who consumed normal water ad libitum; GLLP+SUG: Born from GLLP dams, who consumed sugar solution from PND 21 to PND 90. After PND 90 all animals consumed normal water. The animals were euthanized on PND 90 and 540. An oral glucose tolerance test (OGTT) and the serum metabolic profile analysis was performed on PND 90 and 540. The ventral prostate (VP) was collected for morphological, antioxidant enzymes, immunostaining, western blotting (WB), and proteomics analysis.

Resultados/Results: Total proteins, triglycerides, and glucose did not change at both ages. In the OGTT, the CTR+SUG group showed higher blood glucose in the time of 120 minutes, and in the area under the curve, the CTR+SUG had a significant increase, which characterizes a glucose intolerance. On PND 540 the same analyses did not change, the animals have recovered. The adult body weight had a significant reduction in the GLLP groups and between the CTR+SUG and GLLP+SUG, in aging this significant reduction remained between the groups CTR+SUG and GLLP+SUG. The anogenital distance, on PND 90 there was a significant reduction in the GLLP+SUG group in comparison to the CTR group, while on PND 540 there was a significant reduction in the GLLP group in compared to the CTR group. The adult VP the CTR+SUG, GLLP, and GLLP+SUG groups had smaller and pleated acinus and a smaller lumen, and an increase in the epithelial compartment and inflammatory cells in relation to the CTR group. All restricted groups on PND 90 had a higher rate of Ki67 immunostaining and an increase in the activity of CAT in the GLLP group. For SIRT and SULF WB analysis, did not change in adult animals, but for SULF immunostaining had a reaction stronger in pleated regions of the sugar consumption groups. The histopathological lesions observed on PND 540, were epithelial atrophy, atypical hyperplasia, prostatic intraepithelial neoplasia in all groups, and carcinoma in situ in the CTR+SUG and GLLP groups. On PND 90 the PCA showed a similar distribution of samples among the groups, whereas the old animals had a more distinct proteomic profile among the groups, especially for the GLLP+SUG. We highlight in sugar groups enriches pathways related to sugar metabolism, inflammation, oxidative stress, DNA degradation, RNA processing by spliceosome, autophagy. While LPD acts in the path of cell growth and proliferation.

Conclusões/Conclusions: Therefore, these analyzes show us that the adult animals had some changes but not in terms of impacting the functionality of the prostate, but the LPD and postnatal sugar consumption may have contributed to disorders in aging, altering the morphophysiology and the prostatic environment, in addition, could develop the carcinoma in situ in the CTR+SUG and GLLP groups.

Palavras Chave/Key-words: Fetal Programming, Protein Restriction, Sugar consumption, Prostate.

ID: 3657

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal low protein diet alters offspring steroidogenic profile and miRNA 33-5p intraprostatic pathway with estrogen regulation

Embasamento/Background: In the approach of Developmental Origin of Health and Disease (DOHaD), seeks to establish the relationship of diseases in adult life with events that occurred in intrauterine development and/or early childhood. Experimental model widely used for DOHaD studies, the rodents submission to maternal low protein diet (MLPD), has already been shown a delay in the prostatic development and increase carcinoma in situ incidence in aged rats ventral prostate (VP), both results were associated with increased serum estrogen levels. However, the molecular and physiological mechanisms associated with this disorder have not been well established. Thus, the objective of this project was to evaluate steroidogenesis systemically in these animals, the intraprostatic effects, and to validate the participation of miRNA 33-5p pathway (selected through bioinformatics analysis).

Métodos/Methods: For this, female and male rats of the Sprague Dawley lineage were randomly divided into two experimental groups: CTR group (control, with 17% protein feed, n = 12) and GLLP (gestational and Lactational Low Protein, 6% protein feed during pregnancy and lactation, n = 12), at the postnatal day (PND) 21 the animals were euthanized and blood, VP, and organs that perform peripheral aromatization (testis, adrenal, liver and skin) were collected. From transcriptomic and microRNomic data VP of rats submitted to MLPD, in

silico analyzes were performed to establish a network of estrogen-regulated miRNAs and mRNAs expression. In the blood, were measured DHEA, progesterone, testosterone, and estrogen. In PV, testis, adrenal, liver and skin, were analyzed gene expression of the enzymes Cyp19a1, Srd5a3, Cyp11a1, Hsd17b6, Hsd3b7, and Cyp7b1 and also were analyzed the miR33-5p and its predicted targets: Upk3a, Srl, Tmem182 and Abcg1.

Resultados/Results: Decreased serum concentrations of DHEA and progesterone were identified in animals in the GLLP group, in addition to an increase in testosterone and estrogen concentrations. The gene expression of Cyp11a1 was shown to be increased in PV and skin and decreased in testis and liver, Hsd3b7 was increased in PV and decreased in the liver, Hsd17b6 was shown to be increased in PV and skin, and decreased in liver and testis, Srd5a3 was increased in PV and decreased in testis and adrenal, Cyp19a1 increased in the liver and adrenal and decreased in the testis and Cyp7b1 decreased in the adrenal and PV. MiR-33-5p was shown to be down-regulated in PV, while its predicted targets Srl, Angpt2, Tmem182, and Abcg1 were up-regulated.

Conclusões/Conclusions: Our results show that MLPD causes an imbalance in the levels of steroid hormones indicating that the biochemical pathway is upstream in relation to estrogen production, evidencing the contribution of PV and others organs in this steroidogenic scenario, in addition to placing miR33 -5p as a potential target in the estrogen regulation.

Palavras Chave/Key-words: DOHaD, maternal low protein diet, estrogen, ventral prostate

ID: 3658

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Integrative Omics Analysis of Animals Submitted to Maternal Low Protein Diet: Identification of Possible miRNAs involved in Early Prostate Carcinogenesis.

Embasamento/Background: In the last decades, has been observed an increase in the incidence of cancer in the population. Studies show that cancer can be originate from insults suffered by individuals during intrauterine life, a condition known as DOHaD. The perinatal period is characterized by the ability of the embryo/fetus to adapt to environmental changes, altering gene expression by post-transcriptional mechanisms. Recently, we demonstrated that maternal protein restriction promotes prostate carcinogenesis in elderly rats; however, there is a lack of information about the molecular mechanism involved in this process. Thus, we aim to identify possible deregulated microRNAs in young programmed rats and locate their possible targets associated with prostate carcinogenesis.

Métodos/Methods: Male Sprague Dawley rats born to mothers fed a standard diet (17% protein), control group (CTR), or low protein diet (6% protein), gestational and lactational low protein diet group (GLLP), during pregnancy and lactation, were sacrificed on the postnatal day 21. Blood was collected for hormonal analysis and the ventral prostate was processed for morphology and by sequencing, HigSeq -2500 Illumina, to determine the profile of the microRNoma. The transcriptome and proteomics of the same animals were used to refine miRNA targets prediction that was performed using the Mirwalk website. The Kobas website was used to analyze enrichment of molecular and ontological pathways of the miRNAs prediction targets. At the same time, MiRNA sequencing data from patients with prostate cancer, from the cancer genome atlas (TCGA), were reanalyzed for comparison with the miRNAs differentially expressed in our rat results.

Resultados/Results: We observed a delay in the development of the ventral prostate and increased levels of testosterone and estrogen expression in GLLP rats. In addition, 15 miRNAs were identified as differentially expressed, 5 regulated down and 10 regulated up. After prediction targets and integration with mRNA and proteins we found 144 possible targets up regulated and 131 down regulated. The results of enrichment for down regulated miRNAs (up regulated targets) are related to development and proliferation pathways, while up regulated miRNAs (down regulated targets) with endoplasmic reticulum and migration pathways. Already for the results of the miRNA sequencing of cancer patients from TCGA, we found 229 deregulated miRNAs being 4 in common with the GLLP group. The mir-33 and mir-99 are down regulated in both experiments and mir-206 and mir-184 are up regulated in the GLLP group and down regulated in TCGA samples with cancer. Studies show that the 4 miRNAs are tumor suppressors in prostate cancer.

Conclusões/Conclusions: Maternal low protein diet causes changes in important miRNAs that are related to prostate cancer. In addition to that, the targets regulated by those miRNAs then relate to cancer hallmarkers. Thus, these changes may be the key to the origin of cancer in adulthood, which reinforces the “Gardner hypothesis” that PCa may originate in the uterus.

Palavras Chave/Key-words: DOHaD, Prostate Cancer and MicroRNAs

ID: 3659

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Learning Deficits in Offspring of Obese Mothers or Obese Fathers are Associated with Impaired Tryptophan Metabolism Via the Kynurenine Pathway. Carla Elena Mezo-González1, Amran Daher Abdi1, Sandra Olvera Hernández1, Luis A. Reyes-Castro1,2, Clarissa

Embasamento/Background: Offspring of obese mothers develop cognitive disabilities at adulthood. Learning deficits have also been reported in offspring of obese fathers. However, the mechanisms underpinning the cognitive deficits resulting from parental obesity are poorly understood. Obesity-induced inflammation upregulates the kynurenine (KYN) pathway, the major route of tryptophan (TRP) metabolism, leading to enhanced production of KYN metabolites including Kynurenic (KA) and Quinolinic (QA) acids. Excessive brain accumulation of KYN or QA impairs learning and memory. The aim of the present study was to make a comparative analysis of the impact of maternal and paternal obesity on the different components of the memory process (encoding, consolidation, retrieval), and to determine whether the learning deficits resulting from maternal or paternal obesity are associated with impaired KYN metabolism.

Métodos/Methods: Founders (F0), female and male Wistar rats were fed standard chow or a free-choice high-fat high-sugar (fc-HFHS) diet from weaning to mating (3 months), and, for females, through pregnancy and lactation to constitute 3 first generation (F1) experimental groups: control mother/control father (CM/CF); obese mother/control father (OM/CF); obese father/control mother (OF/CM). All F1 animals were weaned onto standard chow. At the age of four months, F1 male animals underwent a learning test based on the combination of the Novel Object Recognition (NOR) test and the Novel Object Location (NOL) test. At euthanasia, tryptophan and its metabolites were quantified in the brain stem, hippocampus and frontal cortex by Ultra-performance liquid chromatography-tandem mass spectrometry (LC-MS/MS).

Resultados/Results: Both maternal and paternal obesity induced cognitive deficits in offspring. Nevertheless, while maternal obesity impaired the consolidation process of memory, paternal obesity altered the process of memory retrieval. In OM/CF group, memory deficits were associated with an increased concentration of QA in the hippocampus as well as reduced levels of nicotinamide and kynurenine in the frontal cortex. Offspring of obese fathers exhibited a reduced concentration of NAD in the hippocampus as well as reduced levels of nicotinamide in the frontal cortex.

Conclusões/Conclusions: Paternal and maternal obesity induce cognitive deficits in the offspring by affecting different components of the memory process. Nevertheless, in both cases the cognitive deficits are associated with alterations of the kynurenine pathway. Financial support: CMG and ADA are recipients of an international PhD fellowship from, respectively, the Mexican National Council of Science and Technology (CONACYT) and the Ministry of Research and Innovation of the Republic of Djibouti. CAM benefited from a doctoral fellowship from the Brazilian Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES). This work was supported by the French National Research Agency (ANR, grant ANR-16-CE21-0007-01) and CONACYT (award number 2015-16-273510) and by the programme "Food for Tomorrow" of the French Region Pays de la Loire.

Palavras Chave/Key-words: Parental-obesity, Learning-deficits, Kynurenine-pathway

ID: 3660

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Low Protein Diet and Sugar Consumption: Inflammatory Impacts on the Aging of Rats

Embasamento/Background: Epidemiological and experimental studies have been demonstrated a higher rate of obesity, diabetes and cardiovascular diseases in the adult population of individuals whose mothers had inadequate conditions during pregnancy, such as maternal low protein diet (LPD). Recently, experimental studies have demonstrated that the reproductive system and capacity are also affected by maternal LPD in the rats offspring. Linked to this, the increasing consumption of "added sugar" in the world has been associated with the global epidemic of cases of metabolic diseases. Thus, maternal LPD and sugar consumption may be associated with inflammatory processes in the prostate with aging. Therefore, this project aims to investigate the role of inflammation pathways in rats submitted to maternal LPD, which together were exposed to sugar consumption, focusing on the ventral prostate (VP).

Métodos/Methods: Male offspring of Sprague Dawley rats submitted or not to maternal LPD will be used. After weaning, male Sprague Dawley rats born from dams fed with a control diet (CTR, 17% protein) or low protein diet (GLLP, 6% protein) during gestation and lactation period were divided in 4 experimental groups (n=6/group) Control (CTR) consumed control diet and water until PND 90; Control+sugar (CTR+SUG) consumed control diet and sugar solution (10% diluted in water) until PND 90; Gestational and Lactational Low Protein (GLLP) received normal water until PND 90, and GLLP+SUG consumed sugar solution until PND 90. At PDN540 they were anesthetized, weighed, and euthanized. The collected blood was used for systemic analysis and the VP for morphological and molecular analysis.

Resultados/Results: The results demonstrate reduced body weight in the GLLP and GLLP + SUG, in addition to less total fat. Some metabolic parameters such as glucose, triglycerides and total proteins did not show significant differences, which demonstrates that the two parameters were not sufficient to trigger processes such as obesity, diabetes, and metabolic syndrome. VP tissue alterations were observed in all groups. In relation to inflammatory parameters, an increase in CD68 mast cells and macrophages was observed in the PV of all groups, when compared to CTR, with an emphasis on these infiltrates in the GLLP + SUG group. In addition, there was an increase in the inflammatory infiltrate and inflammation, especially in the GLLP + SUG group. We verified high expression of TGF-b and TNF-a molecules in the carcinoma of animals from GLLP and GLLP + SUG group, but the increase in systemic and intra-prostatic form occurred only in GLLP + SUG. Linked to this, the phosphorylated SMAD2/3 was decreased, which can demonstrate that this inflammation pathway is exacerbated in the group that had both adverse conditions.

Conclusões/Conclusions: With these results, it's possible to outline that there is an influence of inflammation in the harmful processes related to aging and VP, both in animals submitted to maternal LPD and sugar consumption, but with greater emphasis on those that had both adverse conditions. This demonstrates that maternal LPD and sugar consumption negatively and directly affect prostatic homeostasis in senility, and may have a relationship between the biology of cancer in this tissue.

Palavras Chave/Key-words: Maternal protein restriction, sugar, ventral prostate, inflammation.

ID: 3661

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Transcriptomic Landscape Reveals Molecular Pathways Connecting Maternal Malnutrition to Early Life Origins of Prostate Cancer in Rats

Embasamento/Background: Maternal exposure to adverse conditions during intrauterine development can drive the origin of metabolic disorders and some types of cancer in offspring throughout postnatal life, a conception known as Developmental Origins of Health and Diseases (DOHaD). Epidemiological evidence shows intrauterine exposure to low protein diet (LPD) can be associated with the development of chronic disease in adult life, additionally it is one of the most used experimental model used in the DOHaD studies. Here, we investigated the effect of maternal LPD in deregulating molecular pathways involved in the rat prostate development that may also be associated with early life origins of prostate cancer (PCa) in older rats.

Métodos/Methods: Male Sprague Dawley rats were divided into two groups: Control, offspring fed with normal protein diet (17% protein); and Gestational and Lactational LPD group (GLLP), offspring fed with LPD (6% protein) during gestation and lactation periods. The rats were weighed and euthanized on postnatal day 21. The biometric parameters were measured, blood was collected for hormonal analysis, and the ventral prostate was collected for morphological and transcriptome analysis. The analysis of differentially expressed genes (DEG) was performed through the Bioconductor edgeR package in the program R. DEGs were analyzed using: Kobas3.0 to perform enrichment analysis and Transcription Factor Enrichment Analysis (TFEA) through x2k Web tool. Our data were compared with The Cancer Genome Atlas (TCGA) dataset through cBioPortal and SurvExpress, and with studies related to high exposure of estrogen by The Ligand Perturbations from GEO platform by Enrichr tool.

Resultados/Results: The LPD alters biometric parameters, hormonal, and prostate morphology in the GLLP group. Heatmap and principal component analysis (PCA) revealed the distinct gene profile between groups. In addition, 710 DEGs, 526 upregulated and 184 downregulated. Of the total DEGs, 106 up and 38 downregulated were enriched in developmental pathways and cancer. TFEA analysis revealed the transcription factors (TF) upregulated genes: SUZ12, MYOD1, EZH2, TP63, and down: SOX2, GATA1, AR, GATA2, associated with cell development, differentiation, regulation of embryonic development, and activated by the steroid hormone. We selected from TFEA six upregulated (Foxa2, Cyp1b1, Msx2, Rspo3 and Tubb2b) and six downregulated (Cyp7b1, Diaph3, Gadd45g, Rtn4p1, Semea3a and Pde10a), targets involved in signaling pathways, cell cycle, apoptosis, mainly estrogen pathway, observed through Ligand Perturbations platform. The survival analysis and gene alterations using TCGA dataset, revealed the up genes were altered in 65% of patients with PCa, while down genes were altered in 62% patients, both were be able to predict shorter survival time for these patients, with significant values the Kaplan-Meier: hazard ratio= 6.77/p-value= 0.01 for upregulated, and hazard ratio= 5.45 and p-value= 0.03 for downregulated. We highlighted Cyp1b1 and Cyp7b1 in the control of prostate growth, leads us to believe that LPD mainly changes hormone-responsive genes in prostate cells.

Conclusões/Conclusions: Our results described potential key molecular pathways deregulated after maternal exposure to maternal LPD that may connect early life exposure to prostate carcinogenesis in rat offspring.

Palavras Chave/Key-words: Prostate, DoHaD, Fetal programming, Transcriptome

ID: 3663

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: The Perinatal Maternal Low Protein Intake Interfers in the Sexual Maturation of Male and Females rats

Embasamento/Background: During famines, such as Dutch and Chinese or following second war, the maternal low protein intake was related with reduced fertility, increase of miscarries and altered metabolism in infants. Some papers also demonstrated this association in experimental animals. The brain continues the development after the birth being susceptible to alterations during the lactational phase. In rodents the 10 first days after birth represents the an important sexual development area of brain. The aim of this study was evaluated the impact of maternal low protein diet in the sexual maturation of males and females offspring.

Métodos/Methods: The dams were fed with 4% low protein diet (LP) or a 23% of protein chow diet (NP) during the first 12 days of sucking phase. The offspring were evaluated in weight, circumference head, abdomen and height through the post-natal (PN) 7, 14 and 21. At 21 days old was collected and weight the reproductive organs from one female and one male of each litter. During the PN 25 to 45 the preputium and vaginal open were evaluated. In females the first estrus was detected after the vaginal open. Also, the estrus cycle was assessed between the PN60 to 75. At PN90, the males and females were weight and sexual organs were obtained and weight.

Resultados/Results: Both male and female from LP dams had a diminished circumference of head and abdomen in all days evaluated, the height and weight also were decreased in this group in the PN 21. Similarly, the weight in both sexes was reduced in LP offspring at PN90. The ovaries and uterus did not differ to control, otherwise the testes and epididymis were reduced in the LP offspring in both PN21 and 90. The preputium and vaginal open showed a delay in the LP groups. Also, the first estrus had a delay in the LP females offspring. But the estrus cycle presented the number of phases similar between the groups.

Conclusões/Conclusions: Both male and female were affected by maternal low protein intake, since the first days of lactation seems to have a role in the sexual brain development and in consequence, the sexual maturation. However, the females were less affected by the LP diet than the males, showed a recover after the adolescence and did not differ in the estrus cycle phase and sexual organs weight. The GnRH, may represent a significant function in the sexuality of males and females, controlling the sexual hormones release, together some studies showed a reduction of this genes after low protein intake in experimental animals. However, more studies are necessaire to confirm the damages caused by maternal LP diet during the first days of lactation in the males and females on sexual development.

Palavras Chave/Key-words: sexual maturation, maternal low protein intake, males and females offspring.

ID: 3664

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: EFFECT OF MATERNAL DIABETES AND POST-WEANING HIGH-LIPID DIET INTAKE ON THE ADULT OFFSPRING: PRELIMINARY RESULTS

Embasamento/Background: Diabetes is a chronic disease characterized by hyperglycemia resulting from defects in the synthesis and/or secretion of insulin by beta-pancreatic cells or resistance to the action of insulin by peripheral tissues. It is known that during pregnancy, high blood glucose levels contribute to an unfavorable intrauterine environment influencing fetal programming. Environmental and genetic changes that may occur during intrauterine life are capable of influencing embryo and fetal development as well as the onset of disease during adulthood. Fetal programming influenced by maternal diabetes raises the risk of obesity, type 2 diabetes, gestational diabetes, cardiovascular disease, and insulin resistance in offspring. Intrauterine hyperglycemia may conduct to the diabetogenic phenotype to the next generation. Therefore, intrauterine programming is more related to the presence of maternal hyperglycemia than to the type of diabetes. Objective: To analyze blood glucose levels after glucose overload in rats with diabetes and their adult offsprings.

Métodos/Methods: Mild diabetes was induced in female Sprague Dawley rats by streptozotocin (beta cytotoxic drug) at the neonatal period. For OGTT, the non-diabetic females received the citrate buffer (vehicle). At adulthood, the control and mildly diabetic rats were submitted fasting of 6 hours, next glycemia was determined. Subsequently, the rats received glucose overload, and after 30, 60, and 120 minutes, glycemic measurement to oral glucose tolerance test (OGTT). About day 120 of life, the diabetic rats were mated to obtain their offspring, which were maintained up to adult life. Similarly to control (C) and mildly diabetic (D) dams, the female offspring born to diabetic dams (OD) were also submitted to OGTT on day 115 of life (n=7 animals/group). For comparative analysis of OGTT glycemia, the Negative Binomial test was used. For all statistical comparisons, a minimum confidence limit of 95% ($p<0.05$) was considered.

Resultados/Results: In the OGTT performed at time zero (fasting), there was no significant difference between the experimental groups (D and OD) compared with the C rats, however the OD group presented glucose intolerance, with a blood glucose value greater than 140 mg/dL. Thirty minutes after glucose overload, the glycemia was higher in the D group (> 200 mg/dL), as well in the OD group (>140 mg/dL), compared with the C group. Similarly, it was observed at 60 minutes after glucose overload. At time 120 min, glycemia was also greater in the D and OD groups (both groups > 140 mg/dL) in relation to the control group.

Conclusões/Conclusions: Our preliminary findings show that the offsprings of diabetic mothers had glucose intolerance demonstrated in OGTT, leading to an unfavorable intrauterine environment that caused a dysregulation in the glycemic homeostasis of the offspring. This corroborates the hypothesis of maternal diabetes-induced fetal programming.

Palavras Chave/Key-words: diabetes, fetal programming, rats, glucose tolerance

ID: 3667

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Reduction of Placental Autophagy in Mice with Maternal High-Fat Diet Induced Obesity Oliveira,J.L[1];Sanches,A.P.V[1];Ferreira,M.S[1];Lima,B.S[1];Salomão,J.S[1];Miyamoto,J.E[1];Simino,L.A.P[1];Milanski,M[1];Torsoni,A.S[1];Torsoni,M.A[1];Ignacio-Souza,L.M[1]

Embasamento/Background: Obesity in women of childbearing age has been growing exponentially and represents an adverse condition, which may establish specific risks, as it predisposes to the development of obstetric complications. Both the high pre-gestational BMI and excessive weight gain during pregnancy lead to metabolic disorders that can lead to complications for the mother and the fetus. Additionally, autophagy has been described as an important process in implantation and fetal development, however it has been reported that obesity has a modulating role in this process. Considering the importance of the placenta in a successful pregnancy, and the high growth of obesity in women of childbearing age, it is necessary to investigate the factors that relate these parameters. Therefore, the objective of this study was to verify the regulation of the autophagy process in the placenta of obese mothers.

Métodos/Methods: The experimental procedures were submitted for approval by the Ethics Committee of UNICAMP (CEUA: 5401-1/2019). Swiss female mice were divided into 2 groups, one received a control diet (CT) and the other a 45% high-fat diet (HF) for 4 weeks before mating and until the 19th day of gestation, when the animals were euthanized. Before and during pregnancy, parameters of ingestion and body weight were evaluated and in euthanasia, placental and fetal parameters. The data were analyzed using Student's t-test and differences were considered significant for $p < 0.05$.

Resultados/Results: The results showed that at the beginning of the experiment the animals did not show any difference in body weight. However, 4 weeks after the introduction of the high-fat diet (pre-gestational moment), the HF group showed greater weight gain compared to the CT group. The final weight gain was greater in the HF group despite the tendency to reduce gestational weight, this difference is due to the fact that the animals have already started pregnancy with a large difference in body weight. Also, the total weight gain may indicate that pre-gestational weight gain is more related to the fetal outcomes that weight gain during pregnancy, at least in this animal model at judge by equal number of fetus but different phenotype. The intake in grams was lower in the HF group and can be justified by the fact that the high-fat diet is high-calorie, complementing this data, the feeding efficiency was higher in the high-fat group, which may justify the increase in the weight of the animals. Fetal weight was lower in the HF group compared to the control group, indicating that consumption of a high-fat diet before mating can lead to impairment in the development of the fetus. The weight of the placenta showed no difference between the groups, however, the relationship between placental and fetal weight shows a placental inefficiency and analysis of autophagy in this tissue showed that the HF group showed impairment in this pathway at least by the reduction in the mRNA expression of ATG7 and p62. Taken together, the results may indicate that the consumption of a high-fat diet could lead to a decrease autophagic process in the placenta, generating changes in fetal development.

Conclusões/Conclusions: The consumption of a high-fat diet can lead to impaired fetal outcome through under regulation of placental autophagy. Support: CAPES, CNPq, FAPESP, FAEPEX.

Palavras Chave/Key-words: Autophagy; maternal obesity; placenta; DOHaD

ID: 3668

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Obesity Affects Hepatic MicroRNAs Modulation and Homeostasis of Second Generation

Embasamento/Background: Background: MicroRNAs may exert a great influence on energetic metabolism. In the liver, downregulation of miR122 leads to an increase in triglycerides synthesis, as well as a decrease in fatty acids transportation and oxidation. Let7 have been reported to be involved with insulin resistance and previous studies from our lab showed that offspring from obese dams presented increased Let7 and decreased miR122 expression in the liver. Therefore, this study aimed to evaluate whether HFD consumption at gestation and lactation would lead to transgenerational deleterious effects that could be triggered by hepatic microRNAs expression.

Métodos/Methods: Female Swiss mice were maintained on a normal chow diet or 45% HFD. HFD group were later subdivided into obese resistant (OR) or prone (OP), according to the weight gain presented during the 4 weeks of exposure. F0 females were mated with control males for F1 generation conception. After weaning, F1 females were fed exclusively a control diet until they were able to be mated with control males to originate the second generation (F2). Experiments were approved by the Ethics Committee on the Use of Animals of the State University of Campinas (CEUA / UNICAMP) with protocol number 3963-1.

Resultados/Results: At the birth day, offspring from obesity-prone grandmothers (F2-OP) had an increase in fasting glycaemia, which was maintained until the 28th day of life, even though the body weight did not differ between groups. Furthermore, in d28, both F2-OP and offspring from obesity-resistant grandmothers (F2-OR) showed an increase in liver fat content in comparison to offspring from control grandmothers (F2-C). F2-OP offspring showed a lower expression of hepatic miR-122 and, on the other hand, they presented higher levels of Let7 in the liver.

Conclusões/Conclusions: Maternal nutrient imbalance during gestational and lactational periods leads to metabolic programming, and it has been shown that the effects of poor maternal nutrition can persist through future generations. miR-122 and Let-7 can be referred as predictors of metabolic disorders and, in the present study, we showed that the second generation of obese prone HFD fed dams present modulation at these microRNAs that may be, at least in parts, adjuvants of glycemia and fat storage in the liver. These findings confirm the need for adequate nutrition and weight gain during the gestation and lactation periods for the good prognosis of the health of the newborns and the prevention of several chronic diseases across the generations.

Palavras Chave/Key-words: microRNAs, maternal diet, obesity, fatty liver

ID: 3671

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Early Exposure to High-Sucrose Diet Hastens Menarche and Deteriorates Ovarian Follicles in Young Female Rats

Embasamento/Background: Early introduction of hypercaloric diets, particularly those rich in table sugar, has been associated to the development of diverse risk factors for metabolic disorders, such as obesity, dyslipidemia, and type 2 diabetes melittus. Of note, those conditions are also related with cognitive and reproductive impairments. Thus, this study sought to evaluate the effect of post-weaning exposure to a high-sugar diet on glycolipid metabolism and reproductive parameters

Métodos/Methods: Weaned Wistar female rats were fed from the postnatal day (PND) 21 to 120 days with a 25% sucrose-rich diet (HSD, n = 8) or standard chow (CTR, n = 8). From PND 35, daily observations were made for determination of the vaginal opening and estrous cyclicity. Upon PND 120, glucose and insulin tolerance tests were performed, and serum samples collected for biochemical profile analysis. Ovary and adipose tissue samples were also collected for histological studies

Resultados/Results: There was no difference in body weight between groups, but visceral adipose tissue depots were increased by 53% in HSD animals. HSD rats also were hyperglycemic at both fasting and fed states, as well as hypertriglyceridemic, which resulted in higher values of TyG index (HSD = 8.05 ± 0.18 vs. CTR = 7.36 ± 0.18), suggesting impairment of peripheral insulin sensitivity. However, there was no difference in both GTT and ITT tests. Regarding the impact of excess sucrose on reproductive parameters, vaginal opening was significantly shortened in HSD rats, as compared to CTR. Nevertheless, HSD rats presented significantly higher counts of antral, atretic antral, and pre-cysts follicles. This ovarian deterioration is possibly associated to the hyperplasia of periovarian white adipose tissue, whose average adipocyte area was increased by 47% (HSD = 553.0 ± 12.8 vs. CTR 375.8 ± 7.6 μm2), as compared to CTR.

Conclusões/Conclusions: All together, our data show that excessive intake of table sugar in critical periods of development may be responsible for causing not only metabolic but also reproductive disorders as observed in the ovarian microenvironment, which might severely compromise the fertility of sucrose-fed young female rats.

Palavras Chave/Key-words: High-sugar diet, ovarian microenvironment, metabolic disorders.

ID: 3673

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: PERINATAL EXPOSURE TO AN ENVIRONMENTALLY RELEVANT PHTHALATE MIXTURE CHANGES THE GENE AND PROTEIN EXPRESSION PROFILE IN THE PROSTATE OF RATS AND THEIR DECENDENTS

Embasamento/Background: The programming of the offspring through maternal exposure in a critical period of development generates late and transgenerational modification. Phthalates are chemical substances widely used in the plastics and cosmetics industry, they are ubiquitous in the environment and act as endocrine disrupting chemicals (EDCs). More than 18 billion pounds of phthalates are used each year, predominantly as plasticizers in polyvinyl chloride (PVC) products such as upholstery, table cloths, shower curtains, pesticides, solvents, and infant toys. Furthermore, some reports have shown that phthalates can modulate epigenetic mechanisms, which can be transmitted to different generations. Several studies indicate the presence of different phthalates in the blood, urine, and placenta of pregnant women. this study aimed to identify the gene expression profile by sequencing and the proteomic profile in the ventral prostate (VP) of rats exposed during gestational and lactational periods to a mixture of the of the six most commonly found phthalates in pregnant women, as well as their descendants.

Métodos/Methods: Pregnant SD rats were randomly assigned to 2 experimental groups: G1: control (vehicle) and G2: 20μg/kg/day, (by gavage). The concentration was selected based in the environmental exposure and in previous results. Pregnant females (F0) were treated from gestational day 10 (GD10) to postnatal day 21 (PND21). Both exposed males and females (PND90-F1) were mated with nontreated

animals to obtain F2. VP was collected on PND22 and 120 at F1 and only in PND22 at F2. mRNAs and miRNAs were sequenced using the HiSeq2500 platform (Illumina) and some selected genes and miRNAs were validated by RTq-PCR (F1 and F2). Proteome was performed using the nanoACQUITY UPLC system coupled with the Xevo Q-TOF G2 mass spectrometer (Waters, Milford, USA)

Resultados/Results: We found that some of the miRNAs differentially upregulated in F1 remained upregulated in the F2 generation. The proteomic results were filtered to identify common proteins between F1 and F2 generations (both in the PND22). The filtrations were made considering up and down-regulated proteins in the comparison among the groups and generations. The crossing of common proteins between generations, have pointed out for 18 upregulated and 96 downregulated proteins. From these proteins, it was highlighted different histones, a dense Rabs' cluster, proteins involved in the regulation of DNA transcription, replication and repair, and chromosomal stability. Although preliminary, the results pointed out important structural changes and alteration in the organization and integrity of DNA, which are transmitted by generation. Rab's family is part of the Ras superfamily of proteins and it is associated with intracellular vesicles traffic, and its expression is upregulated in many types of cancers, including prostate carcinoma. When gene expression and predict targets for deregulated miRNAs were crossed with the proteomic profile, proteins such as Rab6b, Tubb3, tubb4a, rabb3b, among others, emerged as possible altered targets regulated by miRNAs, which may support one of the epigenetic mechanisms associated with the transmission of changes between generations in our model

Conclusões/Conclusions: Our results have demonstrated that the phthalate mixture, at an environmentally relevant dose, was able to alter the genomic and proteomic profile pattern in the rat prostate in F1 and F2 generations.

Palavras Chave/Key-words: PHTHALATE EXPOSURE PROSTATE GENE AND PROTEIN EXPRESSION PROFILE OFFSPRING

ID: 3674

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: ORAL

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Título/Title: Antioxidant Fraction Extracted From Stevia rebaudiana Leaves Mitigates Complications Of Type 1 Diabetes Mellitus.

Embasamento/Background: Stevia rebaudiana produces a series of non-sweetening molecules with a high antioxidant capacity. These substances are obtained by fractioning stevia leaf extracts, with the ethyl acetate fraction (FAE) having the highest antioxidant capacity. FAE has no sweetening potential and has an in vitro insulinotropic effect. In view of these results, this study evaluated the capacity of this fraction to protect against the development of type 1 diabetes mellitus, evaluating its effects on glycemic parameters, on tissue lipoperoxidation and on the morphometry of the pancreatic islets of diabetic rats induced by streptozotocin.

Métodos/Methods: The experimental protocol was approved by the Animal Use Ethics Committee of UEM (nº 9076141116). Wistar rats with 30 days of age were submitted to treatment with FAE (5mg / Kg / day), orally, for 60 consecutive days. The streptozotocin-induced diabetic model was used with a single intravenous application of 60 mg / kg p.c. applied on the 30th day of treatment. The animals were divided into 2 groups: Diabetic Control (DC, n = 10) and Treated Diabetic (DT, n = 10). Plasma parameters were evaluated: fasting blood glucose and insulinemia. Pancreas histology was performed to measure the area of the pancreatic islets. Plasma antioxidant capacity was measured. Data were expressed as mean ± epm and submitted to test t-studant and applied after Bonferroni test with significance level when $p < 0.05$.

Resultados/Results: An increase in plasma antioxidant capacity (8.2%, $p < 0.05$) and reduction in pancreatic and hepatic lipoperoxidation was observed in animals treated with FAE (15.6% and 13.5%, respectively, $p < 0$, 05). The fasting insulinemia of the DT group was about 51.3% higher than that of CD ($p < 0.001$), whereas the fasting glucose did not show any significant difference. However, when the HOMA-β index was evaluated, there was a significant improvement in the DT group (23.4%, $p < 0.01$). Corroborating these results, there was a smaller reduction in the area of pancreatic islets in the DT group (55.8%, $p < 0.01$). Lower levels of AST and ALT (36.7% and 30.3%, respectively, $p < 0.001$) and fructosamines (9.8%, $p < 0.05$) were observed in the treated group. There was a significant increase in hepatic glycogen production in DT (26.7%, $p < 0.01$).

Conclusões/Conclusions: Together, these results suggest that FAE has an important antidiabetic effect, due to its high antioxidant capacity, improving pancreatic and hepatic functions in diabetic animals.

Palavras Chave/Key-words: antioxidant, Stevia rebaudiana, diabetes mellitus, insulin

ID: 3675

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Lipid Content of Donated Human Milk and Maternal Body Mass Index.

Embasamento/Background: Human milk (HM) is considered as an obesity preventive factor. The high variability in its composition depends on maternal factors, like body composition and diet, affecting particularly its lipid and energy content. Objective: To describe the nutritional composition of donated HM according to the nutritional status of the donors.

Métodos/Methods: This is a descriptive study of the macronutrient and energy content in samples of donated HM, from the Human Milk Bank of the Hospital Sótero del Río, between 2015 and 2018. The analysis was performed through infrared spectroscopy. Protein, carbohydrate, and lipid contents (gr/dL) were measured, and the energy content (kcal/dL) was calculated. It was analyzed according to maternal body mass index (BMI). We applied nonparametric tests (Kruskal- Wallis) and linear regression model, considered significant when $p<0.05$. (STATA-13).

Resultados/Results: We obtained 214 samples of donated BM from 125 mothers; whose BMI median was 24.2 (IQR 19.2; 34.5) kg/m2. 51.9% had normal weight (NW), 28.9% overweight (OW) and 19.2% obesity (OB). The HM content for protein was 1.26 (1.2; 1.3) gr/dL, for carbohydrates 6.46 (6.24; 6.79) gr/dL, for lipids 3.15 (IQR 2.41; 3.84) gr/dL, providing 59 (52.5; 66.5) kcal/dL. A direct correlation was observed between carbohydrate and protein content (r: 0.98, p<0,001) and lipids and energy content (r: 0.98, p<0,001). HM from mothers with obesity (BMI≥ 30) had a higher lipid content than HM from women with normal weight (BMI 18.3 to 25): 3.83 (3.19; 4.35) vs. 2.83 (IQR 2.18; 3.75) gr/dL (p=0,006) and also a higher caloric content 65.7 (IQR 57; 73.3) vs. 56 (IQR 49.8; 65.8), without difference in protein or carbohydrates. In the linear regression models, lipids were associated to the mother's age, BMI, newborn gestational age, and infant´s age.

Conclusões/Conclusions: In this study, HM had a high variation in lipid and caloric content. Donated HM from women with obesity had a higher lipid content than HM from women with normal weight. The lipid content seems to be a good predictor of the caloric content of the BM, while protein and carbohydrate content had a high association between them.

Palavras Chave/Key-words: Donated human milk, lipids content, maternal body mass index

ID: 3677

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal High-Fat Diet Increases Thermogenesis Markers and Mitochondrial Damage in Skeletal Muscle of Adult Rat Offspring Independent of the Endocannabinoid System. Dias-Rocha CP1, Almeida MM1, Woyames J1, Mendonça RC1, Souza LL1, Pazos-Moura CC1, Treven

Embasamento/Background: Maternal high-fat diet (HF) during the perinatal period induces obesity in the offspring. Obesity is associated with unbalanced energy metabolism and endocannabinoid system (ECS) over activation. The energy metabolism is a balance between food intake and energy expenditure, which has important contribution of thermogenesis in brown adipose tissue (BAT) and skeletal muscle. The thermogenesis is stimulated mainly by a sympathetic signaling via activation of beta-adrenergic receptors and uncoupling proteins (ARβ2/UCP3 in skeletal muscle and ARβ3/UCP1 in BAT), and it is also regulated by ECS. BAT and skeletal muscle express the cannabinoid receptors (CB1 and CB2) and endocannabinoid metabolizing enzymes (FAAH and MAGL). Recently, we demonstrated that maternal HF diet induces alterations in ECS components and thermogenic markers in offspring BAT both at birth and weaning, possibly associated with early obesity development. We also observed that the HF male offspring showed a compensatory increase of total energy expenditure at adulthood. Thus, we hypothesized that maternal HF diet also changes the ECS in BAT and skeletal muscle of the adult offspring contributing to their compensatory metabolic response.

Métodos/Methods: All procedures using animals were approved by CEUA/CCS/UFRJ (protocol 095/17). Female rats received a standard diet (C; 9% fat) or high-fat diet (HF; 28% fat) during 8 weeks before mating, gestation and lactation. C and HF male offspring were fed a C diet from weaning to adulthood. At 180-day-old, we assessed body weight, food intake, white and brown adiposity and the body lean mass using the carcass method. We collected plasma for analysis of T3, T4, sex hormones, leptin and insulin by radioimmunoassay and glucose by colorimetric assay. We collected BAT and soleus muscle for histology (hematoxylin-eosin staining) and transmission electron microscopy (TEM), respectively. We also evaluated the expression of ECS components and thermogenic markers in these tissues using western blotting. Student's t test was used for comparisons between control and high-fat offspring. * $p<0.05$.

Resultados/Results: Maternal HF diet increased body weight (+7.5%*), white adipose tissue (+27%*) and BAT (+21%*) weight and leptinemia (+313%*) while decreased testosterone (-59%*) in adult male offspring. Maternal HF diet did not affect lean mass content, thyroid hormones, glucose or insulin levels. Maternal HF diet did not change BAT general morphology. However, in skeletal muscle, maternal HF diet decreased the number of viable mitochondria (-25%*) and increased the percentage of injured mitochondria (+8.2%*), suggesting tissue damage. Molecular analysis of soleus muscle showed an increase of UCP3 (+69%*) and TH (+81%*) protein content in HF adult male offspring, without alterations in ARβ2 and ECS components. We found no change in thermogenic markers or ECS components in BAT.

Conclusões/Conclusions: We demonstrated that maternal HF diet induces adult male offspring overweight, increased adiposity accompanied by hyperleptinemia and hypotestosteronemia. Maternal HF diet impacted preferentially skeletal muscle thermogenesis mechanisms compared to BAT in male offspring at adulthood, regardless ECS changes. These data contribute to understanding the dynamics of thermogenesis in the metabolic adaptation of adult male offspring to a maternal dietary insult. Support: Cnpq; Capes; Faperj.

Palavras Chave/Key-words: Obesity; Energy Metabolism; Endocannabinoid System; Thermogenesis.

ID: 3678

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: Post-Weaning Exposure to High-Sucrose Diet Leads to Early Diabetic Cardiomyopathy Onset in Male Rats

Embasamento/Background: In the last decades, the increased prevalence of metabolic syndrome and its comorbidities has been correlated with increased intake of table sugar, mainly fructose, particularly among children and youth. More recently, diabetic cardiomyopathy (DCM) has emerged as a new clinical entity characterized by great metabolic inflexibility, progression to structural changes and heart failure in absence of classic risk factors. Thus, this study sought to investigate the role of early exposure to high-sucrose diet in inducing metabolic abnormalities like deleterious metabolic programming pattern, compatible with diabetic status and the development of histological markers of cardiac remodeling associated to the onset of DCM in male rats.

Métodos/Methods: : Male Wistar rats were fed a 25% sucrose-rich diet (HSD, n = 8) or regular chow (CTR, n = 8) from weaning, at postnatal day (PND) 21, up to PND 120 to allow the assessment of cardiometabolic parameters and heart left ventricle histological studies.

Resultados/Results: HSD rats presented 25% higher periepididymal adipose tissue accumulation, without increased body weight, as compared to CTR. Additionally, HSD rats showed fasting hyperglycemia (HSD= 92,63 ± 1,832 vs. CTR= 85,25 ± 1,048 mg/dL; p= 0,0018), hypertriglyceridemia (HSD= 131,4 ± 24,75 vs. CTR= 75,46 ± 15,48 mg/dL; p= 0,0380) and insulin resistance, as predicted from TyG Index calculation (HSD= 8,57 ± 0,21 vs. CTR= 7,92 ± 0,20; p < 0,05). Of importance, HSD rats also had elevated systolic (HSD,157.9 ± 3.8 vs. CTR 130.3 ± 7.6 mmHg, p<0.05) and diastolic (HSD 128.9 ± 5.5 vs. CTR 107.8 ± 3.3 mmHg; p<0.05) blood pressure, as well as showed histological markers of pathological remodeling in left ventricle samples, such as higher ratio of perivascular fibrosis (HSD 3.17 ± 0.43 vs. CTR 1.44 ± 0.24, p<0.001) and cardiomyocyte hypertrophy (HSD 767987 ± 49121 vs. CTR= 570501 ± 29097 μm2, p<0.01).

Conclusões/Conclusions: Our data show that excess sucrose intake during early life nutrition, particularly following breastfeeding cessation, may lead to premature onset of cardiometabolic syndrome and myocardial abnormalities compatible with a pre-clinical stage of DCM. In this way, our study supports early intake of excess sucrose for longer periods as an animal model to understand the deleterious cardiometabolic programming pattern toward a full DCM phenotype.

Palavras Chave/Key-words: added sugars, cardiometabolic programming, cardiac remodeling.

ID: 3679

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Quantification of Fetal Hormones in Animal Model of Maternal Obesity

Embasamento/Background: Obesity has become a public health problem, with growth mainly in young women of reproductive age. It is known that maternal health can have a significant impact on the intrauterine environment and therefore on fetal development and child health. This occurs as a result of the epigenetic mechanisms of developmental programming, entering into the concepts proposed by Developmental Origins of Health and Disease (DOHaD). During pregnancy, some maternal adaptations should occur and, among them, the development of specific tissues and in the fetal outcome. Thus, considering that obesity may be an important component of self-perpetuation, studying adaptations during the maternal phase becomes important to understand the processes that operate during this phase of life and its relationship with the fetal outcome in a maternal obesity animal model.

Métodos/Methods: The experimental procedures were submitted for approval by the Ethics Committee of UNICAMP (CEUA: 5412-1). Swiss female mice were divided in two groups: control (CT), and high fat (HF). They were fed with standard (CT) or hyperlipidic (HF) diet during four weeks. After, the mating was performed. For each group of two females, it was assigned to a male, held together for three days at 12 hours intervals, when they were examined for the presence of signs of mating and detection of the vaginal plug (day E0.5 of pregnancy). Data on intake and feeding, weight characterization were performed in the pre-gestational and gestational phases. After the gestational period, some fetal tissues were extracted and collected for subsequent fetal hormones analysis.

Resultados/Results: The daily food intake in kcal was the same for both groups, however, the weight gain in the pre-gestational period was significantly higher in the HF group (p<0.005), which could also suggest more accumulation of adipose tissue. In the gestational period, however, no differences were found between the groups regarding weight gain, but the CT group showed a tendency to increase when compared to the HF. As for the fetus hormones, analyzed in the amniotic fluid, the HF group shows an alteration that is usually found in obese individuals, with a higher and lower concentration of prolactin and adiponectin, respectively.

Conclusões/Conclusions: The pre-gestational period was responsible for the greatest weight gain in the gestational period and may suggest a greater accumulation of adipose tissue for the HF group. About the hormones analyzed, the concentrations found may be related to changes in lipid and glycid metabolism during the pre-gestational and gestational periods, which could impact the hormones in question.

Palavras Chave/Key-words: pregnancy, obesity, fetal programming, Dohad

ID: 3680

Área: DOHaD and nutrition

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Título/Title: Positive Effects Of Ketogenic Diet On Metabolic Dysfunction Caused By Early Exposure To A Cafeteria Diet

Embasamento/Background: Obesity is a metabolic dysfunction that has become one of the major public health problems, reaching all ages and with increasing prevalence. Changes in lifestyle, mainly diet related, have a fundamental role in the development of obesity and its comorbidities, especially in the first years of a child's life. Introduction to ultra-processed foods in early childhood is capable of generating increased susceptibility to cronic diseases in adulthood. In this context, nutritional strategies such as the use of the Ketogenic Diet (KD), have been widely used due to their beneficial effects on the improvement of weight loss and metabolic parameters. Despite several studies reporting positive effects, the results are still divergent and little is known about its effects after an early childhood overnutrition. The work aimed to verify the association of the consumption of ultra processed foods in post-weaning animals and the metabolic effects caused by the use of diets in the serum biochemical profile and if the KD is able to reverse the effects of early obesity.

Métodos/Methods: Fifty Swiss post-weaning male mice were divided into two groups, one on a cafeteria diet (CAF) and the other on a control diet (CRT), after 12 weeks they were redistributed to 5 groups that received a CRT, CAF or KD diet for 8 weeks. To evaluate the effects of diets on lipid and glycemic parameters, glucose levels, triglycerides, cholesterol were dosed and for the evaluation of insulin resistance, intraperitoneal insulin tolerance tests (ITTip), oral glucose tolerance test (GTT) and TyG index were performed.

Resultados/Results: Cafeteria diet exposure led to hyperglycemia from 30 days, triglyceride levels increased at 90 days of diet, total cholesterol was higher from 30 days of diet exposure and increased weight from 4 weeks compared to CTR. After changing diets, animals fed with KD showed a weight gain in relation to controls. Although there was no difference between food intake of the animals, there was an increase in caloric consumption between the KD and CAF groups. There was also an improvement in biochemical parameters such as decrease in triglycerides, improvement in fasting and postprandial glycemic levels and improvement in glucose tolerance, in addition to increased sensitivity to insulin in animals that received CAF diet and started receiving DC however, no decrease in cholesterol levels can be observed.

Conclusões/Conclusions: An early introduction to ultra processed foods, highly palatable, rich in calories, sugars and fats, leads to a diabetic phenotype, with worsening in glycemic and lipid levels, in addition to weight gain. The dietary intervention in these animals results in the improvement and prevention of progression to type 2 diabetes, even without reverting the cholesterol levels and obesity previously established by CAF in childhood. Financial support: FAPEMA funded research.

Palavras Chave/Key-words: early childhood; obesity; insulin resistance; ketogenic diet.

ID: 3681

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Biomechanical Responses of Fetoplacental Arteries in FGR: Ex Vivo and In silico Analysis

Embasamento/Background: Fetal growth restriction (FGR) is a severe complication of pregnancy that affects ~10% of gestations, associated with adverse long-term cardiovascular and metabolic outcomes. Besides, several studies show an impairment in functional and structural properties of fetoplacental vessels. A biomechanical analysis from FGR animal model suggest that umbilical arteries develop increased compliance. However, whether this biomechanical behavior occur in umbilical and chorionic arteries from human placenta remains elusive. The main aim of this study is to characterize biomechanically through the tensile test for the constitutive response of the vessel and simulate FGR fetoplacental vessel behavior.

Métodos/Methods: Umbilical and chorionic arteries were isolated from normal (n=5) and FGR (n=5) placentas. Biomechanical responses were determined in arteries samples by uniaxial ring tensile tests. Data obtained from these experiments were used to adjust a Demiray constitutive model and to simulate the arteries responses with Finite element method (FEM). Van Gieson's stain was performed to measure morphometric properties.

Resultados/Results: Differences were found between Control and FGR, either umbilical (UA) or chorionic (CA) arteries. UA shows less strain energy in FGR (0,0312 ± 0,002 kJ/m3) compared to Control (0,0438 ± 0,0048 kJ/m3). CA also shows a diminished strain energy in FGR (0,0205 ± 0,0024 kJ/m3) compared to Control (0,0442 ± 0,003 kJ/m3). Demiray constitutive model was similar to the experimental data, either UA normal (0,0439± 0,0011 kJ/m3), UA FGR (0,0309 ± 0,0018 kJ/m3), CA normal (0,0462 ± 0,0022 kJ/m3) or CA FGR

(0,0227 ± 0,0021 kJ/m3). Finally, in silico simulation also shown similar strain energy responses to the experimental data , either UA normal (0,0433 ± 0,0011 kJ/m3), UA FGR (0,0306 ± 0,0018 kJ/m3), CA normal (0,0474 ± 0,0011 kJ/m3) or CA FGR (0,0245 ± 0,0018 kJ/m3). Morphometric analysis reveals thinners UA in FGR, whilst a thicker FGR CA was observed. UA shown a different percentage of composition for media and adventitia layer compared to control. No differences on layer composition was observed in CA.

Conclusões/Conclusions: These results suggest that FGR results in biomechanical changes, either chorionic or umbilical arteries. The increased biomechanical compliance observed in chorionic and umbilical arteries could arise as a response to the increased placental and systemic vascular resistance occurring in the FGR. Moreover, these biomechanical changes suggest a compensatory mechanism of the arteries in response to low oxygen levels that it is a main feature in FGR fetoplacental blood vessels.

Palavras Chave/Key-words: Fetoplacental arteries, Fetal Growth Restriction, Biomechanical Analysis

ID: 3682

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: MATERNAL OBESITY PROTECTS THE OFFSPRING AGAINST SEPSIS AND MODULATES THE IMMUNE RESPONSE

Embasamento/Background: Sepsis is a clinical condition caused by a dysregulated immune response to infection. Lipopolysaccharide (LPS), a major component of gram-negative bacteria, has been studied as a key mediator of the pathogenesis of bacterial infection and it can lead to an organ dysfunction and hypotension. The obese dams' offspring have increased metabolic damages after inflammatory challenge. The innate immune system is capable of restore the homeostasis and it modulates the activating of the cholinergic anti-inflammatory pathway. This system is dependent of acetylcholine which is released by the vagus nerve stimulated by a central muscarinic receptor signaling and it will inhibit pro-inflammatory mediators' production. We studied if central activation of the M1 muscarinic receptor in the obese dams' offspring can prevent metabolic damages caused by sepsis.

Métodos/Methods: Ethics approval was obtained from the State University of Campinas Ethics Committee (Protocol 5546-1/2020). Female Swiss mice were subjected to either standard chow (SC) or high-fat diet (HFD) during pregnancy and the lactation period. The analyzes were performed in the offspring (SC-O and HFD-O) 28 days. The cholinergic receptor m1 mAChR expression was measured by western blotting, qPCR and immunofluorescence. Survival rate was measured in the offspring after challenge with LPS ip (30mg per Kg body weight) and repeated with antagonist Benztropine administration (ICV). The serum cytokine levels were evaluated in the groups by Elisa. Finally, the immune response was evaluated in the spleen and bone marrow isolated cells by flow cytometry.

Resultados/Results: The hypothalamic level of M1 mAChR protein and the mRNA levels were elevated in the HFD-O offspring compared to the SC-O offspring. M1 expression in HFD-O offspring seems to be more intense in the median eminence. HFD-O offspring was protected against the sepsis induced by LPS. However, this protection was lost when the offspring were treated with M1 antagonist (icv). The cytokines levels, TNFa and IL-10, were reduced in the blood serum of HFD-O group after challenge with LPS but this was prevented by the antagonist administration. The mean number of isolated bone marrow cells was reduced in HFD-O mice compared to the SC-O mice. Flow cytometry analysis was used to predict differences in the immune cells in the spleen and bone marrow cells differentiated. On average, HFD-O mice did not show any significant differences in positive macrophage cells in mature bone marrow cells. However, CD45 + Ly6G +cells (neutrophils) and CD45+ F480+ CD11c+ cells (pro-inflammatory macrophages) seem to be reduced in the spleen of HFD-O offspring. Additionally, CD3+ CD4+ cells (T-helper lymphocyte) was increased and CD3+ CD8+ cells (cytotoxic T- lymphocyte) decreased in the spleen of HFD-O offspring. IL6 and IL-1² cytokine levels seems to be reduced in mature bone marrow cells of HFD-O mice compared with SC-O mice. These findings confirm the difference in the immune response in the HFD-O mice.

Conclusões/Conclusions: Taken together these results show that the central increase of the M1 receptor in the offspring mediated by maternal consumption of HFD plays an important role in the prevention against endotoxic shock caused by sepsis and seems to improve the immune response cells in the offspring.

Palavras Chave/Key-words: M1 mAChR receptor, programming, sepsis.

ID: 3684

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Myricetin Improves Metabolic Profile but not Cognitive Deficit Associated to MSG-induced Obesity in Mice

Embasamento/Background: Flavonoids could be indicated as potential preventive therapy for obesity, metabolic syndrome and even their comorbidities. Myricetin is a flavonoid known for its hypoglycemic and anti-obesity effects, as well as its great scavenger capacity. Rodent obesity induced by monosodium L-glutamate (MSG) is a model of hypothalamic obesity which develops early hyperinsulinemia and mimetizes DM 2, obesity, dyslipidemia, NAFLD/NASH and cognitive deficit. Thus, this study aimed to investigate whether myricetin can revert or ameliorate metabolic and behavioral features in MSG-induced obesity.

Métodos/Methods: Male Swiss mice pups (n= 24) were treated with 4g/Kg/day of MSG or 0.9% saline solution (CTR), by subcutaneous via, in alternate days, during the first ten days of life. Each 30 days of life, blood samples were collected by tail to assess fasting glucose and fasting triglycerides. Lee Index and TyG were calculated. When the animals reached 90 days of life, MSG obese animals were divided into two groups: MCT, treated for 45 days with myricetin suspended in distilled water at dosage of 50 mg/Kg by gavage, and MSG, which received vehicle. Between 120 and 135 days of life, animals performed the following behavioral tests: Morris Water Maze, Elevated Plus Maze, Open Field and Forced Swim. After that, they were euthanized for collection of fat pads (retroabdominal, periepididymal and mesenteric), liver and blood samples. Fat pads and liver were weighted, and liver samples were processed to histology. In liver H&E slides, NAFLD activity score was assessed.

Resultados/Results: After myricetin treatment, MCT had a Lee Index value (349.5 ± 6.8, g1/3.cm-1) significantly lower than MSG mice (376.1 ± 9.1, g1/3.cm-1), but still higher than CTR (313.2 ± 3.2, g1/3.cm-1), what demonstrates that myricetin treatment reduced body mass, albeit has not impacted body weight. Myricetin also reduced the relative weight of periepididymal fat pad (CTR: 0.25 ± 0.03; MSG: 0.52 ± 0.03; MCT: 0.39 ± 0.03 g/10 g of total body weight), but not the other ones. Myricetin treatment improved hyperglycemia (CTR: 99.8 ± 4.1 mg/dL; MSG: 145.1 ± 14.6; MCT: 100.3 ± 10.4 mg/dL) and hypertriglyceridemia (CTR: 70.1 ± 6.0 mg/dL; MSG: 91.6 ± 9.7 mg/dL; MCT: 61.1 ± 9.1 mg/dL). Thus, myricetin restored peripheral insulin sensitivity, as depicted from the decreased TyG value (CTR: 8.1 ± 0.1; MSG: 8.9 ± 0.2 mg/dL; MCT: 7.9 ± 0.3 mg/dL). Besides, MSG mice displayed microvesicular steatosis, which was completely reverted by myricetin treatment. In Open Field, MSG mice exhibited less thigmotaxis than CTR ones, since they remained more time into the inner zone (CTR: 59.2 ± 4.9; MSG: 91.7 ± 12.5 s). Myricetin treatment reverted this behavior because of MCT mice thigmotaxis was even higher than CTR (CTR: 239.9 ± 4.7; MSG: 208.3 ± 12.5; MCT: 270.1 ± 7.4 s). In Elevated Plus Maze, rearing count was significantly lower in MSG group, as compared to CTR and MCT (CTR: 16.7 ± 1.7; MSG: 10.4 ± 0.6; MCT: 16.4 ± 1.7), although no difference had been found in motor activity parameters. MSG mice had marked cognitive deficit, as verified in Morris Water Maze, which was not altered by myricetin treatment. No differences were found among groups in Forced Swim.

Conclusões/Conclusions: Overall, our results suggest that myricetin may be used as a complementary therapy for both metabolic and central comorbidities in obesity and MSG cognitive deficit needs further investigation.

Palavras Chave/Key-words: Myricetin, Monosodium L-glutamate, Metabolic Syndrome, Cognitive Deficit

ID: 3685

Área: DOHaD and exercise

Forma de Apresentação: Ê-POSTER

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Título/Title: Inadequate Physical Training in Pregnancy as Stressful Factor Addressing Metabolic Disturbances in Rat-Offspring

Embasamento/Background: Physical training has been postulated as a healthful practice fighting the metabolic disorders onset and progression. Nevertheless, in case, it be improperly practiced, especially during critical periods of life such as pregnancy, it can become an unhealthy factor, like that a source of physiological stress, imprinting negative programming of metabolism. Herein we was interested on to assess the effect of an inadequately swimming training protocol in pregnancy on the birthweight, catch-up growth, and metabolic parameters of rat offspring.

Métodos/Methods: Female Wistar rats swam, throughout pregnancy and lactation, in one fo the following swimming training protocols: protocol where rats started to swam abruptly at begin of pregnancy (Ab-S group) or protocol where rats started to swam (gradually and previously of conception, Gr-S group), while control group did not swam (Cont group). To assess the stressful effect of the swimming training protocols on rats, a submaximal lactate test was performed. At delivery, birthweight and body length of rats were assessed. Body weight, food and water intake were recorded every two days, since weaning (21-days old) until adulthood, where euthanasia was performed to collect body tissues (retroperitoneal, periepididymal and mesenteric fat pads) as well as blood for further biochemical (lipid profile and glucose homeostasis) analyzes. All experiments were approved by the Ethics Committee of the Federal University of Mato Grosso (protocol number 2108.017073/2019-56).

Resultados/Results: In comparison with Cont rats, Ab-S rat-offspring were smaller at birth, as well as lower than Gr-S rats ($P<0.01$). At adulthood, Ab-S rats displayed an obese phenotype associated with metabolic dyshomeostasis (higher body weight and increased visceral fat pad, $P<0.05$), in addition a reduction in the interscapular brown adipose tissue was observed ($P<0.05$). Ab-S rats were hyperglycemic ($P<0.01$), insulin resistant and hypertriglyceridemic ($P<0.05$) when compared with Cont and Gr-S rat groups. Corroborating findings on metabolic disturbances, Ab-S rats, presented Castelli indexes ($P<0.001$) higher than Cont and Gr-S rat groups.

Conclusões/Conclusions: Inadequately swimming training, in pregnancy and lactation, affects rat offspring birthweight, which seems to be associated with body and metabolic dyshomeostasis in later life.

Palavras Chave/Key-words: Key words: low birthweight, intrauterine stress, swimming training, metabolic syndrome, obesity. Financial Support: CAPES, CNPq, FAPEMAT.

ID: 3686

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Placental transcobalamin receptor (TCblR/CD320) expression and vitamin B12 status in mother and their offspring: the effect of pregestational obesity and sexual dimorphism

Embasamento/Background: Low vitamin B12 status during pregnancy leads to adverse perinatal outcomes. Chile has a high prevalence of obesity and it's have been reported that obesity in non-pregnant and pregnant women decrease their vitamin B12 levels in plasma compared to normal weight. It is not well known whether pregnant women with pregestational obesity have low vitamin B12 levels and what are its effects on pregnancy and in the offspring and if there is some relationship with its placental transport

Métodos/Methods: Pregnant women were enrolled in EpiFat study (NCT04249635). At the time of delivery maternal blood, cord blood, and placenta were collected from women with pregestational normal weight (PG-NW), pregestational overweight (PG-OW) and obesity (PG-Ob): 60 pairs (mother-offspring) and 150 offspring. The placental mRNA expression (RT-qPCR) and protein levels (Western Blot) of TCblR/CD320 were evaluated in PG-Ob (n=40) and PG-NW (n=30) groups. To evaluate Vitamin B12 Status, the maternal and cord blood vitamin B12, and holotranscobalamin (HoloTC) levels were evaluated by ECLIA, homocysteine levels by HPLC, and Methylmalonic acid (MMA) by LC-MS/MS. Kruskal Wallis test was used to evaluate differences between groups; Mann Whitney test was used to evaluate differences between sexes. Component Principal Analysis (CPA) and regression models were used to evaluate the relationship of pregestational obesity over Vitamin B12 Status.

Resultados/Results: No significant differences were found in the mothers between the groups for all biomarkers (Vitamin B12, HoloTC, Hcy and MMA). In cord blood from mothers with PG-Ob and PG-OW Vitamin B12 and Holo-TC were lower and Hcy was higher compared to PG-NW ($p<0.05$). Vitamin B12 and HoloTC were higher in cord blood compared with their mothers in both PG-NW ($p<0.0001$) and PG-Ob ($p<0.001$). In plasma of mothers with female offspring, Total Vitamin B12, HoloTC, Hcy and MMA were lower ($p=0.0476$, $p=0.0157$, $p=0.0280$, $p=0.0116$, respectively). Total Vitamin B12 is lower in female offspring ($p=0.0259$). In placentas from PG-Ob, mRNA expression is lower compared with PG-NW, however, protein levels were not different between groups. Both mRNA and protein of TCblR/CD320 are higher in female placentas than males ($p<0.05$). In PCA, we found two clusters in cord blood of pairs (n=60) and in total cord blood samples (n=145). In Cluster 1 (n=91), was observed an association according to pregestational BMI, showing that 42% (n=38) had mothers with pregestational obesity and 24% (n=22) had mothers with pregestational overweight compared to 26% (n=14) and 15% (n=8) cluster 2 (n=54), respectively (Pearson's Chi-Square test $p=0.0125$). Also, Cluster 1 had lower Vitamin B12 status (low vitamin B12 and HoloTC and high MMA), This association with pregestational obesity and vitamin B12 status in the offspring was also confirmed in the regression models.

Conclusões/Conclusions: Maternal pregestational obesity decreases vitamin B12 status in the offspring of women with pregestational obesity possible due to altered transcobalamin transport in the placentas. Regardless of maternal nutritional status before pregnancy, the female newborn has lower vitamin B12 and HoloTC levels, but higher mRNA and protein expression of TCblR/CD320 possibly because of an adaptation mechanism in the placenta to ensure vitamin B12 delivery to the fetus. There is some relationship between the sex of the fetus and the maternal vitamin B12 status; therefore, we suggest future studies according to sex dimorphism, possible from the beginning of the pregnancy to understand this association, which could be related since placental implantation.

Palavras Chave/Key-words: Vitamin B12 Status, Pregestational obesity, Transcobalamin receptor, sexual dimorphism

ID: 3432

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Effects of Excessive Chronic Omega 3 and Omega 6 Supplementation in Female Wistar Rats Offspring Weight and Mortality at Birth

Embasamento/Background: Excess chronic supplementation of a specific metabolic substrate is known to cause not only adverse effects on metabolic balance but also has an oxidative effect by raising error rate in oxidative metabolism, resulting in increased formation of reactive oxygen species (ROS). The expected consequences of n-3 and n-6 PUFA supplementation, therefore, include a higher probability and rate of stillbirths, compared to a control group, besides the overweight of the offspring along the first trial weeks.

Métodos/Methods: In this trial (CEUA 1303), female Wistar rats in the pregnancy process had their body weight gain and food intake monitored during the 12 experimental weeks. Analyzing the percentual body weight gain of these females, no difference in gain between groups was statistically observed by ANOVA testing.

Resultados/Results: The only differences found were in time and treatments along the trial period. When it comes to food intake, there was no difference between treatments neither of treatments along, only the food intake was increased along time. On the day of birth of the offspring, the animals were manipulated to the counting, sexing, and stillbirth quantifications. The number of live and dead pups was

analyzed by Pearson's Chi-Squared test, not being observed an n-3 and n-6 PUFA supplementation interference on the number of births or a relation between supplementation and number of stillbirths, despite both of which increased the absolute pups' mortality when in comparison to the control group offspring. After normalizing the litters, being fixed the number of eight pups per litter (4 males and 4 females), all offspring were weighed, being observed a higher weight of the litters n-3 and n-6 PUFA supplemented when in comparison to the control group.

Conclusões/Conclusions: Hence, even that chronic supplementation showed no effects on body weight gain on mothers, there was a significant effect on the offspring's body weight gain at birth. And, contrary to expected, there was no statistic relation to supplementation and the number of stillbirths. This research was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

Palavras Chave/Key-words: development; toxicity; fatty acids

ID: 3689

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Ketogenic Diet does not reverse hepatic steatosis of obese animals induced by early cafeteria diet in addition to promoting steatosis in healthy mice

Embasamento/Background: The energy imbalance contributes directly to the installation of the phenotype of obesity, environmental factors when instated in the initial period of life, can serve as an important stimulus to the altered health state. The growth in its prevalence is related to the increase in the incidence of other comorbidities such as non-alcoholic fatty liver disease (NAFLD), which can impact the risk of chronic diseases from childhood to adulthood. Such disease has high prevalence in obese individuals. In this sense, interventions during the primary phases (pregnancy, early childhood and childhood) can be of great importance for public health. Different dietary approaches have been used to control this comorbidity, among them the ketogenic diet (KD). Although some studies report a decrease in weight and an improvement in insulin sensitivity, its effects on the liver are still controversial. The purpose os this work is to elucidate the effects of KD on the lipid and liver profile of mice exposed to obesogenic diet in childhood

Métodos/Methods: To obtain the data we distributed the 50 mice that were exposed to diets immediately after weaning, in 2 groups: one group received control diet (CRT) and the second group cafeteria diet (CAF) diet for 12 weeks. Following this period, these groups were again redistributed to 5 groups that received the CRT, CAF or KD diet and another two groups that continued receiving the induction period diets for another 8 weeks. The weights of the animals were analyzed weekly and every 30 days the lipid profile and glycemia were measured, through the plasma levels of triglycerides, total cholesterol and fasting glycemia, besides the caloric consumption. After euthanasia the liver was collected to perform the hepatic histology.

Resultados/Results: In animals submitted to cafeteria diet, the obesity phenotype was established, resulting in high levels of triglycerides, cholesterol, glycemia and insulin resistance. There was an increase in weight among the animals that consumed the ketogenic diet. In the animals that received CAF and after received KD there was an improvement in triglyceride levels, without changes in cholesterol levels. The restriction of carbohydrates and higher consumption of lipids in animals that were previously fed a CTR and started receiving KD resulted in significantly higher levels of cholesterol and fasting glycemia. In addition, mice in the KD group showed fat accumulation in the hepatocytes, characterizing the presence of hepatic steatosis, animals in the CAF group also showed steatosis, however, the liver of animals that consumed CTR or CAF that changed to KD had an even greater presence of steatosis, showing that KD is linked to the development of NAFLD.

Conclusões/Conclusions: Taken together, the results show that exposure to hypercaloric diets by mice in early childhood promotes metabolic dysfunction generating the phenotype of obesity. However, KD was not a promising therapy for reversing these dysfunctions, leading to steatosis, because the high concentrations of KD lipids lead to a high production of free fatty acids that follow towards the liver, thus increasing their accumulation. Despite the improvement of triglyceride levels and glycemia. Financing: FAPEMA.

Palavras Chave/Key-words: early nutrition, obesity, ketogenic diet, steatosis

ID: 3434

Área: DOHaD and nutrition

Forma de Apresentação: ORAL

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Título/Title: Nutritional Epigenetic Re-Programming Brain Expression Profiling on Rat Pups after the Supplementation of miR-375-3p

Embedded in Biomimetic Vehicles

Embasamento/Background: MicroRNAs are small non-coding RNAs with an average length of approximately 22pb. They regulate post-transcriptional gene expression in the integrated and tuning manner. There are proposed as therapeutic candidates for several nutritional disease. In order to know the therapeutic potential of miR-375-3p we conduced epigenetic alterations induced by an oral bolus on pups rats.

Métodos/Methods: Sprague-dawley pups were oral supplemented with nanovesicles containing miR-375-3p at PND12. The animals were euthanized at PND45, samples of the hypothalamus; brain stem and hippocampus were collected and stored at -80°C. Total RNA was isolated using Quiazol. RT-qPCR were evaluated using SYBR® for transcripts and TaqMan system for the microRNAs. Ct data were normalized by an internally reference β-Actin, β-2 Microglobulin, and GADPH genes geometric mean for messenger, and let-7d, miR-let-7g and miR-146 for microRNAs. Comparison of mean between the groups (Control vs miR-375-3p; n=16) adjusted by gender was done used ANOVA two-way interaction and Post-hoc Bonferroni p adjust value, significant difference were taken at $p<0.05$. The ethics committee in animal experimentation, Pays de la Loire, France (APAFIS 21917), approved this protocol.

Resultados/Results: The three tested tissues present significant differential effect on HTR1B, HTR2C, DRD1, DRD2 messengers at the PND45. We found impact on the expression levels miR-320-3p and miR-132-3p in the three tissues, miR-504 modifier expression on hypothalamus and hippocampus. While miR-16 preferentially affect the hypothalamus.

Conclusões/Conclusions: Conclusions: The early (PND12) supplementation of one high dose of miR-375-3p modified the expression profile of important modulators of eating behavior on the brain regions tested. Showing a potential therapeutic role for the epigenetic modulation in eating disorders, by reprogramming key molecules. Founding RFI Food for Tomorrow/Cap Aliment and Research, Education, and Innovation in Pays de la Loire and CAPES (Finance code 001).

Palavras Chave/Key-words: Therapeutic microRNA, Eating Behaviors Modulation, Exosome-like particles

ID: 3690

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Changes in Metabolic Hormones Due to Intrauterine Undernutrition Can be Triggering Obesity Phenotype in Weaned Rat Offspring

Embasamento/Background: Perinatal stress such as intrauterine malnutrition has been well used as a tool to study the developmental origins of health and diseases. Food scarcity in critical stages of life is a strong factor programming high vulnerability of metabolic diseases later in life. Herein, we aimed to evaluate the effect of intrauterine malnutrition on breasting milk composition and weaned rat offspring body composition, biochemical and metabolic hormones profile.

Métodos/Methods: Seventh five days-old Wistar rats were mated and the pregnancy assessed by the vaginal smear, where the presence of spermatozoa were used to mark the conception. On the 14th day of pregnancy, the amount of food, commonly feed ad libitum by control rats, was reduced by 50% (FR50 group) until delivery, while the control mothers (CONT group) was fed ad libitum throughout pregnancy and lactation. At birth, body weight and the naso-anus length was measured and litter size adjusted to 8 pups per mother. The body weight gain was quantified every 2 days during the breastfeeding period. On the 12th day of breastfeeding, milking was performed for biochemical and creamatocrit analysis. At weaning, fasted overnight rat offspring were euthanized to remove the fat pad stores (mesenteric, retroperitoneal and periepididymal) to quantify body composition and blood for biochemical and hormonal quantification. Peripheral insulin sensitivity was assessed by calculating the TyG index, where fasting blood glucose and triglycerides were used for this. The Ethics Committee approved the experimental procedures (protocol number: 23.108724433/2017-16).

Resultados/Results: At birth, FR50 rats were 9.38% lighter ($P<0.01$) and 9.89% smaller ($P<0.001$) than CONT rats. By other hand, the FR50 rat's body weight gain, over the suckling period, was increased by 62.00% ($P<0.001$), as well as fat pad stores (mesenteric, 83.33%; retroperitoneal, 180.00% and periepididymal, 63.27%; $P<0.001$) in comparison with CONT rats. At weaning, compared to CONT rats, the FR50 rats presented hyperglycemia (+20.78%, $P<0.05$), hypertriglyceridemia (+75.41%, $P<0.01$), hyperghrelinemia (+81.40%, $P<0.05$) and hyperleptinemia (+74.55%, $P<0.001$). Indeed, in relation to the CONT group, the TyG values was increased in FR50 rats (+7.01%, $P<0.001$), characterizing insulin resistance. Breast milk showed high levels of glucose (27.05%; $P<0.01$), triglycerides (1.52%; $P<0.05$); total cholesterol (40.61%; $P<0.05$), fat content (22.10%; $P<0.05$) and energy value (21.32%; $P<0.05$).

Conclusões/Conclusions: Intrauterine malnutrition programs rat offspring to lower birthweight, as well as metabolic hormones and nutrient milk composition, contributing to early obesity and the development of insulin resistance, which is associated with changes in hormones that control energy balance in rat offspring blood.

Palavras Chave/Key-words: Obesity, metabolic programming, insulin resistance, ghrelin.

ID: 3446

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Paternal Programming: Sex-dependent Effects In The Placenta Of Fetuses From Male Diabetic Rats. Daiana Fornes, Florencia Heinecke, Verónica White, Alicia Jawerbaum, Evangelina Capobianco. Centro de Estudios Farmacológicos y Botánicos

Embasamento/Background: Paternal exposure to diabetes can lead to the transmission of metabolic disorders in the offspring. Our aim was to assess sex-dependent lipid alterations in the placenta of fetuses from diabetic males.

Métodos/Methods: Control and type 2 diabetic male rats (diabetes obtained by intrauterine programming in the offspring of streptozotocin-induced diabetic rats, glycemia: 140-190 mg/dL) were mated with control female rats. On day 21 of gestation, the placenta of male and female fetuses was obtained for the evaluation of lipid levels (by TLC) and mRNA of genes involved in lipid metabolism (by RT-qPCR).

Resultados/Results: Fetal weight was increased in both males and females of diabetic group (15%, $p<0.05$) but placental weight and fetal glycemia showed no differences between groups. Triglyceride (46%, $p<0.05$), cholesterol (43%, $p<0.01$) and free fatty acid (47%, $p<0.05$) levels were increased in the male's placenta but not in the female's placenta from diabetic group. The PPARalpha mRNA levels were only increased in the male's placenta from diabetic group (168%, $p<0.001$), and no differences were found in the PPARgamma and PPARdelta mRNA levels in placentas of both male and female fetuses from diabetic group. The mRNA levels of Fasn, Acc1 and Scd-1 (genes involved in lipid synthesis) show no differences between groups, and the mRNA levels of Aco (42%, $p<0.05$), Fatp1 (96%, $p<0.01$), Lipg (121%, $p<0.05$) and Lpl (79%, $p<0.01$) (genes involved in lipid oxidation and transport) were increased only in placentas of male fetuses from diabetic group.

Conclusões/Conclusions: Paternal diabetes has sex-dependent effects on the regulation of lipid metabolism in the placenta, where only males were affected with an increase in lipid accumulation and an increase in the mRNA expression of enzymes involved in lipid oxidation and transport pathways.

Palavras Chave/Key-words: Fetal Programming. Paternal Diabetes. Placenta. Lipids.

ID: 3457

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: ORAL

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Título/Title: Impact of the Treatment with Mometasone Furoate over Pancreatic Beta Cells Mass in Rats

Embasamento/Background: Synthetic glucocorticoids (GCs) are anti-inflammatory and immunosuppressive drugs, commonly used for treating asthma, rheumatoid arthritis, and multiple sclerosis as well as after organ transplants to prevent possible immune responses against the newly transplanted organ. GCs efficacy is undeniable but depending on the degree of drug exposure adverse effects will be present such as skin and muscle atrophy, osteoporosis, and delayed growth. Excess of GCs also result in significant alterations over the glucose metabolism including reduction in the peripheral insulin sensitivity and impairment of glucose tolerance. Glucose intolerance is possibly due to an uncouple between beta-cell function or mass with the metabolic demand, as observed in rats treated with dexamethasone. Most of undesirable metabolic effects of GCs occurs through upregulation of genes containing glucocorticoid responsive elements. An already existing GC, mometasone furoate (MF), could be a candidate for maintaining the GC efficacy with lesser adverse effects, due to its preferential binding in vitro to the Farsenoid X receptors. MF is applied for topic/inhaled purposes and there is no study evaluating its systemic effects due to its low bioavailability. We aimed to evaluate the impact of MF administration on pancreatic beta-cell mass and to compare these findings with those obtained in rats treated with DEX.

Métodos/Methods: The experimental protocol was approved by the institutional Committee for Ethics in Animal Experimentation (5012250518). Three-month-old Wistar rats received daily injection of the following compound during seven consecutive days: corn oil (1 ml/kg b.m., o.g.) or NaCl 0.9% (1 ml/kg b.m., i.p.) as controls, DEX 1 mg/kg b.m. i.p or o.g. diluted in saline and MF 1 mg/kg b.m. i.p. or diluted in corn oil. After the last day of treatment, the animals were euthanized, and their pancreas was processed for insulin immunofluorescence. Morphometric analyses were done using ImageJ software. One-way ANOVA followed by post hoc Tukey test (GraphPad Prism 8.0.1.) was applied for multiple comparisons of parametric data. The significance level adopted was $P < 0.05$.

Resultados/Results: Preliminary data indicate rats treated with MF through i.p. exhibited higher beta cell mass (32,95 mg) compared with their control group (corn oil-treated), in contrast with the o.g. group which did not exhibit modification of beta-cell mass. DEX treatment resulted in higher absolute beta-cell mass for both i.p. (32,82 mg) and o.g. (44,23 mg) groups than in the control group (saline-treated).

Conclusões/Conclusions: Treatment with MF through o.g. is not associated with change in beta-cell mass. This data may indicate rats treated with the anti-inflammatory MF through o.g. have either unaltered insulin sensitivity and glucose tolerance or this unaltered beta-cell mass is not sufficient to avoid glucose metabolism disturbances, a matter to be investigated.

Palavras Chave/Key-words: beta cells, mometasone furoate, dexamethasone, glucose homeostasis

ID: 3463

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Fructose consumption by adult rats exposed to dexamethasone in utero exacerbates intestinal gluconeogenesis

Embasamento/Background: Fructose consumption by rodents modulates both hepatic and intestinal lipid metabolism and gluconeogenesis. We have previously demonstrated that in utero exposure to dexamethasone (DEX) interacts with fructose consumption during adult life to exacerbate hepatic steatosis in rats. The aim of this study was to clarify if adult rats born to DEX-treated mothers would display differences in intestinal gluconeogenesis after excessive fructose intake.

Métodos/Methods: Female Wistar rats were treated with DEX during pregnancy and control (CTL) mothers were kept untreated. Adult offspring born to CTL and DEX-treated mothers were assigned to receive either tap water (CTL-SC and DEX-SC) or 10% fructose in the drinking water (CTL-fructose and DEX-fructose). Fructose consumption lasted from the 80th to the 160th day of life. All rats were subjected to a 40-hour fasting before sample collection.

Resultados/Results: Rats born to DEX-treated mothers displayed reduced birth weight (18% lower than CTL; P=0.033). Both DEX-SC and DEX-fructose had shorter small intestine when compared to CTL-SC (respectively 8% and 7% shorter; P<0.05). DEX-fructose rats have increased glucose (144% higher than CTL-SC and 83% higher than CTL-fructose; P<0.01), and reduced lactate in the portal blood (26% lower than CTL-SC; P<0.05). Jejunum samples of DEX-fructose rats have enhanced PEPCK activity (14% higher than CTL-SC; P<0.05), decreased hexokinase activity (ca. 50% lower than all remaining groups; P<0.01), increased GLUT2 (60% higher than CTL-SC and 73% higher than DEXA-SC; P<0.01), and GLUT5 contents (75% higher than CTL-fructose; P<0.05). Morphological analyses also show increased villous height (27% higher than CTL-SC and 39% higher than DEX-SC; P<0.05 and P<0.01), crypt depth (25% higher than DEX-SC and 43% higher than CTL-fructose; P<0.05 and P<0.01), and PCNA staining (48% higher than CTL-SC, 78% higher than DEX-SC and 43% higher than CTL-fructose; P<0.0001).

Conclusões/Conclusions: The current data reveal that consumption of fructose by adult rats exposed to DEX during fetal life leads to an exacerbation in intestinal gluconeogenesis and recapitulates morphological features in the jejunum that are commonly found during neonatal life. These data provide a new mechanism to explain the increased prevalence of metabolic disturbances in humans that were born with low birth weight.

Palavras Chave/Key-words: fructose, dexamethasone, intestinal gluconeogenesis

ID: 3472

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: Ê-POSTER

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Título/Title: ANGIOTENSIN-(1-7) IMPROVES CARDIAC LEFT VENTRICULAR BIOENERGETICS AND MITOCHONDRIAL FUNCTION IN A RAT MODEL OF NEONATAL HIGH OXYGEN-INDUCED CARDIOMYOPATHY.

Embasamento/Background: The cardiac transition to extra-uterine life requires significant bioenergetics and mitochondrial (mito) adaptation, and the immature heart is particularly susceptible to deleterious neonatal conditions. Impaired cell bioenergetics and mitochondrial function are a hallmark of cardiac disease-associated hypertrophy and are determinant in the progression to heart failure. We previously showed that angiotensin II contributes to the cardiomyopathy induced by transient neonatal exposure to hyperoxia in rats, a model of preterm birth. We here postulated that oxygen-induced cardiomyopathy (OIC) is associated with impaired cell bioenergetics that can be reversed by treatment with Ang-(1-7), a counter-regulatory peptide of the renin-angiotensin system.

Métodos/Methods: Sprague–Dawley litters were kept in 80% O2 from day 3 (P3) to P10 of life (OIC group) or in room air (Ctrl group). Male offspring were studied. At P22, osmotic minipumps containing Ang-(1-7) (24 µg/kg/h) were implanted. At P28 cardiac echo was performed and at P34, the rats were euthanatized, the heart was removed and the left ventricle (LV) sampled for molecular analyses and mitochondria isolation. Results are mean±SEM; Ctrl vs. OIC vs. OIC Ang-(1-7) are compared using one-way ANOVA with Fisher (n=6/group. P<0.05).

Resultados/Results: The treatment with Ang-(1-7) restored LV ejection fraction (75±4 vs. 65±3 vs. 70±2%) and fractional shortening (45±4

vs. 37±2 vs. 40±1%) at P28. Ang-(1-7) also restored the oxygen consumption rate during the oxidative phosphorylation (state 3) of LV isolated mitochondria respiration (228±12 vs. 187±15 vs. 243±25 nmol O2/mL/mg protein), the protein expression (relative to GAPDH) of mitochondrial electron transport chain complexes III (1±0 vs. 0.6±0.05 vs. 0.86±0.13) and V (1±0 vs. 0.67±0.03 vs. 0.95±0.03), normalized LV cardiomyocytes marker of mitochondria abundance citrate synthase mRNA (0.93±0.02 vs. 1.11±0.07 vs. 0.87±0.05), and hexokinase expression, a marker of less efficient bioenergetics (1.04±0.12 vs. 1.76±0.28 vs. 1.01±0.23).

Conclusões/Conclusions: Our results indicate that Ang-(1-7) treatment of juvenile rats subjected to neonatal high oxygen exposure prevents LV systolic dysfunction and restores LV mitochondrial dysfunction. This study identified a potential therapeutic target for impaired cardiac function observed in children and young adults born very preterm.

Palavras Chave/Key-words:

ID: 3483

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: MiR-29a-c Regulate PGC-1α, PEPCK and G6Pase Expression in Liver of Weaning Rats Exposed to Dexamethasone in utero

Embasamento/Background: Fetal excess of glucocorticoids is one of the main insults that lead to metabolic impairment in the liver, generated in cases of malnutrition or stress during pregnancy. In the present study, we used an experimental model to induce metabolic reprogramming: maternal treatment with dexamethasone (DEX) during the third period of pregnancy. A master regulator of mitochondrial biogenesis and a primary regulator of liver gluconeogenesis is the peroxisome proliferator-activated receptor gamma coactivator 1 alpha (PGC-1α). PGC-1α plays a pivotal role in the transcription of genes that encodes gluconeogenesis-limiting enzymes, and is modulated by epigenetic mechanisms such as cytosine methylation and miRNAs. This study aimed to evaluate whether hepatic changes in PGC-1α expression and epigenetic mechanisms occur to explain the glucose intolerance and persistent upregulation of gluconeogenesis enzymes of weaning rats exposed to DEX in utero.

Métodos/Methods: Male Wistar rats born to mothers treated or not treated with dexamethasone during the last week of pregnancy (DEX and CTL, respectively) were used in the experiments. After birth, the offspring were euthanized on the first day of lactation (L1), eighth day of lactation (L8) and at weaning (21st day of lactation - L21) for sample collection and analysis.

Resultados/Results: On the 21st day of life, rats exposed in utero to DEX displayed glucose intolerance (71% higher than CTL; P = 0.002) and increased conversion of pyruvate into glucose (53% higher than CTL; P = 0.02). In the liver, either Pck1 mRNA expression, PEPCK protein content and PEPCK activity were upregulated (respectively 106%, 21% and 16% higher than CTL; P = 0.0006, P = 0.008 and P = 0.02) along with enhanced G6pc mRNA expression, G6Pase protein content and G6Pase activity (respectively 270%, 32% and 89% higher than CTL; P = 0.0008, P = 0.019 and P = 0.001). Rats born to DEX-treated mothers exhibited increased hepatic PGC-1α protein content at L21 (43% higher than CTL; P = 0.006). Conversely, there was a progressive decrease in Ppargc1a mRNA expression throughout early postnatal life, reaching the lowest value at L21 (6.7-fold lower than L1 and 6.1-fold lower than L8; P<0.0001 and P = 0.0019, respectively) and an increase in the Ppargc1a promoter cytosine methylation at L21 (90% higher than CTL; P = 0.01). Such rise in PGC1α protein content, instead, was paralleled by decreased miR-29a-c expression (2.5-fold lower than CTL; P = 0.01). Of note, miR-29a-c are validated negative regulators of Ppargc1a gene translation. In addition, rats born to DEX-treated mothers presented impaired lipid metabolism, which was associated with reduced PPARα protein content (37% lower than CTL; P < 0.0001), altered expression of putative PPARα target genes and increased lipid density in hepatocytes (65-fold higher than CTL; P = 0.0003).

Conclusões/Conclusions: Our data suggest that a reduction in miR-29a-c expression prevail over an increase in promoter methylation, resulting in greater hepatic PGC1α content. Such results reveal a novel mechanism to explain the upregulation of key enzymes of gluconeogenesis and demonstrate the genesis of fat accumulation in hepatocytes of rats subjected to metabolic programming.

Palavras Chave/Key-words: dexamethasone, gluconeogenesis, miR-29a-c, PGC-1α, liver

ID: 3486

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: Ê-POSTER

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Título/Title: Safety of Neonatal Venlafaxine on the Mammary Gland Development and Risk for Breast Tumorigenesis in Female Offspring F1 Rats.

Embasamento/Background: Maternal depression during pregnancy and/or postpartum periods is a growing health issue worldwide, which can lead to serious effects on both the mother's and the child's health Venlafaxine (Venl), a serotonin and noradrenaline reuptake inhibitor,

has been used to treat a wide spectrum of mood disorders, including maternal depression. However, some case reports have indicated adverse effects as galactorrhea, mammoplasia and gynecomastia associated with Venl therapy. In addition, this drug has one of the most significant absolute infant plasma concentrations, in comparison with other commonly used antidepressants. Thus, this animal study aimed to investigate the effect of maternal Venl exposure during lactation on the mammary gland growth and morphology and susceptibility to chemically-induced mammary carcinogenesis in female offspring at adulthood.

Métodos/Methods: For this purpose, dams (Wistar strain rat) were treated orally with Venl during lactation (21 days) at doses of 3.8, 7.7 and 15.4 mg/kg. Female offsprings were euthanized for mammary gland development and ovary weight and morphology analyses on the post-natal day (PND) 21 and 30 (1 pup/litter/period). At PND 21, other females (2 pups/litter) received a single intraperitoneal dose of N-nitroso-N-methylurea (MNU, 50 mg/kg) and were euthanized on PND 250 for tumor assay. Tumor incidence and latency were recorded and representative samples were collected for histopathology.

Resultados/Results: The findings indicate the neonatal Venl exposure did not alter the overall development of the mammary glands (ductal elongation or mean number of terminal end buds) or of the ovary (weight and morphology) on PND 21 or 30 neither tumor incidence and latency in female offspring on PND 250.

Conclusões/Conclusions: Thus, the results indicated that Venl exposure did not appear to exert any significant adverse effect on the mammary gland development at early-in life or on breast tumorigenesis late in life.

Palavras Chave/Key-words: Maternal depression, Venlafaxine, Breast

ID: 3489

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Modulation of Gonadotropins After Prepubertal Exposure to Isoflavones. Oliveira, J.M., Sleiman, H.K., DalForno, G.O., Cavallin, M.D., Romano, M.A. Romano, R.M. Department of Medicine/Reproductive Toxicology Laboratory/ Unicentro. Guarapuava, PR-Brasil.

Embasamento/Background: Prepubertal period is considered critical in the development of the organism, characterized by the maturation process of the hypothalamic-pituitary-testicular axis (HPT) and the secretion of gonadotropins (LH and FSH), important in the development of secondary sexual characteristics and regulation fertility. During this maturation process, the integration between genetic, endocrine and environmental factors, can alter the axis homeostasis leading to the manifestation of pathologies and dysfunctions later in life. Isoflavones (ISO) are compounds present mainly in soy, used as a substitute in the vegan, vegetarian diet and in soy-based milk formulations for individuals with lactose intolerance. They have a chemical structure similar to the endogenous hormone 17β-estradiol, and because of this, they can interact with estradiol receptors and trigger stimulatory or inhibitory actions on the axis. Thus, this study aimed to investigate the actions of ISO and genistein (GEN) isolated, on the HPT axis after pre-pubertal exposure.

Métodos/Methods: Forty-two male Wistar rats were divided into 5 groups, being a control group, which received only the vehicle (corn oil), the groups exposed to 0.5, 5 or 50 mg / kg of ISO, and the groups exposed to 0.5 or 5 of GEN by gavage technique from the 23rd postnatal day (PND23) to PND60. The animals were kept on a soy-free diet (PragSoluções Bioscências), water ad libitum, a 12:12 hour light / dark cycle and controlled temperature (23 ± 1ºC). At the end of the experiment (PND60), the animals were euthanized and the samples were collected and stored at -80ºC for further analysis. In the blood, the quantification of the hormones LH, FSH, testosterone and estradiol was carried out by the chemiluminescence method. The hypothalamus, pituitary and testicles were subjected to reverse transcription analysis, followed by RT-qPCR for the analysis of the relative expression of genes: Gonadotropin releasing hormone 1 (Gnrh1), Androgen receptor (Ar), Estrogen receptor 1 (Esr1) and 2 (Esr2) present in the hypothalamus, Gonadotropin releasing hormone receptor (Gnrhr), Luteinizing hormone beta polypeptide (Lhb), Follicle stimulating hormone beta subunit (Fshb), Ar, Esr1 and Esr2, present in the pituitary, and the genes Luteinizing hormone / choriogonadotropin receptor (Lhcgr), Follicle stimulating hormone receptor (Fshr), Cyp19a1 (aromatase) and Inhibin beta B subunit (Inhbb). The data were analyzed statistically by ANOVA followed by the Dunnet post-test ($p < 0.05$) (CEUA/ UNICENTRO 005/2017).

Resultados/Results: In the hypothalamus, there was an increase in the expression of Esr1 in exposure to ISO, while in exposure to GEN there was a decrease in Esr2. In the pituitary, the expression of Gnrhr increased and the expression of Ar and Lhb decreased in the exposure to ISO, whereas in the exposure to GEN, it was possible to observe a reduction in the expression of the Gnrhr and Fshb genes. In the testicles, both treated groups increased the expression of the Lhcgr gene. Exposure to ISO increased the serum concentration of LH and FSH, and decreased the concentrations of testosterone and estradiol.

Conclusões/Conclusions: In this study, exposure to ISO and GEN modulated the expression of genes and the serum level of hormones related to the HPT axis, interfering in the signaling mechanisms of the beginning of puberty, showing that there is an endocrine dysregulation in this period extending to life adult, in addition, GEN showed a different response pattern, which shows that other types of ISO may be involved in these changes. Support: CAPES

Palavras Chave/Key-words: Endocrine disrupting, Isoflavones, genistein, hypothalamic-pituitary-testicular axis

ID: 3494

Área: DOHaD and xenobiotic exposition

Forma de Apresentação: Ê-POSTER

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Título/Title: Maternal Exposure to an Mixture of Phthalates Increases the Susceptibility to Chemically-Induced Mammary Carcinogenesis in Female Offspring Rats. Moreira CM; Zapaterini JR; Brito CP; Freitas T; Scarano WR; Barbisan LF. Depto. BEF/UNESP/Botucatu

Embasamento/Background: Adverse influences early in development, especially during intrauterine life, can result in permanent changes in physiology and metabolism with increased disease risk in adulthood. Maternal exposure to phthalates (Pht), may increase the susceptibility to many cancer types, such as breast cancer. However, much of the experimental research focuses on exposure to a single phthalate, whereas humans are exposed to many. Thus, further investigation using an environmentally relevant mixture of phthalates is necessary to explore their effects on the mammary gland. This study aimed to evaluate the noxious effects of maternal exposure to a mixture of six different phthalates at different doses on the development of the mammary gland and susceptibility to carcinogenesis in the female offspring at prepubertal and adult life, respectively.

Métodos/Methods: Pregnant female Sprague-Dawley rats were exposed to a Pht mixture or vehicle by daily oral gavage. Four groups were established (n=8): Non-treated (control group exposed to corn oil), Low dose (20 µg/kg/day), Moderate dose (200 µg/kg/day) and High dose (200 mg/kg/day). Dams received the respective doses of the Pht mixture in the following proportion: 21% DEHP (Bis (2-ethylhexyl) phthalate), 35% DEP (Diethyl phthalate), 15% DBP (Di-n-butyl phthalate), 8% DiBP (Diisobutyl phthalate), 5% BBzP (Butylbenzyl phthalate), and 15% DiNP (Diisononyl phthalate), during gestational day 12 (DG12) to postnatal day 21 (DPN21). After weaning (PND22), female offspring from each group (n=10) were euthanized and were performed as morphometric measurements of the mammary gland. The others animals (n=16) received a single dose i.p. of N-methyl-N-nitrosurea (MNU, 50 mg/kg) and were maintained until PND 180. The tumor latency, development, and incidence were recorded until PND 180.

Resultados/Results: At PND 22, the mammary gland growth, measured by area and perimeter, was higher in exposed phthalates groups when compared to the control group, but it was not significant (p=0.248 and p= 0.551, respectively). The total tumor number was higher in exposed phthalates groups (n= 12; 15; 21, respectively) when compared to the control group (n=6) and the tumor latency was lower in the higher-dose group when compared to the low-dose group (p=0,031). Finally, the tumor incidence was also higher in the group exposed to a high dose of phthalates than in the control group (p= 0.006).

Conclusões/Conclusions: These findings indicate that Pht mixture exposure, during gestation and lactation, increases the susceptibility to MNU-induced mammary carcinogenesis in adult female offspring.

Palavras Chave/Key-words: Fetal Programming, Mammary Carcinogenesis, Phthalates, Sprague-Dawley Rats.

ID: 3506

Área: DOHaD and nutrition

Forma de Apresentação: Ê-POSTER

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Título/Title: Low protein diet during adolescence induces cardiovascular autonomic dysfunction in male adult rats.

Embasamento/Background: Exposure to low protein diet in perinatal life induces hypertension related to cardiovascular autonomic dysfunction in adulthood. However, it is not known if this insult during adolescence affect the cardiovascular system. This study aims to evaluate whether low protein diet during adolescence induces hypertension related to autonomic dysfunction in adult male rats.

Métodos/Methods: The research ethics committee approved the study under CEUA nº 4833210519. Thirty-day-old Wistar rats were fed a low protein diet (4% protein as casein) for 30 days and subsequently fed a 20.5% normal protein diet for a 60-day recovery period (LP). Control animals (NP) were fed a 20.5% protein diet throughout life. At 120 days of age, direct measurements of arterial pressure were recorded from conscious animals, histological analysis of heart and aorta were performed, and oxidative stress was evaluated. Statistically significant differences were evaluated by T-Student test.

Resultados/Results: LP rats were hypophagic (-13%; p<0,021) until 60 days. LP animals has smaller body weight (-10%; p<0,0003) and body length (-4%; p<0,015), hyperphagia (+21%; p<0,001), hyperglycemia (+13%; p<0,0081) but the lipid profile and visceral fat deposits were similar to NP. Systolic (SBP), diastolic arterial pressure and mean arterial pressures (MBP) were increased in LP (+19%, 23% and 20%, respectively; p <0.0003, p <0.005 and p < 0.002) but heart rate was unchanged. In the spectral analysis, the LP rats showed a greater amplitude in the low frequency zone (LF) of MBP (+41%; p<0,035). In the pulse interval, the LP group showed an increase in LF, LF/HF ratio and total variability (+73%, 45% and 37%, respectively; p<0,014, p<0,048 and p<0,011) but the high frequency zone (HF) was similar to NP. After intravenous injections of atenolol (4mg/kg) and methylatropine (3mg/kg), the bradycardia and tachycardia responses and the intrinsic heart rate were similar to NP. The MBP response to phenylephrine (8 µg/kg, iv) was increased in LP (+26%; p<0,049) but the baroreflex sensitivity (ΔHR/ΔMAP) in response to phenylephrine (8 µg/kg, iv) and sodium nitroprusside (50 µg/kg, iv) was similar between groups. The LF-MBP decrease and depressor response to the ganglionic blocker, hexamethonium (30 mg/kg, iv), was greater in the LP group (57% and 36%; p<0,032 and p <0.006, respectively). The histological analysis showed a decrease in the aortic media wall thickness (-9%; p<0,0001), ventricular hypertrophy in the heart (+10%; p<0,044) in LP, but perivascular fibrosis was not different between

groups. The levels of protein carbonyl (PC) in the heart were decrease in LP (-28%; p<0,0305), but the activity of catalase was lower at the LP (-40%; p<0,0016). The levels of PC were lower in the brainstem of LP (-33%; p<0,002) and the superoxide dismutase and catalase activity were lower (13% and 28%; p<0,044 and p<0,012), but the levels of reduced GSH and total glutathione were higher (+27%; p<0,039 and p<0,038).

Conclusões/Conclusions: Low protein diet during adolescence leads to hypertension later in life, sustained by a greater sympathetic activity which may lead to a structural vascular and cardiac alteration and depend on a disorganization of the redox state.

Palavras Chave/Key-words: low protein diet; high blood pressure; autonomic nervous system.

ID: 3549

Área: DOHaD and non-transmissible chronic diseases

Forma de Apresentação: ORAL

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Título/Title: Facilitation of Corticostriatal Transmission by Phosphodiesterase 10A Inhibition Attenuates L-DOPA-Induced Dyskinesias

Embasamento/Background: Long-term treatment for Parkinson's disease (PD) with L-DOPA has been associated with side effects called L-DOPA-induced dyskinesias (LIDs). The striatum is a key structure of the basal nuclei related to LIDs. The medium spiny neurons (MSNs) make up approximately 95% of the neurons in the striatum and constitute the direct or indirect pathways of motor control. Chronic treatment with L-DOPA is able to modulate these pathways. Much evidence suggests that LIDs would emerge as a result of an imbalance between the direct and indirect pathways. The enzyme phosphodiesterase 10A (PDE10A) is mainly expressed in MSNs in the striatum and metabolizes the second messengers (cAMP and cGMP), thus exercising a strong modulation of the activity of MSNs. Thus, our hypothesis is that inhibition of phosphodiesterase 10A would have an anti-dyskinetic effect by modulating the activity of MSNs.

Métodos/Methods: All procedures were approved by the local ethics committee (CEUA-FFCLRP / USP (18.5.35.59.5). 6-OHDA lesioned rats were chronically treated with L-DOPA (5 mg/kg/day plus benserazide 12,5 mg/kg/day, subcutaneously) once daily for one week. After this period, dyskinetic rats received either vehicle (n = 6) or PDE10A inhibitor (PDE10Ai) (1 mg/kg/day, oral gavage; n=7) one hour before L-DOPA, once daily for two additional weeks. Behavioral analyzes were performed regarding the LIDs that affect the anterior, axial and orofacial limbs of parkinsonian animals. The walking test was performed once a week, 1 hour after the administration of L-DOPA to monitor the effect of L-DOPA antiparkinsonian activity in the animals. After treatment, extracellular electrophysiology was performed in vivo in the parkinsonian striatum to characterize the activities evoked through cortical stimulation, and spontaneous MSNs activities.

Resultados/Results: PDE10Ai (1 mg/kg) decreased axial and forelimb dyskinesias in the third week of treatment (p<0.05 vs. vehicle + L-DOPA) but didn't interfere with the incidence of orofacial dyskinesias (p>0,05 vs. vehicle + L-DOPA). PDE10Ai (1 mg / kg) increased the probability of triggering MSNs evoked by stimulation of the primary motor cortex (p<0.05 vs. vehicle + L-DOPA). The MSNs of the animals treated with PDE10Ai (1 mg/kg) showed spontaneous activity significantly higher than the animals in the control group (p <0.05 vs. vehicle + vehicle).

Conclusões/Conclusions: These data reinforce the discussion that animals treated with PDE10A inhibitors may have their dyskinesias attenuated due to facilitated transmission of the cortico-striatal pathway and an increase in spontaneous activity of MSNs in the striatum. Financial support: this work was funded by CAPES and FAPESP (processes 2017/00003-0 and 2018/12956-5)

Palavras Chave/Key-words: Dyskinesias, L-DOPA, Phosphodiesterase 10A, Corticostriatal

ID: 3565

Área: DOHaD and pregnancy-related disorders

Forma de Apresentação: ORAL

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Título/Title: Effects of Excessive Chronic Supplementation of Omega 3 and Omega 6 on Weight and Body Development of Wistar Rats Offspring After Weaning. Diego Francis Saraiva Rodriguez2, Matheus Felipe Zazula1, Shersey Gonçalves de Oliveira1, Suellen Cristina Baal1, A

Embasamento/Background: Excessive polyunsaturated fatty acids (PUFAs) can have adverse effects on energy metabolism. Knowing this, excessive intake of PUFAs rich in omega 6 (ω-6), and omega 3 (ω-3), during pregnancy and lactation, can modify the body development of the offspring. However, few studies have investigated the body evolution of Wistar rat's offspring, from the excessive supplementation of PUFAs ω-6, and ω-3.

Métodos/Methods: In this study (CEUA 1303), the offspring of 30 Wistar rats supplemented with PUFAs rich in ω-6 and ω-3, were separated from weaning, at 21 days of age, and formed experimental groups according to sex: (CTLE-M and CTLE-F) control male and female

animals, from mothers who were not supplemented; (SPL3-F), females from mothers supplemented with PUFAs rich in ω-3; (SPL3-M), males from mothers supplemented with PUFAs rich in ω-3; (SPL6-F), females from mothers supplemented with PUFAs rich in ω-6; (SPL6-M), males from mothers supplemented with PUFAs rich in ω-6. Body weight (BW), naso-anal length (CNA), and LEE index, were measured at 21, 30, 45 and 60 days of life and analyzed by Repeated Measurements ANOVA.

Resultados/Results: It was observed that, after 45 days of life, the offspring of SPL3 females had lower body weight when compared to CTLE and SPL6. In the same way, both males and females SPL3, as well as the offspring of males SPL6, had lower CNA compared to the CTLE, throughout the experimental period. However, it was observed that the animals of both genders SPL3 and SPL6, presented a higher LEE index in relation to the CTLE, and in males this increase occurred after 30 days of life.

Conclusões/Conclusions: Thus, it is possible to conclude that the chronic supplementation of ω-6 and ω-3, contrasts alterations on the development of the offspring of Wistar rats after weaning, delaying body growth, as seen in the groups of both genders, and reducing weight gain in the offspring of supplemented females, however influencing the increase in the LEE index of these animals.

Palavras Chave/Key-words: Metabolism, Fatty acids, Pregnancy

# SBFIS ePoster Abstracts / Resumos

ID: 2816

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: VASCULAR REACTIVITY IN THE PROCESS OF CARDIOVASCULAR EVOLUTION Duran, L.M.1, Moraes, L. H. O.2, Filogonio, R.1, Rodrigues, G. J.2, Leite, C.A.C.1 1 Departamento de Ciências Fisiológicas, Laboratório de Zoofisiologia e Bioquímica Comparativa 2 Departa

Introduction: Tetrapods had to face diverse new hemodynamic challenges during the evolutionary process to leave the aquatic environment regarding thermoregulation, water balance, gas exchange and cardiovascular modulation to deal with the effects of gravity. Besides, the majority of tetrapod species possesses vascular communication between systemic and respiratory circulation requiring hemodynamic control for effective shunt adjustments. Experimental evidence indicates parasympathetic vascular innervation of the pulmonary artery is the main modulatory mechanism for cardiac shunts in reptiles. We hypothesized that the modulatory mechanism is a primitive character and so that should be present in all tetrapods with cardiac shunts.

Objective: We evaluated the presence of effective parasympathetic vascular innervation in the bullfrog, a basal tetrapod species.

Methods: For the experiments, we used 3 mm vascular rings from systemic and respiratory vessels obtained from bullfrogs, Lithobates catesbeianus (n = 24): The vessels were mounted in a wire myograph and maintained in Krebs solution with gas with 98% O2 and 2% of CO2. After normalization, we used electrical field stimulation (EFS - 0.5 – 16 Hz, 60 V, 30 s) to investigate the presence of vascular innervation. After response curve was defined, we used cholinergic and adrenergic vasoactive drugs to address the nature of the autonomic stimulus such as: Atropine, Phentolamine and Propranolol (EFS – 16 Hz, 60 V, 30 s after 30 minutes incubation) (CEUA - UFSCar: 6616040220)

Results: Pulmonary artery presented further blockage after atropine, indicating the presence of parasympathetic innervation and also, that vascular contraction mediated by muscarinic receptors is the main nervous modulatory source in that segment. Mesenteric artery contraction was blocked after both (Phentolamine and Atropine) indicating a significant presence of adrenergic type β receptors and cholinergic receptors. Propranolol did not cause any significant blockade in any vessel. The femoral vein was the only vascular segment that did not respond to the electric stimulation, thereby the blocker protocol was not applied to this vessel.

Conclusions and Support: The present study brings experimental evidence on the primitive condition for tetrapod vascular modulation. Cholinergic nervous influences are present in both systemic and respiratory circuit and it is the main source of nervous stimulus for contraction in the pulmonary artery.

ID: 3073

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: ANTI-INFLAMMATORY RESPONSE OF BACTERIAL BIOCELLULOSE AND ALGINATE GEL IN SKIN BURN

Introduction: Engineering of new materials having therapeutic applications is a major issue in biomedicine. The biotechnology research field aims at the use of natural and synthetic polymers, emerging materials with various properties. Among natural polymers, polysaccharides such as cellulose and alginate have been considered for biomedical application because of their high availability and biocompatibility. Bacterial

cellulose has been shown to be promising for wounds and burns healing, standing out for its appropriate physicochemical properties, nanotechnology facet and nanofibres organized in a threedimensional network, which provides mechanical properties, high crystallinity, malleability, porosity and hydrophilicity. Alginate is a malleable structure and easily associated with bivalent ions, such as calcium to form hydrogel that resembles the extracellular matrix and wound moisture preservation. Ion exchange between calcium from the biomaterial and sodium from the wound leads to the formation of a stable gel.

Objective: Evaluate neutrophils and macrophages activity, IL-10 and TGF-β1 antiinflammatory response by treating skin burns with cellulose and alginate gel.

Methods: The Animal Ethics Committee of the Hermínio Ometto Foundation (CEUA_053/2018) previously approved the use of animals. Male Wistar rats were anaesthetised with ketamine (75mg/kg) and xylazine hydrochloride (25mg/kg). An aluminium metal plate (2.0cm diameter) was kept in contact with the animals back for 20 seconds at 120ºC constant temperature. Oral analgesic dipyrone sodium (50mg/kg) and tramadol injection (5mg/kg) was considered during 72 hours of the burning procedure. Four experimental groups: untreated, CMC (Carboxymethylcellulose), Cellulose (CMC with bacterial cellulose) and Cellulose/alginate (CMC with bacterial cellulose and alginate). The animals were followed by 7/14/21/28/35 days. Myeloperoxidase (MPO) and nacetylglycosaminidase (NAG) enzymes levels were evaluated to determine neutrophil and macrophage activation, respectively, by biochemical assay. Moreover, IL-10 and TGF-β1 levels were assessed by immunohistochemistry.

Results: Cellulose/Alginate group presented lower level of MPO on the 14th, 21st and 28th days compared to other groups. On the 21st experimental period, cellulose groups also presented lower level compared to untreated and CMC groups. NAG evaluation also showed lower levels for cellulose and cellulose/alginate groups compared to untreated and CMC groups, especially for cellulose/alginate on the 21st day. The other experimental periods all groups presented similar levels of MPO and NAG. Cellulose/Alginate group presented higher level of TGF-β1 on the 21st day compared to the untreated group, and both of them, IL-10 TGF-β1 were also higher in Cellulose/Alginate and Cellulose groups in the 28th day. The use of cellulose seems to reduce neutrophils activation; however, the association of cellulose with alginate faster mediated the effect. Such association also contributed to reduce the macrophage activation, an anti-inflammatory effect, without impairing the transition to tissue formation phase, since the association of cellulose and alginate enhanced IL-10 and TGF-β1 stimulation.

Conclusions and Support: The use of cellulose/alginate gel reduced the neutrophil and macrophageactivation, and enhanced IL-10 and TGF-β1 levels, which could contribute to regulate the inflammatory response, a positive impact to treat chronic wounds and burn injuries. SUPPORT: FAPESP 2019/14977-2

ID: 2819

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

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Title: GAME-BASED LEARNING IN THE PROMOTION OF LEARNING IN MEDICAL SCIENCES: A SYSTEMATIC REVIEW

Introduction: Game-based learning (GBL) refers to an innovative approach derived from the use of games with educational value for teaching purposes. Although several studies carried out related to games and teaching, just a few studies explored the effectiveness of using game-based learning in the education of medical courses. This is how GBL aims to improve the assessment and analysis of the teaching and learning process.

Objective: Therefore, this work aims to develop a systematic review to evaluate the effectiveness of this new methodology teaching the medical field.

Methods: The pursuit for scientific evidence started by defining the terms, their combinations, and the boolean operators for association. International electronic databases were chosen for the research (Web of Science, PubMed, BVS and Cochrane) to cover the most diverse areas of health sciences. Original articles published between 2009 and 2019. Papers were selected by its relation with game-based learning strategy, specially applied for the apprehension of knowledge in Medical Sciences undergraduated courses. International electronic databases were chosen to compose this search, namely: Web of Science, PubMed, Biblioteca Virtual em Saúde (BVS) and Cochrane Library. The number of bases was determined due to their ability to filter articles published in the most diverse areas of health sciences.

Results: After searching on chosen databases, 31 papers were recovered. Applying inclusion and exclusion criteria, 6 were selected for analysis to constituite this study. It is observed that there are few studies involving GBL being published in the last 10 years, considering the inclusion and exclusion criteria chosen. These works come from medical schools from different countries, concentrated in North America (Canada and USA), Europe (Spain, United Kingdom and Germany) and Oceania (Australia). It is noticed that the subjects presented as learning objectives deal with the basic cycle of medical training, with games focusing on anatomy. Besides, into the medical specialties, such as uroanalysis, neonatology and radiology, there are some GBL strategies. Most studies have a positive position in related to the use of games in the teaching-learning process. The parameters used to assume this conduct are based mainly on the comparison between the GBL methodology with the traditional methodologies .

Conclusions and Support: It is possible to conclude that the use of Game-Based Learning (GBL) techniques is capable to promote the learning process in topics associated with Medical Sciences in Higher Education. The studies analyzed in this work managed, through their own parameters, certification methodologies to prove that the GBL was efficient in the teaching process and that the students presented satisfactory performance compared to the tradicional teaching methods. It is important to point out that, although GBL is a clear strategy for the construction of active learning valid for the education of young people and adults, the games developed in the medical sciences may not yet be, in fact, instruments that allow the student to be the center of the your own learning process. More research must be carried out to assess whether the applied GBL techniques promote real active learning. However, the capacity of GBL to promote important aspects for the construction of active teaching episodes is undeniable, such as peer interaction, engagement, motivation and fun.

ID: 3075

Área: FISIOLOGIA GERAL

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Title: ASTROCYTE TO NEURONS LACTATE SHUTTLE (ANLS) MECHANISM IS INVOLVED IN WATER AND SODIUM SODIUM INTAKE INDUCED BY ANGIOTENSIN II (ANG II) IN THE SUBFORNICAL ORGAN (SFO).

Introduction: Studies showed that ANLS mechanism activites GABAergic neurons involved with sodium avoidance behavior induced by hypertonic Na+solution. We recently observed that inhibition of glial cells attenuates sodium intake induced by central ANG II. However, the involvement of the ANLS mechanism in the water and sodium intake induced by ANG-II remains to be elucidated.

Objective: To analyze the involvement of the ANLS mechanism in the water and sodium intake induced by ANG II in the SFO.

Methods: Guide-cannula was implanted in the SFO of male Wistar rats [(280-320g) Ceua/CBiotec/UFPB n.133/2015]. Before the experimets, the rats were adapted to drinking Na+solution in metabolic cages containing bottles of the water and sodium (0.3 M NaCl) for 5 days. Next, we performed microinjections (100nl) of sterile saline (0.9%), ANG II (20 ng), α-CHCA [(4.5 µg) lactate transporter inhibitor - MCT or Lactate (2 µg) into SFO, followed by water and sodium intake analysis during 2h. Statistical analysis: One-way (ANOVA), Newman-Keuls post-test, $P<0,05$.

Results: ANG II into SFO produced increase in water (10.3 ± 2.8 vs. 0.6 ± 0.3 mL/2h, p=0.009, n=08) and sodium intake (5.7 ± 1.3 vs. 0.1 ± 0.1mL/2h, p= 0.002, n=08). Previous Lactate microinjection attenuated water (3.1 ± 0.8 vs. 10.3 ± 2.8mL/2h, p=0.03, n=08) and sodium intake induced by ANG-II (2.3 ± 0.9 vs. 5.7 ± 1.3 mL/2h, p=0.04, n=08). Furthermore, α-CHCA potentiated water (18.2 ± 2.6 vs. 10.3 ± 2.8 mL/2h, p=0.04, n=05) and sodium intake induced by ANG II into SFO (12.6 ± 1.8 vs. 5.7 ± 1.3 mL/2h, p=0.01, n=05).

Conclusions and Support: Our results suggest that ANLS mechanism is involved in the water and sodium intake responses induced by ANG-II in the SFO. Financial Support: CAPES, CNPq.

ID: 3076

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: HYPERCALORIC AND RESTRICTIVE DIETS AFFECT HISTOLOGICAL AND INFLAMMATORY PATTERNS IN THE LIVER OF MICE DAMS

Introduction: A variety of conditions, such as unbalanced maternal nutrition, exposure to environmental insults, infection or stress, occurring during fetal development can lead to health dysfunctions in the offspring. Studies with rodent models have demonstrated an association between hypercaloric diet (HD) exposition during gestation, and a higher risk of adverse outcomes in the offspring, for instance, congenital anomalies, and of developing obesity and metabolic syndrome. It is known that HD promotes liver dysfunction, such as nonalcoholic steatohepatitis (NASH).

Objective: Analyze the effects of the diet interventions in the dams, assessing the histological characteristics of the liver related to cellular damage and inflammation.

Methods: The Institutional Animal Care and Use Committee of UFCSPA (#388/15) approved this study. Thirty female BALB/c albino mice (60 days old) were separated in 3 different groups (n=10/group) and individually housed. To the control group (CONT) was administrated a standard mice chow ad libitum, with a total energy content of 3.4 kcal/g; the restrictive diet group (RD) had 30% reduction in the standard chow amount, compared according to the consumption of CONT group; and the hypercaloric diet group (HD) was fed with a special chow ad libitum, with total energy content of 4.9 kcal/g. Diet adaptation lasted 25 days, after they were housed with males for mating. When pregnant they were housed in separate cages until delivery. On the first postpartum day, litters were standardized at 6 pups. After weaning, the dams were euthanized, and hepatic tissue was collected for further analysis. In the liver, four-micrometer sections of formalin-fixed and paraffin-embedded tissue slices were stained with hematoxylin-eosin. A pathologist, blinded to experimental protocol, analyzed all liver fragments using light microscopy. The histological features were grouped into 3 broad categories: steatosis, inflammatory lymphocyte infiltration and ballooning. These features were used for diagnostic categorization of NASH according a scoring system described by Kleiner et al. (2005). Liver concentrations of interleukin 6 (IL-6) and tumor necrosis factor alpha (TNF-alfa) were analyzed by enzyme-linked immunosorbent assay (ELISA) (Sigma-Aldrich), according to the manufacturer's instructions.

Results: Histological evaluation of the liver demonstrated the presence of low lobular inflammatory infiltrate, hepatocellular ballooning and mild steatosis in HD-fed mice. Our findings are graded as 1 for inflammatory infiltrate, 2 for hepatocyte ballooning and 2 for steatosis. According Kleiner's system, scores $\geq 5$ are correlated with a diagnosis of NASH, which is the case for HD-fed dams. CONT and RD groups did not show features of liver injury. The ELISA assay shows that IL-6 had no differences among the groups. There is an increase in TNF-alfa in HD dams compared to CONT and RD (p=0.046).

Conclusions and Support: In our findings HD-fed dams' hepatic tissue had low lobular inflammatory infiltrate, hepatocellular ballooning and mild steatosis, which according to Kleiner's system, represent scores correlated with a diagnosis of NASH. Our findings also showed an increase in TNF-alfa in the liver of HD dams, compared to CONT and RD, indicating a pro-inflammatory status. Support: CAPES, CNPq, UFCSPA

ID: 3588

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF LINSEED OIL SUPPLEMENTATION ON GLYCEMIA AND LIPID PROFILE IN PHYSICALLY ACTIVE MEN SUBMITTED TO A HIGH INTENSITY EXERCISE

Introduction: The linseed oil has increased omega-3 fatty acid concentration and has been considered as a potential oil source for improvement of glyco-lipid variables.

Objective: The aim of study was to investigate the effects of linseed oil supplementation on blood pressure levels, serum glucose levels and lipid profile in physically active men submitted to a high intensity physical exercise.

Methods: The study was approved by the research ethics committee of the medical science center, Federal University of Paraiba (protocol nº 3.066.373). Twenty male subjects, aged 18 - 39 years, physically active and who do not have chronic non-communicable diseases. The subjects were randomly distributed into 03 groups: Group 01- Placebo + Exercise; Group 02- Flaxseed Oil (6g/day) + Exercise; Group 03 - Flaxseed Oil (12g/day) + Exercise. Supplementation was performed for 07 days. Participants were submitted to a running session on a treadmill for 40 minutes, consisting of 05 minutes of warm (4-5Km/h), 30 minutes with the intensity determined by the heart rate reached in 70-75% of VO2 maximum and 05 minutes of warm (4-5Km/h). Blood pressure, maximum heart rate, anthropometric variables [weight, height, waist circumference, body mass index (BMI) and fat percentage] and biochemistry (glycemia and lipid profile) were measured.

Results: Height, weight, body fat percentage, body mass index (BMI) and waist-hip ratio (WHR) were similar between the groups. Levels of systolic and diastolic blood pressure were similar between the groups, and did not differ before and after the intervention with supplementation and physical exercise. Fasting serum glucose levels were significantly reduced (98.90 ± 12.23 vs 89.99 ± 11.98 mg/dL, $p<0.05$) in participants who received 06g/day of linseed oil. HDL and LDL levels were similar in all groups.

Conclusions and Support: Supplementation with 06g/day of flaxseed oil for seven days effectively reduced serum glucose levels, but did not result in differences in blood pressure and lipid profile.

ID: 3589

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF CLIMATE CHANGE ON THE PHYSIOLOGY OF MARINE ANIMALS

Introduction: The uptake of CO2 by the ocean induces changes in seawater chemistry that could have drastic impacts on ecosystems and in the biology of animals. The increase in atmospheric CO2 concentration has been associated with global temperature elevation and ocean pH reduction. It is estimated that ocean pH might be reduced from 8.1 to 7.7 until the end of the century it may get to 7.4 until 2300. Mean global sea surface temperature increased 0.13oC per decade since 1979. Although some species may be more resilient than others and adaptative processes could reduce some of the negative consequences expected, studies have shown that ocean acidification, temperature increase, and salinity alterations, resulting from sea level rise, may alter the biology of several species.

Objective: Changes in pH, temperature and salinity might alter important physiological processes, such as metabolism, acid-base balance, respiration, osmoregulation, cardiac beat, thermal tolerance, nitrogen excretion, chemoreception. If these alterations persist after long-term exposure, the alterations might have as a result the impairment of survive, growth and reproduction. In addition such responses are also expected to compromise marine biodiversity through species local extinctions (species stop occurring in a specific area) and species invasions (species growing in the places where they have never existed before). Compared with terrestrial ecosystems, the impacts of climate change on the aquatic fauna are likely to be more dangerous, since fishes and invertebrates are ectotherms. Additionally, organisms that inhabit the intertidal zone live at their maximum tolerance limit and climate changes might impose bigger challenges than these organisms can tolerate.

Methods: Understanding the effects of climate change on the physiology of living beings is one of the challenges confronted by current science. The number of studies investigating the effects of climate changes over the physiology of marine animals has increased. However, there is a gap when it comes to investigations that involve long-term exposition (e.g., several generations), early ontogenetic stages, the tradeoffs involved in adaptation and the synergistic effects among several environmental factors related to climate changes.

Results: Furthermore, researchers should establish links between field studies reporting a climate change-induced effect at the ecosystem level and laboratory studies explaining the reasons for such an effect. The few studies that evaluated the combined effect of acidification with other variables have suggested that this synergy may alter more drastically the physiology of animals. These studies could contribute to advance the current knowledge in climate change and aid in forming of the mitigation and adaptation measures.

Conclusions and Support: The United Nations proclaimed a Decade of Ocean Science for Sustainable Development, to be held from 2021 to 2030. Key actions include promoting the Ocean Decade among the scientific community, accelerating scientific initiatives, and exploring opportunities for fundraising.

ID: 3078

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: CONDITIONAL DELETION OF RIC-8B GENE IN OLFACTORY SENSORY NEURONS LEADS TO INCREASED HYPERCAPNIC VENTILATORY RESPONSE

Introduction: The main physiological function of breathing is the maintenance of blood gases (CO2 and O2) homeostasis. For this fine tuning to take place, the central nervous system (CNS) must receive refined and accurate information. Among the neural clusters that control respiratory activity, the ventral medullary surface region of the brainstem, namely the retrotrapezoid nucleus (RTN) is capable of detecting increases in the partial pressure of CO2, composing the process of central chemoreception. It is characteristic of chemoreceptors in addition to their sensitivity to CO2 and pH, an excitatory neurochemical phenotype and projections to the respiratory pattern generators. It is also known that rodents can detect CO2 by the olfactory and taste system. CO2-sensitive olfactory epithelium neurons (GC-D+) project to a sequence of caudal glomeruli in the olfactory bulb that are anatomically segregated from other olfactory projections, forming a distinct subsystem of the main olfactory system.

Objective: Considering that Ric-8B conditional knock-out mice are anosmic, and this may reveal a possible contribution of this olfactory chemoreception system to the central one, our hypothesis is to test the functional consequences of the Ric-8B gene knock-out in the olfactory epithelium neurons to the chemoregulation control of breathing. Therefore, our proposal will be to evaluate baseline and the hypercapnic ventilatory response (HCVR) among Ric-8B conditional knock-out mice (cKO) presenting none of the Ric-8b protein in the olfactory epithelium sensory neurons and wild-type conscious mice.

Methods: To fulfill our goals, we used the whole-body pletismography technique. Conscious mice were kept in a sealed chamber whereby ventilatory parameters can be obtained. Hypercapnia was induced by increasing CO2 up to 7% for 10 minutes. Ventilation (VE), tidal volume (VT) and respiratory frequency (fR) were quantified every 30 seconds of a section of the 10-minute-record.

Results: Hypercapnia (FiCO2 = 7%) showed a further increase in VE (7627,9 ± 1779,9, vs. wild-type: 5758,7 ± 957,5 ml/min/g), VT (22,3 ± 2,7, vs. wild-type: 17,6 ± 2,1 ml/g) and fR (337,1 ± 62,5, vs. wild-type: 324,5 ± 27,8 breaths/min) in Ric-8b compared to wild-type mice.

Conclusions and Support: Our preliminary data suggest that the olfactory epithelium sensory neurons chemoreception may also contribute to the process of central chemoreception once the lacking of Ric-8B gene in the olfactory epithelium sensory neurons leads to further increase in the ventilatory responses to CO2. Financial Support: FAPESP, CAPES/PROEX and CNPq. CEUA Nº 8033310719.

ID: 3591

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: FACILITATION OF CORTICOSTRIATAL TRANSMISSION BY PHOSPHODIESTERASE 10A INHIBITION ATTENUATES L-DOPA-INDUCED DYSKINESIAS

Introduction: Long-term treatment for Parkinson's disease (PD) with L-DOPA has been associated with side effects called L-DOPA-induced dyskinesias (LIDs). The striatum is a key structure of the basal nuclei related to LIDs. The medium spiny neurons (MSNs) make up approximately 95% of the neurons in the striatum and constitute the direct or indirect pathways of motor control. Chronic treatment with L-DOPA is able to modulate these pathways. Much evidence suggests that LIDs would emerge as a result of an imbalance between the direct

and indirect pathways. The enzyme phosphodiesterase 10A (PDE10A) is mainly expressed in MSNs in the striatum and metabolizes the second messengers (cAMP and cGMP), thus exercising a strong modulation of the activity of MSNs. Thus, our hypothesis is that inhibition of phosphodiesterase 10A would have an anti-dyskinetic effect by modulating the activity of MSNs.

Objective: To investigate how the modulation of MSNs influences the anti-dyskinetic effects of a new PDE10A inhibitor (PDE10Ai) in a mouse model with PD.

Methods: All procedures were approved by the local ethics committee (CEUA-FFCLRP / USP (18.5.35.59.5). 6-OHDA lesioned rats were chronically treated with L-DOPA (5 mg/kg/day plus benserazide 12,5 mg/kg/day, subcutaneously) once daily for one week. After this period, dyskinetic rats received either vehicle (n = 6) or PDE10Ai (1 mg/kg/day, oral gavage; n=7) one hour before L-DOPA, once daily for two additional weeks. Behavioral analyzes were performed regarding the LIDs that affect the anterior, axial and orofacial limbs of parkinsonian animals. The walking test was performed once a week, 1 hour after the administration of L-DOPA to monitor the effect of L-DOPA antiparkinsonian activity in the animals. After treatment, extracellular electrophysiology was performed in vivo in the parkinsonian striatum to characterize the activities evoked through cortical stimulation, and spontaneous MSNs activities.

Results: PDE10Ai (1 mg/kg) decreased axial and forelimb dyskinesias in the third week of treatment ($p<0.05$ vs. vehicle + L-DOPA) but didn't interfere with the incidence of orofacial dyskinesias ($p>0,05$ vs. vehicle + L-DOPA). PDE10Ai (1 mg/kg) increased the probability of triggering MSNs evoked by stimulation of the primary motor cortex ($p<0.05$ vs. vehicle + L-DOPA). The MSNs of the animals treated with PDE10Ai (1 mg/kg) showed spontaneous activity significantly higher than the animals in the control group ($p <0.05$ vs. vehicle + vehicle).

Conclusions and Support: These data reinforce the discussion that animals treated with PDE10A inhibitors may have their dyskinesias attenuated due to facilitated transmission of the cortico-striatal pathway and an increase in spontaneous activity of MSNs in the striatum. Financial support: this work was funded by CAPES and FAPESP (processes 2017/00003-0 and 2018/12956-5)

ID: 2827

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: Ê-POSTER

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Title: HISTAMINERGIC MODULATION OF BREATHING AT THE LEVEL OF VENTRAL MEDULLARY SURFACE

Introduction: Histaminergic neurons of the posterior hypothalamic tuberomammillary nucleus (TMN) are pH-sensitive and contribute to behavioral responses to CO2 including arousal and increased respiratory activity.

Objective: Considering histaminergic neurons project to several brainstem respiratory centers including the ventral medullary surface near the retrotrapezoid nucleus (RTN), and since chemosensitive RTN neurons are an important source of CO2/H+-dependent respiratory drive, in the present study our aim is to investigate how histamine modulates chemosensitive RTN neurons in brain slices and in anesthetized rats.

Methods: In brain slices obtained from rat pups (7-12 days old), chemosensitive RTN neurons were identified in cell-attached voltage-clamp mode by their characteristic firing response to CO2 ($\geq$ 0.8 Hz increase in activity in response to 10% CO2. We also measured mean arterial pressure (MAP) and diaphragm muscle activity (DIAEMG) in urethane-anaesthetized, vagotomized and artificial ventilated male Wistar rats.

Results: We found that most chemosensitive RTN neurons showed a dose-dependent increase in activity in response to bath application of histamine dihydrochloride (HD: 1-25 μM). The increased activity of RTN neurons by HD (25 μM) was completely blocked after bath application of the H1 receptor antagonist DPH (diphenhydramine hydrochloride; 100 μM) (1.1 ± 0.1 Hz to -0.06 ± 0.2 Hz; n = 7) or the H2 receptor antagonist ranitidine (ranitidine hydrochloride; 10 μM) (1.0 ± 0.2 Hz to 0.3 ± 0.3 Hz; n = 5). In urethane-anesthetized rats, unilateral injection of HD (25 mM - 50 nl) into the RTN increased DIAEMG amplitude (19.5 ± 4.3 vs. saline: -1.1 ± 1.3%), without changes DIAEMG frequency or MAP. Bilateral injections of DPH (0.5 mM) into the RTN decreased DIAEMG amplitude (-62.6 ± 14.5. vs. saline: -1.1 ± 1.3%), DIAEMG frequency (-66.4 ± 13.4 vs. saline: -1.5 ± 1.9%) and MAP (-43.67 ± 8,4 vs. saline: -3.2 ± 1.7 mmHg). Besides the massive reduction of basal breathing activity, the hypercapnic ventilatory response was preserved in urethane-anesthetized.

Conclusions and Support: These results suggest that histamine directly activates chemosensitive RTN neurons by activation of H1 and H2 receptors and that histaminergic signaling in the RTN could be involved in the modulation of breathing. Financial Support: FAPESP, CNPQ and NIH.

ID: 3084

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: CONTINUOUS USE OF ORAL CONTRACEPTIVE COMPOSED BY DROSPIRENONE AND ETHINYLESTRADIOL CHANGES VAGINAL CYTOLOGY AND WEIGHT OF UTERUS IN SWISS MICE

Introduction: The combined oral contraceptive (COC) is an effective method of contraception used by 9% of the world's female population of reproductive age. Many women choose continuous use of contraceptives to avoid menstruation and symptoms of premenstrual tension. However, there is poor information about the effects of this use in morphology of uterus.

Objective: The aim of this study was to evaluate the effects of continuous use of combined oral contraceptives composed of drospirenone and ethinyl estradiol in the uterus of female mice.

Methods: Swiss mice of 80 days old received daily 0.6 µg of ethinyl estradiol and 60 µg of drospirenone (COC group n = 6) or vehicle (distilled water; CTL / control group n = 6) by gavage for 35 days. Vaginal cytology was recorded weekly, and after 35 days of treatment, mice were euthanized and uterus was removed, weighed and processed to perform morphological analyze (CEUA UFRJ-Macaé approval number: MAC039).

Results: During treatment, the COC group stopped cycling normally and vaginal cytology showing characteristics of the metestrus and proestrus phases, this effect is known as "COC hormonal stimulation". The uterus weight differed significantly between groups (COC: 5.7 ± 0.3 mg / g BW and CTL: 4.7 ± 0.3 mg / g BW). n morphological analyzes no alteration of histology of uterus was seen when compared to control group.

Conclusions and Support: The continuous treatment with the combined oral contraceptive drospirenone and ethinyl estradiol had hormonal action proved by increasing the uterine weight and changing the cyclic pattern of vaginal cytology, but but did not change the uterine morphology

ID: 3087

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: QUERCETIN ENHANCES VASCULAR ENDOTHELIAL GROWTH FACTOR AND MUSCARINIC RECEPTOR EXPRESSION IN PANCREATIC ISLETS AND REVERSES HYPERTENSION OF THE 2K1C RATS

Introduction: Hypertension often occurs in association with insulin resistance and other components of the cardio metabolic syndrome. It has been indicated by experimental evidence that oxidative stress plays an important role in the hypertension. Increased angiotensin II increases oxidative stress and may compromise pancreatic function. The pancreas is susceptible to oxidative stress due to the low expression of antioxidant enzymes in the islets and consequently promotes the deterioration of the islets. Quercetin supplementation promote improvement of the hypertensive clinical condition due to their anti-oxidative function.

Objective: The aim of this study was to evaluate the anti-oxidant action of quercetin in 2K1C (two-kidney, one-clip) hypertensive rats, and to define the molecular mechanisms in pancreatic islets.

Methods: This project was approved by the ethics committee of the Hermínio Ometto University Center (number 013/2019). Surgery was performed to make 2K1C hypertensive Wistar rats. Animals were anesthetized with a mixture of ketamine and xylazine, then a silver clip was inserted on the left renal artery. Sham rats received the same treatment except for placement of silver clips. Systolic blood pressure (SBP) was measured once a week by tail cuff plethysmography and rats with SBP>160mmHg were considered hypertensive and used for experiments. Three months after surgery, rats were randomly divided into three groups: group Sham rats received vehicle, carboxymethyl-cellulose, group hypertensive rats received vehicle, and group rats received quercetin (50mg/kg/day, orally, 35 days). Glucose tolerance test (GTT), insulin tolerance test (ITT) were performed before and after quercetin supplementation. Blood was collected at the time of euthanasia, via cardiac puncture, and pancreatic islets were isolated by collagenase digestion of the pancreas. Serum biochemical analyses of lipid profile and TBARS were performed. The western blotting was performed for catalase, SOD-2, VEGF (vascular endothelial growth factor), muscarinic receptors 1 and 3 in isolated islets. Results are presented as means ±SEM, statistical significance ($p<0.05$) was assessed using ANOVA-Tukey's multiple comparisons test.

Results: Our results showed that the left kidney weight (g) (1.3±0.006) was reduced compared to the right kidney weight (1.5±0.007) in the clipped rats and prove the animal model of hypertension (p=0.03). Hypertension (mmHg) was reduced in quercetin rats (126±5) at the level of Sham rats (135±7) and hypertension decreased by 40% compared to the hypertensive rats (218±6). Serum levels of TBARS (mM/mg protein) were reduced in quercetin rats (0.0005±0.0001) compared to the hypertensive rats (0.001±2.6e-005) and prove the anti-oxidant effect of quercetin (p=0.0002). The lipid and glycemic profile, GTT, ITT and levels of oxidative stress markers in isolated islets, catalase and SOD-2 were not different in all rats. However, we observed an increase in quercetin rats of VEGF (1.38±0.1) and Muscarinic receptor 1 (0.63±0.1) in pancreatic islets compared to the hypertensive rats (0.36±0.1) and (0.28±0.05), p=0.02, respectively.

Conclusions and Support: Renal hypertension was reversed by quercetin and it suggests preventing the progression of pancreatic dysfunction, ensuring greater vascular endothelial growth factor that important to blood supply and a greater muscarinic receptors expression that regulate insulin secretion. Support: Hermínio Ometto University Center.

ID: 3343

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de São Paulo - Ribeirão Preto - Sao Paulo - Brasil

Title: KATP CHANNELS IN GLYCINERGIC NEUROTRANSMISSION IN THE DORSAL COCHLEAR NUCLEUS

Introduction: Cartwheel neurons from the dorsal cochlear nucleus (DCN) are glycinergic interneurons and the main source of inhibition on the fusiform neurons, the main excitatory neuron in the DCN. Changes in DCN inhibition may be relevant to the development of tinnitus, which related to DCN hyperactivity. Cartwheel (CW) neurons are mostly spontaneously active producing a strong tonic glycinergic inhibition of the fusiform neurons Data from our laboratory demonstrated that open ATP-sensitive potassium channels (KATP) are responsible for the existence of a small fraction of silent CW neurons that do not fire spontaneously, hyperpolarizing the membrane potential below AP threshold.

Objective: The objective of our work is to investigate the impact of of the KATP channels modulation on glycinergic neurotransmission between cartwheel and fusiform neurons in the DCN.

Methods: We used Wistar Hannover rats between 17-22 days of age. The animal handling protocol was approved by the Animal Use Ethics Commission (CEUA) of FMRP-USP (protocol 006/2020). The animals were anesthetized with isoflurane and quickly beheaded to remove the brainstem and coronal slices of 200 µm were obtained. Electrophysiological recordings were performed using whole-cell patch-clamp techniques using an electrode internal solution with potassium gluconate as main ion. The effect of drugs was statistically analyzed using the paired Student's t-test in external saline with 10 mM glucose.

Results: The application of the KATP antagonist tolbutamide, increased the frequency of inhibitory postsynaptic currents (sIPSCs) in fusiform neuron from 17.7 ± 2 Hz to 24.1 ± 3 Hz (n=7; p= 0.01) as well as the amplitude (from 52.2 ± 7 pA for 61.9 ± 7 pA; n=7; p=0.06). On the other hand, the activation of the KATP channels with diazoxide decreased the frequency of sIPSCs from 18.6 ± 1.2 Hz to 11.5 ± 1.4 Hz (n=5; p=0.002) and the amplitude of 60.4 ± 6.6 pA for 40.9 ± 2.5 pA (n=5; p=0.02). We also compared the glycinergic neurotransmission in the fusiform neuron in 5 mM glucose, and the frequency and amplitude of the sIPSCs were similar to those of 10 mM glucose (dados) suggesting that KATP channels are not affect by deacresing glucose in half. We performed recordings of cartwheel neurons using aCSF with 5 mM glucose and the proportion of quiet and active neurons remained as 20% of quiet neurons versus 80% of active neurons (n=5 quiet and n=16 active), the same was previously observed in 10mM glucose. The membrane potentials of the quiet neurons were more hyperpolarized, similar to those observed in 10 mM glucose (active: -78.7 ± 1.7 mV, silent: -89.2 ± 4.6 mV, p=0.0191).

Conclusions and Support: We conclude that glycinergic neurotransmission in the fusiform neuron is affected by the activity of the KATP channel and that variations in external glucose seen to have little impact on the inhibitory CW neuron activity and glycinergic neurotransmission. Thus modulation of KATP channel can have a relevant impact on DCN excitability.

ID: 3600

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: THE NEW LET-7/AMPK AXIS MAY BE INVOLVED IN THE GENESIS OF OBESITY-INDUCED FATTY LIVER

Introduction: Let-7 represent a family of microRNAs (miRs) and were one of the first miRs to be discovered. Processing and maturing of Let-7 are controlled by LIN28, an RNA-binding protein, and the Let-7/LIN28 axis has been recently implicated in the regulation of multiple aspects of glucose metabolism and lipid metabolism. On the other hand, AMPK is a serine/threonine kinase known as a cellular energy sensor. Its activation in the liver leads to the suppression of fatty acids (FA) and triglycerides (TAG), while it activates oxidative processes. Although previous bioinformatic analysis of our laboratory demonstrated that Prkaa2, the gene that encodes AMPK protein, may be a target of Let-7 repression, there are no studies describing the role of Let-7 in the regulation of AMPK activity.

Objective: To investigate whether Let-7 plays a role in the regulation of AMPK in two different models of obesity-induced fatty liver.

Methods: Two different models of obesity-induced fatty liver were applied: 1) Male swiss mouse were fed standard chow (SC) or an high-fat diet (HFD – 45% fat) for eight weeks; samples of the blood and liver were collected for the analysis; 2) Female Swiss mice were fed SC or HFD for 4 weeks and then mated with control male mice; blood and the liver of the male offspring were collected at the delivery day for the analysis. A mouse hepatocyte cell line (AML12) was cultured to evaluate lipid accumulation and Let-7/AMPK axis after treatment with FA, glucose and insulin.

Results: Obese male mice that received HFD for eight weeks had higher serum glucose, insulin and TAG. At the time, they presented fat accumulation within the liver and higher expression of hepatic Let-7, with lower Prkaa2 levels. Accordingly, offspring from obese dams had higher levels of glucose, insulin, TAG and FA in serum, along with fat accumulation in the liver and modulation in hepatic Let-7/Prkaa2 expression. Interestingly, the treatment with either FA or glucose in AML12 lead to fat accumulation and Prkaa2 downregulation, while the transfection with Let-7 inhibitor rescued Prkaa2 levels and prevented lipid accumulation. Finally, Let-7 inhibitor transfection into liver samples of offspring from obese dams rescued LIN28 and pAMPK content.

Conclusions and Support: The results show strong evidence that Prkaa2, the gene that encodes AMPKa2, may be regulated by Let-7 microRNA levels, and that the potential Let-7/AMPK axis may be involved in the obesity-induced fatty liver development. Financial Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), grant #2015/01947-7. Ethics Committee on the Use of Animals of the State University of Campinas (CEUA/UNICAMP): Protocol #3963-1

ID: 3093

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: NEUROSCIENCE AND EDUCATION: A NECESSARY DIALOGUE TO IMPROVE THE TEACHING-LEARNING PROCESS.

Introduction: Educational processes require knowledge of how to teach and learn. “Neuroeducation” is an interdisciplinary field that articulates neuroscience and education to promote a better understanding of how the brain work, including the cognitive and emotional processes related to learning.

Objective: To report on the workshop “Contributions that the dialogue between neuroscience and education can bring to the improvement of teaching-learning processes”, offered to undergraduate students of teacher training courses of the Federal University of Pampa.

Methods: This study was approved by the Research Ethics Committee of Federal University of Pampa (3.138.705). Seventeen future teachers participated in the workshop, 58.82% of them were female (n = 10), 29.41% (n = 5) male and 2 did not report (11.76%). The first part of the workshop aimed to understand students’ perceptions about neuroscience; for this, we use an online tool (mentimeter.com) and asked participants to indicate the first word that came to their minds when they hear “neuroscience”. In the sequence, we discussed the importance of neuroscience in our everyday, and asked: “Nowadays neuroscience is in fashion, but is everything that we know about the brain true?”. After, we applied a questionnaire containing affirmations and myths related to neuroscience. The participants should indicate whether they agreed, disagreed, or had no opinion for each one. We use the affirmations presented in the questionnaire to work on some important concepts of neuroscience and education, as neuroplasticity, emotions, learning consolidation, and others.

Results: In the first activity, the most mentioned words were “learning”, “brain” and “scientific study”. In the questionnaire applied latter, we verify that most of the students consider true some verdict information about the brain function. For example, when we affirmed that neuroscience investigate the functions of the central nervous system, 82.35% agreed; 11.76% disagreed; and 5.88% had no opinion. When we affirm that learning is the process of new acquisitions constituted through new and/or different experiences, 94.12% agreed; and 5.88% (n = 1) had no opinion. But some brain important concepts are not clear to the futures teachers. One example was the neuroplasticity. When we affirm that the nervous system has the ability to change, adapt and shape along neuronal development, what is called neuroplasticity, 58.82% agreed; and 41.18% had no opinion. In the same way, some participants also believe in neuromyths. When we affirmed that we use only 10% of brain capacity 29.41% agreed; 58.82% disagreed; and 11.76% had no opinion. In the statement that after some critical periods in childhood some things cannot be learned, 17.65% agreed; 58.82% disagreed; and 23.53% had no opinion. In the evaluation of the workshop, after discussions and elucidations about neuroscience, the participants evaluated the workshop positively, highlighting the methodology, the importance of topics addressed, as neuromyths, and understanding of brain functioning.

Conclusions and Support: Our results demonstrate that the training of educators in neuroscience can positively help education, as it promotes a better understanding of the learning process, and avoid misconceptions about brain functioning. Support: IBRO/IBE-Unesco. PROEXT/ Unipampa.

ID: 2838

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: HYPERCAPNIA INDUCES SELECTIVE ACTIVATION OF MICROGLIA AT THE LEVEL OF RETROTRAPEZOID NUCLEUS

Introduction: Microglia are resident immune cells in the brain considered constitutively active because of their continuous surveillance function. They survey the activity of neuronal circuits via fine processes and respond to a broad range of brain insults which can disrupt brain homeostasis.

Objective: The current study examines the hypothesis that microglia cells can exhibit changes in their morphological characteristics elicited by high levels of CO2 (hypercapnia) in the ventral medullary surface in a region called retrotrapezoid nucleus (RTN).

Methods: C57Bl/6 mice (CEUA: 8256040619) were subjected to hypercapnia (7% CO2, 21% O2, bal N2) or normocapnia (N: 21% O2, bal N2) for 1 hour. The microglia branches and number of endpoints/cell were quantified from immunohistochemistry images of RTN region

using skeleton and fractal analysis. The expression of P2Y12 receptors (selective marker for microglia in the central nervous systems) was also analyzed using optical density (OD) method.

Results: Quantitative analysis reveals that exposure to hypercapnia decreased the number of branches of microglia cells in the RTN region: (branch number/cell: 1437 ± 87, vs. N: 1623 ± 29, p = 0.034) and (end points/cell: 54 ± 3, vs. N: 63 ± 2, p = 0.024). However, after fractal analysis, no differences were observed in the circularity of microglia in the group exposed to hypercapnia (0.847 ± 0.006, vs. N: 0.850 ± 0.007, p = 0.6). According to our data, hypercapnia decreased P2Y12r expression (0.6580 ± 0.010 vs. N: 0.5520 ± 0.038, p = 0.026) indicating an activation state of microglia cells.

Conclusions and Support: Our partial findings illustrate that microglia activation after hypercapnia includes both decreased cell ramification and decreased expression of P2Y12 receptors within RTN region. Importantly, the quantitative analyses of microglial morphology and phenotype are feasible and would assist in the comprehensive identification of neuroinflammatory condition caused by increased CO2 levels. Financial support: FAPESP, CAPES/PROEX and CNPq

ID: 2839

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: INHIBITION OF ANANDAMIDE HYDROLYSIS AS A STRATEGY TO COUNTERACT RESPIRATORY ABNORMALITIES OBSERVED IN AN ANIMAL MODEL OF PARKINSON'S DISEASE. Luara A. Batista1, Thiago S. Moreira2, Ana C. Takakura1. 1Department of Pharmacology, 2Department of Physiology

Introduction: Anandamide is an endocannabinoid with therapeutic potential to treat neurological and psychiatric disorders. Here, we tested the hypothesis that URB597, an anandamide hydrolysis inhibitor, counteracts the impaired response to hypercapnia observed in an animal model of Parkinson's Disease (PD).

Objective: To test the effects of URB597 in the respiratory and neuroanatomical deficits observed after lesion of the substantia nigra

Methods: Male Wistar rats (300-360g; CEUA: 5513240518) received 6-OHDA (12 mg/2 mL) or vehicle into the dorsal striatum bilaterally and after 40 days respiratory parameters (respiratory frequency (fR), tidal volume (VT) and ventilation (VE)) were recorded by whole-body plethysmography. For the recordings, animals received intraperitoneal injections of URB597 (0.3 mg/kg) or vehicle and were exposed to 15 min of normoxia (21% O2, 79% N2), 15 min of hypercapnia (7% CO2, 79% N2), and 15 min of recovery. Immunohistochemistry was also performed to evaluate expression of tyrosine-hydroxylase (TH) in the Substantia Nigra (SN) and Phox2b in the retrotrapezoid nucleus (RTN).

Results: Injections of 6-OHDA in the striatum led to a decrease in the total number of TH neurons in SN (6-OHDA + vehicle: 178±17 and 6-OHDA + URB597: 190±25 vs. vehicle + vehicle: 702±69, $p<0.05$) and Phox2b neurons in the RTN (6-OHDA + vehicle: 69±14, vs. vehicle + vehicle: 178±31 neurons, $p<0.05$). URB597 was able to decrease the number of Phox2b neurons in the RTN (Vehicle + URB597: 75±22, vs. vehicle + vehicle: 178±31 neurons, $p<0.05$). Animals treated with 6-OHDA and URB597 also presented a decrease in the number of Phox2b neurons in the RTN (6-OHDA + URB597: 59±20, vs. vehicle + vehicle: 178±31 neurons, $p<0.05$). Regarding ventilation, when data were analyzed as a time-course (10 sec interval) 6-OHDA animals presented higher variability for resting fR when compared to vehicle animals (6-OHDA + vehicle: 13.41, vs. vehicle + vehicle: 8.96% Coefficient of Variation, $p<0.05$). Treatment with URB597 was able to increase this variability when compared to 6-OHDA animals (6-OHDA + URB597: 21.17, vs. 6-OHDA + vehicle: 11.29% Coefficient of Variation, $p<0.05$). Data were also analyzed as means during three time points (minutes 5, 10 and 15). We observed a reduction in fR during hypercapnia in lesioned animals (6-OHDA + vehicle: 109±20, vs. vehicle + vehicle: 138±11 breaths/min, $p<0.05$). The means of VT and VE were not altered in lesioned animals. The attenuated tachypneic response observed in 6-OHDA-treated animals was not reversed by URB597 treatment (6-OHDA + URB597: 101±16 vs. 6-OHDA + Vehicle: 109±20 breaths/min, $p>0.05$). URB597 by itself also reduced fR (93±8 vs. vehicle + vehicle: 138±11 breaths/min, $p<0.05$) and VE during hypercapnia (830±95, vs. vehicle + vehicle 2663±310 mL/min/kg, $p<0.05$). Animals treated with URB597 that received 6-OHDA presented a reduction in fR during hypercapnia (100±9 vs. vehicle + vehicle 138±11 breaths/min, $p<0.05$). There were no changes in VE or VT in animals with lesion of the SNpc that were treated with URB597.

Conclusions and Support: Conclusion: we observed that the respiratory dysfunction observed in an animal model of PD may be of central origin. In addition, inhibition of anandamide hydrolysis by URB597 is not an effective treatment for the respiratory symptoms, which may have implications for the consideration of the endocannabinoid system as a target to develop treatments for PD. Support: FAPESP, CAPES and CNPq.

ID: 3095

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Santa Catarina - Florianópolis - Santa Catarina - Brasil

Title: P2X3 RECEPTOR EXPRESSION IN CARDIOVASCULAR TARGET ORGANS IN RATS WITH CARDIOVASCULAR DISEASE

Introduction: Cardiovascular diseases (CVD) are the leading causes of death in Brazil and worldwide. Previous studies have demonstrated increased purinergic P2X3 receptor subtype expression in the carotid body from hypertensive rats and human patients with CVD. In hypertensive rats, systemic antagonism of P2X3 receptors normalized carotid body dysfunction, reduced arterial pressure and basal sympathetic activity. Recent data from our laboratory showed that chronic systemic inhibition of P2X3 receptors prevented the progression of heart failure (HF) in rats supporting the novel idea that P2X3 receptors are a potential new therapeutic target for treating CVD. Nevertheless, to the best of our knowledge there are no reports describing expression levels of P2X3 receptors in the heart or blood vessels in CVD. Therefore, we tested the hypothesis that expression of P2X3 receptors changes in target organs, of rats with CVD.

Objective: To evaluate P2X3 receptor expression in the left ventricle, aorta, mesenteric artery and perivascular tissue of the aorta from HF rats, and rats fed with a high-fat diet (HFD).

Methods: All animal care and experimental procedures were approved by the Committee of Animal Research Ethics from Federal University of Santa Catarina (CEUA/UFSC, number 2351090518). Rat groups included: sham coronary ligation (Sham; n=3-5), HF (n=5-8), standard diet (n=4-6) and HFD (n=4-6). HF was induced by ligation of the left anterior descending coronary artery; rats were studied 6 weeks after the surgical procedure. Sham-operated rats underwent similar surgical procedures but did not undergo coronary artery ligation. The HFD consisted of standard rat chow, peanuts, milk chocolate and sweet biscuits in the proportion of 3:2:2:1. The rats were fed with the HFD for 7 weeks. P2X3 receptor expression was quantified by Western blotting.

Results: HF animals demonstrated increased cardiac (T-Test, t= 4.446, p= 0.001) and pulmonary index (T-Test, t= 3.448, p= 0.005), reduced left ventricle contractility (T-Test, t= 4.571, p= 0.001) and relaxation (T-Test, t= 4.060, p= 0.003). HFD showed higher body weight compared to the standard diet group (Two-way ANOVA, p=0.0001). The receptor was present in each of the organs studied (left ventricle, aorta, mesenteric artery and perivascular tissue of the aorta). However, no difference in a detectable level between rat groups was observed, i.e. HF rats compared with the Sham, or HFD compared to standard diet rats.

Conclusions and Support: We show that P2X3 receptor expression was detectable in cardiovascular structures such as heart, aorta, arteries and perivascular fat but neither HF nor a HFD altered expression levels, which is in stark contrast to that detected in the carotid body of rats with CVD. Support: CNPq, CAPES and FAPESP.

ID: 3351

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF AEROBIC EXERCISE ON HEMODYNAMIC AND CARDIOMETABOLIC PARAMETERS IN RATS TREATED WITH CISPLATIN

Introduction: The antineoplastic drug cisplatin (CP) is associated with an increased risk of cardiovascular events due to its cardiotoxic effects and metabolic disruption developed during or after treatment. Although exercise training is widely recognized as an important promoter of cardiovascular health, its role in preventing CP-induced cardiovascular and metabolic changes is poorly understood.

Objective: Thus, the objective of this study was to compare the effects of low (LIT) and moderate (MIT) intensity aerobic exercise training on the hemodynamic and cardiometabolic parameters in female wistar rats treated with CP.

Methods: The animals were randomly divided into 4 groups (n=6): C+S, sedentary control; CP+S, treated with CP and sedentary; CP+LIT, treated with CP and submitted to LIT (45 to 50% of the maximum capacity); CP+MIT, treated with CP and submitted to MIT (70% of the maximum capacity). The training protocols consisted of running on a treadmill, 5 days/week, for 8 weeks. The CP+S, CP+LIT and CP+MIT groups received a single dose of cisplatin (5 mg/kg, i.p.) and 07 days later they were euthanized by decapitation. The heart rate (HR), systolic (SBP) and diastolic (DBP) arterial blood pressures were monitored in awake rats by a programmable tail-cuff sphygmomanometer. The concentrations of total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) and postprandial glycemia were analyzed using a colorimetric method through an automatic biochemical analyzer. The concentrations of low density lipoprotein (LDL) and very low density lipoprotein (VLDL) were determined by Friedewald formula [LDL = (TC-HDL) - (TG/5)]. This study was approved by the Ethics Committee in Animal Experimentation of the UFBA/IMS (protocol 056.2018). Data are presented as mean±SEM. Statistical differences were defined when $p<0,05$.

Results: The results shows that CP+LIT (343.7±4.447) and CP+MIT (344.4±6.221) groups had a lower HR compared to the C+S (370.4±6.603) ($p<0.05$) and CP+S (367.9±6.196) ($p<0.05$) groups. Both exercise protocols were able to decrease the values of SBP in

CP+LIT (102.1±1.714) and CP+MIT (104.4±2.882) in relation to the C+S (110.9±1.446) ($p<0.05$) and CP+S (117.2±4.027) ($p<0.05$) groups. Similarly, both trained groups had lower serum TC levels compared to C+S (82.13±4.561) ($p<0.05$), however only CP+MIT (53.25±3.111) showed a reduction compared to CP+S (72.73±7.406) ($p<0.05$), but not the CP+LIT group (58.27±5.407). The training protocols were able to decrease the serum LDL levels of CP+LIT (14.42±4.168) and CP+MIT (13.46±2.182) compared to C+S (35.28±4.200) ($p<0.05$) and CP+S (25.65±2.773) ($p<0.05$). Only MIT reduced the TC/HDL ratio of the CP+MIT group (1.971±0.059) ($p<0.05$) compared to the C+S (2.525±0.045) and CP+S (2.644±0.232); LIT was not able to change this parameter in CP+LIT (2.186±0.111). Both the CP+LIT group (0.516±0.143) and the CP+MIT group (0.434±0.087) demonstrated a lower LDL/HDL ratio in relation to the C+S (1.083±0.108) ($p<0.05$) and CP+S (0.927±0.091) ($p<0.05$). Both training were able to decrease the levels of postprandial glycemia in CP+LIT (109.3±3.993) and CP+MIT (106.3±4.918) in relation to C+S (133.2±11.17) and CP+S (134.6±5.642) ($p<0.05$) groups.

Conclusions and Support: In conclusion, although both training protocols brought cardioprotective effects, greater benefits were achieved with MIT, since only it was able to reduce the TC/HDL ratio.

ID: 2842

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: IMPORTANCE OF THE ANGIOTENSINERGIC MECHANISMS OF THE MEDIAL SEPTAL AREA FOR THE CONTROL OF FLUID DEPLETION INDUCED SODIUM INTAKE.

Introduction: Sodium and/or water intake is important to control blood volume and/or osmolarity if water and/or sodium are reduced in the body. Sodium and/or water intake is induced by the action of facilitatory mechanisms like the renin-angiotensin-aldosterone system and osmoreceptors acting in brain areas. On the other side, water and sodium intake are also controlled by inhibitory mechanisms of the lateral parabrachial nucleus (LPBN). An important central area that facilitates dipsogenic responses is the medial septal area (MSA), nevertheless, its participation in the control of sodium intake is not clear.

Objective: In the present study, we investigated the possible participation of angiotensinergic and cholinergic mechanisms of MSA on water and 0.3 M NaCl intake in rats with blockade of the LPBN inhibitory mechanisms.

Methods: (CEUA nº 42/2014) Male Holtzman rats with stainless steel cannula implanted in the LPBN and MSA were used. Water and NaCl intake was induced the injection of the diuretic furosemide (FURO, 10 mg/kg) + the angiotensin-converting enzyme blocker, captopril (CAP, 5 mg/kg). Moxonidine (α2 adrenergic/imidazoline agonist, 0.5 nmol/0.2 µl) or vehicle was injected into the LPBN combined with losartan (AT1 receptor antagonist, 10 µg/0.5 µl), atropine (muscarinic antagonist, 2 nmol/0.5 µl) or saline into the MSA.

Results: Rats treated with FURO + CAP + moxonidine into the LPBN + saline into the MSA ingested a strong amount of 0.3 M NaCl (30.9 ± 4.7, vs. FURO + CAP + vehicle into the LPBN + saline into the MSA: 3.0 ± 1.0 ml/120 min, $p < 0.05$, $n = 8$). The injection of losartan into the MSA reduced 0.3 M NaCl intake in rats treated with FURO + CAP + moxonidine into the LPBN (13.4 ± 4.8 ml/120 min; $p < 0.05$; $n = 8$), not in rats treated with FURO + CAP + vehicle into the LPBN. FURO + CAP-induced water intake was not modified by moxonidine or losartan alone or combined. The injection of atropine into the MSA produced no change in 0.3 M NaCl in rats treated with FURO + CAP + vehicle or moxonidine into the LPBN (atropine + moxonidine: 30.6 ± 6.6, vs. saline + moxonidine: 25.8 ± 6.9 ml/120 min; $p > 0.05$; $n = 8$).

Conclusions and Support: The results suggest that angiotensin II release within the MSA to act on its AT1 receptors is part of the mechanisms that facilitate sodium intake induced by FURO + CAP combined with the deactivation of inhibitory mechanisms with moxonidine injection into the LPBN. No involvement of muscarinic cholinergic receptors of the MSA in sodium intake in this condition was found. Keywords: sodium intake, angiotensin II, septal area. Financial support: CNPq/PIBIC, FAPESP.

ID: 3099

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: OBESITY AS A POTENTIALIZATION FACTOR FOR INFLAMMATORY RESPONSE AND OXIDATIVE DAMAGE IN OSTEOARTHRITIS

Introduction: Osteoarthritis (OA) is a chronic disease of high prevalence that presents an inflammatory and degenerative condition of the joints. In turn, obesity is characterized by a chronic low-grade inflammatory process with high levels of inflammatory proteins and oxidative damage. Currently, it is believed that excess adipose tissue increases levels of cytokines, such as C-reactive protein (CRP), causing systemic inflammation that, in addition to joint overload, can contribute to the development and worsening of OA.

Objective: This study aimed to evaluate the effects of obesity on serum levels of CRP and oxidative stress in obese and non-obese animals with OA.

Methods: All procedures were approved by the Ethics Committee on the Use of Animals (CEUA / UNIPAMPA) under protocol number 039/2019. 36 Wistar rats were used, with an initial weight of approximately 200 grams, under a 12-hour light / dark cycle, and under controlled temperature conditions (22 ± 2 ° C). The animals were divided into a control group (C), control with OA (COA), obese (OB) and obese with OA (OBOA). Groups C and COA (n = 18) received balanced industrial food and water ad libitum. The OB and OBOA groups (n = 18) received a cafeteria diet consisting of commercial feed plus pate, chips, bacon, chocolate and biscuits in a ratio of 2: 1: 1: 1: 1: 1 and water ad libitum. The obesity induction protocol lasted 60 days. For OA induction, on the 60th day, animals in the COA and OBOA groups were anesthetized and will receive an intra-articular injection in the right knee of sodium monoiodoacetate at a dose of 1.5mg. C and OB rats received an intra-articular injection of sterile saline. The animals were evaluated weekly for their body weight and to measure obesity, the adiposity index was used. After 5 days of OA induction, euthanasia was performed and whole blood was collected by cardiac puncture to determine serum levels of CRP and oxidative parameters such as TBARS and carbonyl. Statistical analysis was performed using two-way ANOVA for multiple comparisons, with $p < 0.05$ being considered.

Results: Our results show that the OB and OBOA animals showed a significant increase in body weight and adiposity index compared to groups C and COA. As for the levels of CRP, it was observed that the animals COA, OB and OBOA showed a significant increase in comparison to C. Still, the group OBOA had a significantly higher level of CRP compared to the other groups. It was observed in the analysis of oxidative stress, by the TBARS and carbonyl methods, that the COA, OB and OBOA groups showed greater oxidative damage. Like the result observed in the analysis of the PCR level, the OBOA animals differed from the other groups with high oxidation values. However, it is noteworthy that the OB group also had significantly higher values of oxidative damage compared to the C and COA groups.

Conclusions and Support: Our study shows that obese animals have high levels of CRP and oxidative stress in the systemic circulation, even at baseline. It should be noted that, as for oxidative stress, OB animals showed greater damage, even than non-obese animals with OA. In addition, we found that the association between obesity and OA resulted in an exacerbated inflammatory and oxidative response compared to the isolated analysis of these diseases. Thus, it can be suggested that obesity generates a systemic inflammatory and oxidative process, and that when related to OA, it promotes the potentiation of these processes.

ID: 3355

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF 24H-WATER DEPRIVATION ON THE DIPSOGENIC, RENAL AND CARDIOVASCULAR RESPONSES OF RATS FED WITH HIGH-FAT DIET

Introduction: Obesity is defined as the excessive accumulation of fat that presents a risk to health. Recent data from our group demonstrated a reduction in daily water intake and the pressor effect, but not the dipsogenic response to the icv injection of angiotensin II (ANG II), was potentiated in the high fat (HFD) rats. In addition to central ANG II, other mechanisms are also able to lead to cardiovascular and hydroelectric changes, such as during water deprivation.

Objective: To verify if in HFD rats there is a change in dipsogenic, renal and cardiovascular response induced by water deprivation

Methods: Animals were divided into two groups: one group was fed with a standard diet (SD, 11 % calories from fat) and the other with HFD (45% calories from fat). After 6 weeks, the rats were deprived from water for 24 h and the urine was collected for the 24 h period. After 24 h, water was provided for the animals and the water intake was measured for a 4 h period. In another group of SD and HFD, a cannula was inserted into the femoral artery and in the next day mean arterial pressure (MAP) was recorded in euhydrated rats, thereafter they were water deprived and MAP was recorded in the same animals after 24 h.

Results: After 24 hours of water deprivation, HFD rats showed a reduction in urinary volume compared to SD rats [0.6 ± 0.04 vs. SD: 1.1 ± 0.08 ml/100 g body weight (b. wt.), $p < 0.05$], furthermore, HFD rats drank less water after water deprivation compared to SD rats (3.4 ± 0.1, vs, SD: 4.8 ± 0.2 ml/100 g/4 h b. wt.; $p < 0.05$). HFD animals presented a higher BP compared with SD rats before water deprivation (118 ± 2.2, vs, SD: 104 ± 1.7 mmHg, $p < 0.05$) and after 24 h of water deprivation (126 ± 2, vs. SD: 115 ± 2 mmHg, $p < 0.05$), although the increase in MAP was comparable between groups (HFD: 7 ± 2 and SD: 10 ± 1 mmHg; $p > 0.05$).

Conclusions and Support: The present results show a lower water intake and urine volume after 24-h water deprivation. In addition, the HFD group presented a higher MAP levels before and after water deprivation. Maybe the lower water intake observed in HFD after water deprivation is due to a higher water retention and/or the higher levels of MAP in these animals. Support: FAPESP (2019/22767-8), CAPES – 001, CNPq.

ID: 3100

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF STANDARDIZED EXTRACT OF Gingko Biloba (EGb) ON DIFFERENT TYPES OF MEMORY IN A STREPTOZOTOCIN-INDUCED ANIMAL MODEL OF SPORADIC ALZHEIMER'S DISEASE

Introduction: Alzheimer's disease (AD) affects around 47 million people worldwide and represents about 60-70% of dementia cases according to data from the World Health Organization (2019). AD is characterized by a progressive loss of neural cell, predominantly in the hippocampal formation, which is associated with impairments of cognitive functions, including the ability to form new memories. Currently, AD is also correlate with changes in the brain insulin signaling, similarly to that observed in the streptozotocin intra-cerebroventricular (STZ-icv) animal model. Despite advances in our understanding of neural basis of AD, the pharmacological treatments available are not completely effective. Our lab has shown cognitive enhancer effect of standardized extract of Ginkgo biloba (EGb) in healthy adult and middle-aged rats.

Objective: To improve our understanding about EGb effects in memory, this study assessed the effects of STZ-icv (STZ - 3 mg/kg) in novel object recognition memory (NOR), object localization memory (OLM) and in plus-maze discriminative avoidance task (PMDAT) in middle-aged rats. Additionally, we analyzed the effects of treatment with standardized extract of EGb following STZ-icv in the same tasks (CEUA n. 6052310818).

Methods: Twelve-month-old male Wistar rats were administered citrate buffer (icv) + vehicle (0,9% saline) or EGb (0.25 g/kg, 0.5 g/kg or 1.0 g/kg); STZ (icv) + vehicle or EGb (0.25 g/kg, 0.5 g/kg or EGb 1.0 g/kg) and STZ (icv) + 5 mg/kg donepezil hydrochloride for 14 days and naive group (n=10/group). Except for the naive group, all groups were submitted to stereotaxic surgery before starting treatment. For the memory analysis, the animals were submitted to NOR, OLM and PMDAT.

Results: Our data showed that all doses of EGb were able to reverse the short and long-term memory impairment caused by the administration of STZ. The animals were able to discriminate the new and familiar object, presenting a high rate of exploration as well as object localization memory. Similarly, all doses of EGb prevented the STZ-icv induced memory impairment in the discriminated avoidance task. EGb-treated animals were able to discriminate both enclosed arms (aversive and non-aversive) during the training session (short-term memory). In addition, we observed that animals treated with EGb at doses 0.25 g/kg and 1.0 g/kg following STZ had discriminative avoidance long-term memory maintenance evaluated during test session.

Conclusions and Support: Altogether, our data showed protective and cognitive enhancer effects of EGb treatment in both aversive and non-aversive memories evaluated in recognition and discriminated avoidance tasks. Financial support: FAPESP.

ID: 2845

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Lusófona - - - Portugal

Title: LOOKING FURTHER INTO THE IN VIVO EFFECTS OF

Introduction: Essential oils are complex mixtures of volatile low molecular weight compounds (terpenoids and phenylpropanoids) extracted from plants and are responsible for the characteristic aroma in that plant. These products are widely used in food, drinks, pharmaceuticals, and cosmetics and toiletries.

Objective: Despite the wide use of L. angustifolia (lavender) and S. officinalis (sage) essential oils in cosmetic and dermatological formulations, information about its mechanism of action and efficacy is still insufficient. Thus, our objective is to contribute to understand the impact of these oils on skin's physiology in healthy volunteers.

Methods: These two oils have been obtained by hydrodistillation of the plants' aerial parts. Commercially available almond oil (PYL, Celeiro, Portugal) was used as vehicle for four formulations containing 5% and 10% of each essential oil and as reference (blank). Eleven healthy volunteers (5 men and 6 women) mean age 31.3 ± 10.0 years old were selected after informed consent. All procedures were conducted according to the principles of the Declaration of Helsinki and respective amendments and have been approved by the Ethics Committee from the School of Sciences and Health Technologies, Universidade Lusofona (approval number 03/13). Six areas (3cm x 3cm) were drawn in both forearms to test all formulations. The application order was previously randomised, keeping one square empty as the negative control. Applications were done with a small spatula (2mg/cm2 ) and left in contact with the skin for 30 minutes. The epidermal barrier function was assessed through an evaporimeter (Tewameter TM300 CK electronics GmbH, Germany) which allows the quantification of the Transepidermal Water Loss (TEWL). Epidermal hydration was measured using a MoistureMeter SC and a MoistureMeter D (Delphin Technologies, Finland) for superficial and deep hydration, respectively. Skin biomechanics were assessed by the Cutometer®MPA580

system (CK electronics GmbH, Germany). All variables were measured before and 30 min after applications. Nonparametric statistical comparisons were applied ($p<0.05$).

Results: A significant decrease of TEWL, as well as a significant increase of superficial and deep epidermal hydration, were observed 30 min after the application of all the formulations tested. Regarding skin biomechanics, significant increase of maximum elongation amplitude, maximum relaxation, elasticity, and viscoelastic ratio were found but only for the 5% concentration of both sources.

Conclusions and Support: Our results have shown that essential oils from L. angustifolia (lavender) and S. officinalis (sage) improve the "barrier" function, epidermal (deep and superficial) hydration, and skin biomechanical properties. Our results underline the superficial action of these compounds, probably by reinforcing epidermal cohesion due to their lipid character. These findings make them an interesting source for the development of dermatological formulations to improve human health and well-being. Support: Fundação de Ciência e Tecnologia (FCT) UIDB/04567/2020 and UIDP/04567/2020

ID: 2846

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: TELMISARTAN REDUCES PERIODONTAL DISEASE-INDUCED ALVEOLAR BONE LOSS IN SPONTANEOUSLY HYPERTENSIVE RATS

Introduction: Periodontal disease (PD) is an inflammatory disorder of the tooth surrounding soft tissues and alveolar bone, initiated by bacteria biofilm accumulation. The coexistence of systemic conditions, as hypertension, can exacerbate inflammatory response, enhance bone resorption, and studies have demonstrated that the local renin-angiotensin system (RAS) have a role in PD progression.

Objective: To evaluate the effect of telmisartan (TELM, AngII receptor type 1 antagonist) in the local RAS components modulations and PD progression on mandibles of Wistar (W) and Spontaneously Hypertensive Rats (SHR).

Methods: Ten-week old male Wistar and SHR were subjected to 15 days of PD (induced by bilateral silk ligature placed in the first inferior molars), and concomitantly treated with TELM (10 mg/Kg daily by oral gavage). Hemimandibles were harvested for micro-computed tomography, expression of RAS components by immunohistochemistry and qRT-PCR (Agt, Ace, Agt1r, Agt2r, Ace2, and Masr), production of inflammatory mediators by ELISA (TNF-α, IL-1β, IL-6, CXCL3 e CCL2), and expression of bone formation and resorption markers by qRT-PCR (Runx2, Osx, Catnb, Alp, Col1a1, Opn, Ocn, Bsp, Bmp2, Trap, Rank, Rankl, cathepsin K, Mmp-2 and -9, Vtn, Itga5, Itgb5, and Oscar). Institutional Animal Care and Use Committees Approval (School of Dentistry of Araçatuba; #00686-2016).

Results: The group SHR+PD showed increased alveolar bone loss compared to W+PD, and treatment with TELM significantly prevented this response, especially in the SHR+PD+TELM group. In addition, TELM was able to reduce the production of TNF-α, IL-1β and CXCL3, only in SHR animals. In groups W and SHR+DP we observed an increase in Agt expression and a reduction in Agtr2, and TELM was able to reduce Agtr1 expression and increase Agtr2, in W and SHR+PD+TELM. PD did not lead to major changes in bone formation markers, except for the lower Alp expression. Regarding the resorption markers, the SHR+DP group had greater expression of Mmp9, Ctsk, Oscar and Vtn, compared to the respective control (SHR+PD) and the W+DP group, and TELM significantly prevented these alterations, except for the Oscar expression, in addition to increase the expression of Runx2 and Alp.

Conclusions and Support: Our results suggest a protective effect of TELM in the progression of PD mainly in the hypertensive animals, seen by the lower alveolar bone resorption, in part explained by the modulation of the angiotensin II receptors expression (Agtr1 and 2), decreased production of inflammatory mediators, lower expression of bone resorption markers and increased expression of bone formation markers. This work was supported by FAPESP (Grant #2015/03965-2) and CAPES (Finance code 001).

ID: 3615

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: SEASONAL METABOLIC CHANGES IN LIVER, MUSCLE AND PLASMA IN A SOUTH AMERICAN FROG BOANA

PULCHELLA

Introduction: Surviving in environments with a range challenges of temperature requires that ectothermic animals undergo changes from a behavioral, biochemical and physiological to deal with the decrease in available resources such as food, access to water and oxygen and with changes in environmental parameters as temperature, salinity and humidity. In Hylidae family, reproductive phenology is partially restricted by thermal sensitivity. However, Boana pulchella, a Rio Grande do Sul Hylidae, seems to be able to survive low temperatures and still maintain its active reproductive during coldest months. Due to this particularity, this species is an interesting animal model in studies that involve physiological adaptations to, in the same period, be able to withstand the cold and reproduce.

Objective: Evaluate the energetic metabolic patterns during seasons in liver, muscle and plasma of B. pulchella, identifying possible metabolic pathways that would be modified during year providing data for understanding the biology of these animals.

Methods: We capture B. pulchella males (n=33) during winter (n=12), spring (n=5), summer (n=10) and fall (n=6) in Rio Grande do Sul, Brazil. Immediately after capture, animals were brought to laboratory, made euthanasia and realized biochemical analysis. Pieces of liver and muscle was used to verify hepatic oxidation 14C glucose to CO2, glycogen synthesis from 14C glucose and glycogen concentration. Glycerol and lactate concentrations were made in liver by PBS homogenization and muscle lactate concentrations by saline homogenization following colorimetric test. Plasma was used to determinate glucose, glycerol and lactate concentrations. Statistical analysis: normality was checked using the Kolmogorov-Smirnov test and the differences among groups were tested by one-way ANOVA followed by Tukey post hoc test or Kruskal Wallis followed by Dunn's post hoc test. Values of $p < 0.05$ were considered significant (Prism® software). This study was approved by CEUA - UFRGS (35562) and the collected authorized by SISBIO (63115-1).

Results: Glucose oxidation in summer was higher than spring season in liver and higher in summer than spring and fall in muscle tissue ($p<0.05$). Glucose synthesis in liver was the same in all seasons but, in the muscle, was higher in summer than spring and fall ($p<0.05$). Muscle tissue glycogen were higher in fall than summer and spring ($p<0.05$) and in liver didn't changes between seasons. Glycerol, urea, triglycerides and lactate liver concentrations didn't vary throughout the seasons but in muscle lactate were lower in summer than winter ($p<0.05$). Plasma glucose was higher in winter and spring than fall ($p<0.05$).

Conclusions and Support: During the summer, B. pulchella has a higher rate of glycolytic oxidation in liver and muscle tissue and a higher production of glycogen from glucose, indicating the main energetic substrates during the summer is glucose. The higher concentration of muscle glycogen and the lower plasma glucose concentration in the autumn may indicate an anticipatory deposit of this reserve for the most thermally complicated month: winter. Thus, B. pulchella has a seasonal variation in the concentration of some substrates during year and can occur because it reproduces in all seasons where temperature and resources is not the same throughout the year. This study was supported by Laboratório de Metabolismo e Endocrinologia Comparada - LaMEC and Conselho Nacional de Desenvolvimento Científico e Tecnológico - CNPq

ID: 3106

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: IMPAIRMENT OF METABOLIC PERFORMANCE IN NILE TILAPIA, OREOCHROMIS NILOTICUS, EXPOSED TO A SUBLETHAL LEVEL OF ATMOSPHERIC PARTICULATE MATERIAL

Introduction: Introduction: The atmospheric particulate matter (PM) is a relevant source of air pollution that can be produced by anthropogenic processes. The PM produced by steel industry consists of a complex mixture of particles that includes a large number of metallic nanoparticles. PM was reported to cross-contaminate aquatic environments becoming a potentially relevant problem to aquatic biota and human population. PM contamination has been reported to remain in sublethal level in some Brazilian areas, although questions have been raised about its safety.

Objective: Objective: We evaluated how sublethal contamination by rough PM (96 h) affects general physiological performance to support metabolic increasing and swimming in fish.

Methods: Methods: We recorded the aerobic metabolic rate (under swimming protocol - Steffensen-type swim-tunnel) of Nile tilapia, Oreochromis niloticus (180 ± 98g) exposed to acute contamination (96h) to raw PM (1 g.L-1; PM group, n = 10) and Ctrl group (n = 10). After 96h, each fish was placed in a swim-tunnel adapted for respirometry (volume 13.4 L), in normoxic water (PwO2 of 100%, at 25 ± 1°C) for the swimming protocol while oxygen consumption (MO2 - mMolO2.kg−1.h−1) was measured by intermittent respirometry (optode system - OXY-4 mini PreSens). The used system allows for calculations of metabolic and swimming indexes: standard metabolic rate (SMR), maximum metabolic rate (MMR), aerobic scope (AS), critical swimming speed (Ucrit), net metabolic cost of swimming (COS), swimming efficiency (Eswim), and maximum swimming (Emax). Then PM fish underwent a recovery protocol, with uncontained water for 96h (Rec group, n = 10) and swum again (CEUA-UFSCar #8105110718).

Results: Results: PM contamination changed the profile of energy mobilization after exposure reducing AS (Ctrl, 10.13 ± 0.19; PM, 7.19 ± 0.24 mMolO2.kg−1.h−1) and SMR (Ctrl, 4.65 ± 0.16; PM, 3.32 ± 0.05 mMolO2.kg−1.h−1). Therefore, PM impacted critical swimming speed, Ucrit (Ctrl, 5.68 ± 0.07; PM, 3.41 ± 0.06BL.s−1), and compromising maximum swimming, Emax (Ctrl, 1.86 ± 0.10; PM, 1.12 ± 0.02 µmolO2 Kg-1.BL-1). The alterations after acute PM contamination were not recovered after 96h (AS, Rec 8.09 ± 0.26; SMR, Rec, 3.42 ± 0.09; Ucrit, 4.15 ± 0.77; Emax, 1.51 ± 0.05).

Conclusions and Support: Conclusion: PM evoked sublethal alterations that compromise the physiological support to face fundamental aspects of fish survival, such as energy allocation, aerobic scope, and swimming capacity. In the environment, such problem will develop as a reduction in migratory potential, foraging, and reproduction. Therefore, it might impair species survival and ecological relations. We suggest that physiological indexes such as swimming performance and aerobic metabolic biomarkers are relevant to understand environmental monitoring and for identification of important levels of sublethal contamination before ecological damage is present. Financial support:

CAPES; FAPESP (2019/08491-0)

ID: 3109

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: GLUCOCORTICOIDS MODULATE THE TRIACYLGLYCEROL SYNTHESIS AND REDUCE THE THERMOGENIC CAPACITY IN BROWN ADIPOSE TISSUE OF RATS

Introduction: The maintenance of adequate triacylglycerol (TAG) stores is essential for a normal brown adipose tissue (BAT) functioning and requires a continuous supply of glycerol-3-phosphate (G3P). The glucocorticoids (GC) present contrasting metabolic effects depending on adipose tissue locations and, therefore, have determinant effects on TAG storage. However, the role of these hormones in the control of G3P generation pathways for TAG synthesis and in the function of the BAT is still unknown.

Objective: The aim of this study was to evaluate the effect of GC treatment on TAG content and G3P generation pathways, as also its role in the BAT thermogenesis of rats.

Methods: Male Hannover rats (~180 g) received a single daily injection of dexamethasone (Dexa) (1 mg/Kg) or saline 0,9% during 7 days. Blood was collected for biochemical assays and BAT was excised for G3P generation pathways analyses {2-Deoxi-1-[14C]-glucose uptake, pyruvate incorporation in glycerol-TAG, phosphoenolpyruvate carboxykinase (PEPCK) activity, glycerol-U-[14C] incorporation in glycerol-TAG, and glycerokinase (GyK) activity} and western blot measurements (CEUA protocol 195/2018, FMRP-USP). The results were expressed as mean ± SEM. Unpaired Student t test was used and $P \leq 0,05$ was taken as the criterion of significance.

Results: Dexa treatment increased the lipid content of BAT (~40%) with a consequent increase in tissue weight (~2,5x). These results were accompanied by reduced lipolysis (~50% glycerol and fatty acid release; and ~65% pHSLser660 protein content) and increased lipogenesis when compared with control rats. Dexa treatment did not change the glucose uptake rates (glycolytic pathway) and the incorporation of 1-[14C]-pyruvate in glycerol-TAG (glyceroneogenic pathway) and the activity of the enzyme PEPCK. On the other hand, Dexa treatment increased the activity (~40%) and protein content (~55%) of GyK even with reduced rates of glycerol-U-[14C] incorporation in glycerol-TAG (~55%). This study also demonstrated that Dexa treatment reduced the BAT functional and mitochondrial markers protein content, such as UCP-1 (~40%), VDAC (~40%), citrate synthase (~50%), Tom20 (~36%) and some complexes of the electron transport chain, suggesting a reduction in the thermogenic capacity of the tissue. This hypothesis was corroborated by the reduction (~13%) of tissue capacity to increase the temperature after stimulation with noradrenaline. In addition, the noradrenaline content in BAT of the treated animals was reduced by 53%.

Conclusions and Support: These data suggest that the GCs affect the TAG synthesis in BAT and the direct phosphorylation of glycerol pathway is responsible for maintaining the adequate supply of glycerol-3-phosphate required for fatty acid esterification and storage of TAG. In addition, Dexa treatment seems to suppress the thermogenic capacity of BAT, interfering in the response to sympathetic nervous system stimulation. FAPESP; CNPq.

ID: 3113

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: MATERNAL PERIODONTAL DISEASE PROMOTES INSULIN RESISTANCE, DECREASE OF AKT SERINE PHOSPHORYLATION STATUS AND INCREASE OF TNF-α CONTENT IN PERIEPIDIDYMAL WHITE ADIPOSE TISSUE OF ADULT OFFSPRING

Introduction: It is well established that the fetal environment is linked to maternal health, and abnormal stimuli or aggressions during intrauterine life can result in changes in the physiology and metabolism of offspring, increasing the risk of disease in adult life, this phenomenon is known as fetal programming. Previous studies have demonstrated that maternal periodontal disease (PD) promotes insulin resistance, increased plasma concentrations of cytokines, reduced GLUT4 content and its plasma membrane translocation index in muscle tissue in its adult offspring. And cytokines, such as TNF-α, have been linked to reduced GLUT4 expression through the activation of nuclear transcription factor kappa B (NF-κB). In addition, this cytokine can stimulate some serine kinases including IκB kinase (IKK), c-Jun amino-terminal kinase (JNK) and extracellular signal–regulated kinases (ERKs) that are involved in insulin resistance.

Objective: These findings evidenced the need for further studies to verify whether another tissue, such as adipose tissue, also shows these changes in adult offspring. The aims of the present study were to evaluate in adult rats, offspring of rats with PD: 1) birth weight and during the 75 days of age; 2) glycemia and insulinemia; 3) phosphorylation of Akt serine phosphorylation status in periepididymal white adipose tissue (WAT); 4) TNF-α content in WAT.

Methods: Female Wistar rats were distributed into a control group and an experimental periodontal disease group, in which the disease is induced by ligation with silk thread around the 1st molar. Seven days after ligature placement, animals from both groups mated and daily vaginal smears were taken to verify the presence of sperm. Pregnant rats were kept in individual cages. The body weights of the offspring were measured once weekly from birth until 75 days of age. When male offspring of these rats completed 75 days, the experiments were performed: 1) glycemia and insulinemia; 2) phosphorylation of Akt serine phosphorylation status in WAT; 3) TNF-α content in WAT.

Results: The results demonstrated that maternal periodontal disease promotes in its adult offspring low birth weight (LBW), insulin resistance, decrease of Akt serine phosphorylation status and increase of TNF-α content in WAT.

Conclusions and Support: Therefore, this study is of fundamental importance for the understanding of some of the mechanisms involved in the relationship between maternal periodontal disease and insulin resistance in adult offspring. In addition, it shows that ideal maternal oral health can help prevent future illnesses in adult offspring. Support: São Paulo Research Foundation (FAPESP) [grant #2019/04183-9] São Paulo, SP, Brazil.

ID: 2858

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: BISPHENOL-A EXPOSURE AGGRAVATES WHITE AND BROWN ADIPOCYTE HYPERTROPHY INDUCED BY HIGH-FAT DIET CONSUMPTION IN OVARIECTOMIZED MICE

Introduction: Bisphenol-A (BPA) is an endocrine disrupter (ED), which has estrogenic, antiestrogenic and anti-androgenic actions. Recently, we demonstrate that BPA exposure in postmenopausal mice aggravates hepatic steatosis, but whether this ED can impair adipose tissue in this period of life in females, needs further investigations.

Objective: Herein, we evaluated the effects of BPA exposure on white and brown adiposity in ovariectomized (OVX) female mice fed on a high-fat diet (HFD).

Methods: Adult Swiss female mice were OVX and submitted to a normolipidic diet or HFD and drinking water without (OVXCTL and OVXHFD groups respectively) or with 1 μg/mL BPA (OVXCBPA and OVXHBPA groups respectively), for 3 months. The rectal temperature was measured weekly throughout the experimental period, subsequently, the adiposity and the morphology of the retroperitoneal white adipose tissue (rWAT) and of the interscapular brown adipose tissue (iBAT) were performed (CEUA UFRJ Macaé approval: MAC035). Data were analyzed by Shapiro-Wilk and compared using ANOVA or Kruskal-Wallis ($P<0.05$).

Results: OVXHFD females displayed increased body weight (BW; 59 ± 3 g), food consumption (6 ± 0.7 Kcal/24h), rWAT (1 ± 0.2mg/g BW), perirenal white fat pad (0.5 ± 0.04mg/g BW), and iBAT weights (0.6 ± 0.04mg/g BW), when compared with OVXCTL (47 ± 2g; 3 ± 0.6 Kcal/24h; 0.5 ± 0.07; 0.2 ± 0.02 and 0.3 ± 0.03mg/g BW, respectively). BPA exposure did not modify these parameters in OVXHBPA (58 ± 2g; 6 ± 0.8 Kcal/24h; 1 ± 0.2; 0.4 ± 0.05 and 0.8 ± 0.2mg/g BW, respectively), when compared to OVXHFD. The rectal temperature of OVXHFD females was slightly greater (37.3 ± 0.04 ºC), through the experimental period, when compared to OVXCTL (36.9 ± 0.05 ºC). BPA exposure did not alter this parameter in OVXHBPA group (37.5 ± 0.05 ºC), in comparison to OVXHFD. Morphological analysis of rWAT revealed adipocyte hypertrophy in OVXHFD females which was evidenced by an increased adipocyte diameter (70 ± 0.4 μm) and a reduction in the number of adipocytes/field analyzed (60±2), when compared to OVXCTL (54 ± 0.4μm and 87 ± 2, respectively). BPA exposure aggravated fat deposition in OVXHBPA, since the rWAT exhibited an increase of 22% in adipocyte diameter (86 ± 2μm) and reduction of 11.6% in the number of adipocytes/field (53 ± 0.9), in comparison to OVXHFD females. OVXCBPA females also increased the

adipocyte diameter (60 ± 0.2 µm) and reduced the number of adipocytes/field (70 ± 2) in rWAT, when compared to OVXCTL. Furthermore, OVXHFD females displayed increased adipocyte area (503 ± 12µm2) and number of lipid vacuoles (9 ± 0.1), but a reduction in the number of adipocytes/field (84 ± 3) in iBAT, when compared to OVXCTL (319 ± 4 µm2; 6 ± 0.09 and 119 ± 5, respectively). BPA exposure in OVXHBPA aggravated the hypertrophy of iBAT adipocytes, increasing in 30% the adipocyte area (656 ± 8 µm2), 67% the number of lipid inclusions/adipocyte (10 ± 0.1) and reduced in 16% the number of brown adipocytes/field (70 ± 1), in comparison to OVXHFD.

Conclusions and Support: Exposure to BPA in the postmenopausal worsens the deposition of lipids in rWAT and iBAT associated with the normolipidic diet, but this effect is exacerbated when associated with HFD. These data warn that postmenopausal ED can lead to the onset of chronic diseases predisposed by increased adiposity. Support: CAPES.

ID: 3115

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: SUCCESSFUL ALTERNATIVES IN THE WEB-TEACHING OF HUMAN PHYSIOLOGY DURING THE COVID-19 PANDEMIC.

Introduction: In Brazilian universities, with the start of the pandemic caused by the Coronavirus disease (Covid-19), traditional methods of face-to-face classes were suspended indefinitely. As an alternative to maintain the interaction of students with our university during the Covid-19 pandemic, we proposed a free online course.

Objective: To describe a Human Physiology web course offered to undergraduate students and evaluate the students' perceptions about it.

Methods: The course proposal included activities carried out during May 2020 and was approved by the Institutional Education Committee (IRB No. 10.069.20). We offer 50 vacancies. Students should be regularly registered in an undergraduate program of Federal University of Pampa/Brazil, and have prior approval in the Human Physiology course or equivalent. We proposed to students synchronous and asynchronous activities, using active teachig methods (flipped class) to address topics considered important for understanding and review different Human Physiology systems. For asynchronous activities, developed according to the preferred time of each student, we used different online tools and platforms, such as Lt® Plataform (ADInstruments), Socrative®, social medias, etc. To promote a real time interaction between students and teachers, synchronous activities on Zoom® and interactive questions using the Mentimeter® were proposed.

Results: Considering the 50 students that started the course, 58% (n = 29) completed at least 70% of the total course, and 16% (n = 8) completed at least 60%. 40 students answered to the evaluation questionnaire. In general, the students' expectations about the course included the Human Physiology contents' review and the opportunity for new learning (about the content and the remote teaching) – in this sense, the course fully to the expectations of 85% of students (n = 34). For most students (90%; n = 36) this was the first web course with this type of method. About the different online tools and activities used during the course, the students inducated that they liked more the exercised in Lt® Platform (100%; n = 40), followed by Zoom®'s interactions (77.5%; n = 31), Mentimeter® webquizzes (60%; n = 24) and Youtube® videos (57.5%; n = 23). The dynamic used in the activities was well accepted by students and most of them considered that it contributed to their understanding of the content (85%; n = 34). Moreover, most students (80%; n = 32) considered the dynamic of the activities as important to increase their frequency of studies during the quarantine period. Considering a scale from 0 (bad) to 10 (excellent), the average grade attributed by the students to the course was 9.15 ± 1.23.

Conclusions and Support: Here we report that a web course designed to review the main topics in Human Physiology during the Covid-19 quarantine was well accepted and approved by students. The methods proposed can be considered as a successful alternative to the webteach of Physiology, especially in the current moment that requires social distancing due to the Covid-19 pandemic.

ID: 3119

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE ESTADUAL DE CAMPINAS - LIMEIRA - Sao Paulo - Brasil

Title: SHORT-TERM SWIMMING OR STRENGHT PHYSICAL EXERCISE AFTER AN INFLAMMATORY INSULT REDUCE THE CHRONIC MUSCLE PAIN

Introduction: Our prior study demonstrates that regular physical exercise prevents the onset of acute muscle hyperalgesia induced by an inflammatory insult.

Objective: This study aimed to evaluate whether short-term physical exercise performed after an inflammatory insult prevents the chronic muscle hyperalgesia.

Methods: Swiss male mice from CEMIB/UNICAMP (Ethics Committee n°. 5295-1) were subjected to injection of Carrageenan (Cg, 100 µg) into gastrocnemius to induce acute muscle hyperalgesia and, 10 days later, an injection of Prostaglandin E2 (PGE2, 1µg) at the same place, to evidence the chronic-latent muscle hyperalgesia. Randall-Selitto test was used to quantify the muscle hyperalgesia in both periods of acute (from day 1 to day 6) and chronic (from day 10 to day 17) muscle hyperalgesia. Two different protocols of short-term physical exercise were used: 1. Swimming: starting 24h after Cg, 30 min/day for 8 consecutive days, without load or with loads of 1.5%, 3% and 4% of body weight. 2. Strength: starting 24h after Cg. At least three sessions, with intervals of 24h between them, were performed by 3 repetitions of 12 climbs (steps), on a 70 cm vertical ladder with a load device attached to the tail. The loads were 20%, 40% or 60% of the Maximum Voluntary Load Capacity test. Area Under the Curve was used to evaluate the chronic period of muscle hyperalgesia (from day 10 to day 17) and the statistical analysis was performed by ANOVA with Tukey post hoc test.

Results: All loads of swimming exercises, including the group without load, reduced the chronic muscle hyperalgesia when compared to sedentary ($p<0.05$, ANOVA, Tukey test). However, the loads of 3% and 4% induced an increase in acute and chronic behavior responses induced by saline/PGE2 when compared to sedentary animals that were also subjected to saline/PGE2 ($p<0.05$, ANOVA, Tukey test). All loads of strength exercises reduced the chronic muscle hyperalgesia when compared to sedentary ($p<0.05$, ANOVA, Tukey test). Because 20% was the minimal efficient load, we tested whether more sessions after PGE2 administration would also reduce chronicity. The results showed that more sessions of strength exercises with a load of 20% were also efficient ($p<0.05$, ANOVA, Tukey test).

Conclusions and Support: We conclude that both protocols of short-term physical exercise reduce the chronic muscle hyperalgesia. Therefore, the strategy of using short-term exercise to decrease the intensity of chronic muscle hyperalgesia seems to be interesting. New studies are necessary to investigate the mechanisms by which the performance of a short-term physical exercise after an inflammatory insult induce a reduction of the intensity of chronic muscle hyperalgesia. Support: FAPESP (17/17919-8), CNPq/UNICAMP.

ID: 3376

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: TRANSLATIONAL EFFECTS OF PEPTIDE KEF-1 FROM SYNBIOTIC KEFIR: ANTIHYPERTENSIVE AND ANTIOXIDANT ACTIVITY IN HYPERTENSIVE MICE

Introduction: In a previous proteomics study, were identified 35 peptides inhibitors of angiotensin converting enzyme (ACE) in Kefir. However, it is not well known how these peptides are involved in the antihypertensive effect by Kefir consumption

Objective: To evaluate the effects of an ACE inhibitor peptide, named Kef-1, derived from Kefir on blood pressure (BP) and its antioxidant activity in an experimental model of arterial hypertension

Methods: Kef-1 inhibitory activity on ACE was evaluate in vitro. For in vivo protocols, C57Bl/6 male mice were submitted to clipping of the left renal artery to produce 2K1C hypertension. In the Sham mice, same surgical procedures were performed except for artery clipping. After 2 weeks, mice were divided into 3 groups: SHAM (n=8; water), 2K1C CON (n=8; water) and 2K1C KEF-1 (n=8; 10 mg/kg/day, gavage). BP and heart rate (HR) were measured by plethysmography after 3 hours and 7 days of Kef-1 administration. After 7 days, mice were euthanized, and blood collected. In the blood cells, reactive oxygen species (ROS) production, lipidic peroxidation and DNA damage were analyzed. Inflammatory cytokines were determinate in plasma. The thickness of the aorta midlayer was evaluated by staining with hematoxylin and eosin. ROS production, viability, and cellular apoptosis, as well, NADPHox and mitochondrial membrane potential (MMP) were evaluated in smooth muscle cells (SMC). Data are reported as mean ± SEM. Animal Ethics Committee-UVV (#489-2018).

Results: Kef-1 was able to inhibit at 59.6% of ACE activity in comparation to captopril. After 3 hours, Kef-1 reduced ($p<0.05$) systolic BP (SBP), diastolic BP (DBP) and media BP (MBP) when compared with vehicle (-25.8±3.9, -26.0±3.8, -26.4±4.3 mmHg, respectively). SBP, DBP and MBP also were reduced ($p<0.05$) after 7 days of Kef-1 treatment (-22.2±3.9; -31.6±2.6; MBP: -24.3±3.2 mmHg, respectively. At 7 days, ROS production, lipidic peroxidation and DNA damage was lower in blood cells ($p<0.05$) vs. 2K1C CON (~10%, ~23%, ~54%, respectively). Kef-1 reduced ($p<0.05$) pro-inflammatory cytokines levels when compared to 2K1C CON (TNFα: ~34%, IFNγ: ~22%, MCP1: ~33%, IL-6:~16%). Thickness of aorta was reduced (~28%, $p<0.05$) in 2K1C KEF-1 vs. 2K1C CON. In SMC, Kef-1 reduced ($p<0.05$) ROS production (~22%) and cellular apoptosis (~58%) vs. 2K1C CON. In 2K1C group, NADPHox represented major oxidative source in SMC vs. SHAM group. Kef-1 contributed to attenuate NADPHox participation in SCM. When MMP was evaluated, 2K1C CON showed higher formation of monomer (5.0±0.5%, $p<0.05$) vs. SHAM group (3.0±0.3%), while Kef-1 treatment no was able to attenuate ($p>0.05$) this disruption of PMM (4.4±0.1%).

Conclusions and Support: These findings highlight the anti-hypertensive and antioxidant potential of the Kef-1 peptide, a promising prototype candidate for antihypertensive drugs obtained from natural food and clarify the beneficial effects of kefir consumption. Financial support: CNPq; FAPES; CAPES (Finance Code 001).

ID: 3632

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: IGA, ANTI-INSULINA AND CYTOKINES OF COLOSTRUM IN DIABETIC MOTHERS: INTEGRATIVE REVIEW

Introduction: Inadequate glycemic control during pregnancy seems to alter the phases of lactogenesis, making breastfeeding difficult. In addition, maternal hyperglycemia can interfere with the composition and immunological mechanisms of colostrum. However, little is known about the immunological components of colostrum in nursing mothers who have had pregnancies complicated by hyperglycemic disorders.

Objective: In this sense, this article aimed to make an integrative review

Methods: integrative review of the literature on the subject through the databases: PUBMED, SCOPUS, MEDLINE, LILACS, CINAHL and Google Scholar.

Results: Six studies were included, of which five are Brazilian. Such evidence pointed out that the concentration of IgA is significantly lower in the milk of diabetic mothers compared to normoglycemic mothers, however there were no differences in the concentrations of cytokines: IFN-

Conclusions and Support: The need for more evidence on possible changes in the milk of diabetic nursing mothers is relevant, as breastfeeding is one of the main measures to combat infant morbidity and mortality.

ID: 3633

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: INFLUENCE OF CONCURRENT TRAINING ON PHYSIOLOGICAL AND FUNCTIONAL ASPECTS OF OBESE ADULTS.

Introduction: The sedentary lifestyle is an actual global problem and its consequences are associated with metabolism dysfunction in a variety of organs, and as results with diseases such as heart diseases, dyslipidemias, reduced functional capacity, among other problems. The physical exercise is one of the main ways to get over physical inactivity, and some studies has been shown the reduction of fat adiposity in animals submitted at physical exercise.

Objective: Investigate the influence of 6 weeks of concurrent training on physiological aspects, functional capacity and body composition of 4 middle-aged men with grade II and III obesity.

Methods: 4 man with Body Mass Index (BMI) above 35, and with grade II and III of obesity was submitted to 6 weeks of concurrent training. The training was composed by a combination of resistance and endurance training. The frequency of each training was 1 hour, 3 times a week.

Results: A1: increased body weight (2,1%), lean mass (5%) and functional capacity on Bruce test (0,5%) while got reduced values for fat mass (-1,8%), fat percentage (-1,6%), heart rate (-4,7%) and resting systolic blood pressure (-7,6%). A2: increased functional capacity on Bruce test (64,1%) and got reduced values for body weight (-5,5%), lean mass (-1,8%), fat mass (-14,5%), fat percentage (-2,9%), heart rate (-2,3%) and resting systolic blood pressure (-13,3%). A3: increased body weight (0,2%), fat mass (0,9%) and functional capacity on Bruce test (12,3%) while got reduced values for lean mass (-1,6%), fat percentage (-1,6%), heart rate (-1,1%) and resting systolic blood pressure (-7,6%). And A4: increased lean mass (0,3%), heart rate (5,9%) and functional capacity on Bruce test (8,8%) while got reduced values for body weight (-2,1%), fat mass (-5,3%), fat percentage (-1,5%), and resting systolic blood pressure (-7,6%).

Conclusions and Support: Concurrent Training has proven to be a hypotensive training method, with large increases in the autonomy of its practitioners and with the potential for weight loss and lean mass gains. So, this training can be indicated for obese man, as a way to reduce the consequences of obesity.

ID: 3378

Área: NEUROFISIOLOGIA

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Title: ZINC IMPROVES NEUROINFLAMMATION AND COGNITIVE PERFORMANCE IN CAFETERIA DIET-FED RATS

Introduction: Obesity triggers a chronic inflammatory profile that affects the central nervous system culminating in neuroinflammation, which leads to cognitive damage. In the brain, Zn is involved in cell survival signaling, has immunomodulatory properties, and modulates hippocampal glutamatergic synapses. Thus, Zn could be used to improve the pathological outcomes of obesity in the brain.

Objective: This study aims to evaluate whether zinc supplementation (10mg/kg/day by gavage) would reduce neuroinflammation and cognitive decline in obese rats after consuming a cafeteria diet.

Methods: Twenty-eight animals were divided into four groups (n=7/group): CT (control diet), CT+Zn, CAF (cafeteria diet), and CAF+Zn. The animals received CAF for 20 weeks containing palatable foods broadly consumed in Western societies, while supplementation began in the 16th week and lasted until the end of the experiment. Weight gain, plasma glucose, triglyceride, and insulin levels were quantified. To evaluate astrocyte and microglial responses after the treatment, GFAP and Iba-1 were evaluated in the cerebral cortex by Western blot. TLR-4 expression was also evaluated in the cerebral cortex and hippocampus. Long-term memory was assessed through the object recognition test. The experiments were approved by the Institutional Animal Care and Use Committee of UFCSPA with protocol No. 570/18.

Results: Our results showed that CAF-fed animals had increased weight (diet effect, $F1, 23 = 69.28$, $p < 0.0001$), blood glucose (diet effect: $F1, 20 = 18.12$, $p < 0.0004$; Zn effect: $F1, 20 = 5.21$, $p < 0.03$; interaction: $F1, 20 = 15.66$, $p < 0.0008$) and triglycerides (diet effect: $F1,17 = 21.70$, $p < 0.0002$). Although Zn can reverse the hyperglycemia caused by the diet, it does not appear to act on the other metabolic parameters. When analyzing the expression of Iba-1 in the cerebral cortex, treatment with Zn decreased microgliosis caused by CAF (Zn effect: $F1.14 = 7.05$, $p < 0.01$; interaction: $F1.14 = 9.14$, $p < 0.009$). Still, post hoc test evidenced that CAF+Zn had decreased Iba-1 expression compared to CAF group ($p<0.01$). In regard to hippocampus, we found an increase in TLR-4, which was also reversed by Zn supplementation (diet effect: $F1.13 = 10.52$, $p < 0.007$; Zn effect: $F1.13 = 5.3$, $p < 0.04$; interaction: $F1.13 = 6.5$, $p < 0.03$). CAF caused memory decline, however, it was reversed by zinc (interaction between diet and supplementation, $F1.17 = 13.14$, $p < 0.003$).

Conclusions and Support: Zn has interesting therapeutic properties against neuroinflammatory manifestations and cognitive deficits caused by obesity. Further studies are necessary to understand the mechanisms by which Zn exerts its neuroprotective role. This research was supported by FAPERGS, CAPES and CNPq.

ID: 2868

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF PHYSICAL EXERCISE PERFORMED BY THE MOTHER DURING PREGNANCY IN THE MEMORY OF ADULT RATS SUBMITTED TO MATERNAL SEPARATION IN THE EARLY-LIFE

Introduction: Maternal separation (MS) in early life can result in neural changes and make infants more susceptible to psychopathologies in adulthood. In contrast, maternal exercise can be used to improve cognitive performance and reduce anxiety-like behavior of offspring. Physical exercise increases levels of brain-derived neurotrophic factor (BDNF), involved in brain development and synaptic plasticity.

Objective: To investigate if the physical exercise (PE) performed by the mother before and/or during pregnancy reduce memory deficits induced by MS.

Methods: First, 24 female Wistar rats were divided into 3 groups: Control (CT); Pre-gestational and Maternal exercise (PGE), and; Maternal exercise (ME). PGE dams were submitted to physical exercise in a treadmill for 4 weeks before pregnancy (50min/day; 5x/week; 60-70% VO2máx). After, 12 male Wistar rats were used to induce pregnancy. During pregnancy, PGE females continue to exercise, and ME females started, both in the same intensity (8m/min until pregnancy day 14; 6m/min until the end of pregnancy). After birth, male offspring were divided into 2 subsets of groups: No intervention (NI) and MS. MS groups were separated from their mothers from postnatal day 1 (PND 1) to PND 10, for 3h/day. In PND 60, social and object recognition tasks were used to evaluate recognition memory. Barnes maze (BM) task was used to assess spatial memory. $P \leq 0.05$ was considered significant for all results. This study was approved by the Ethics Committee on the Use of Animals of the Institution (protocol 042/2018).

Results: In the OR test, all groups no submitted to MS consolidated the memory, exploring the new object for a longer time (CT+NI: P=0.01; PGE+NI: P=0.01; ME+NI: P=0.01). However, the MS animals presented a memory deficit (CT+MS: P=0.07). The MS deficit was prevented by physical exercise started during pregnancy (ME+MS: P=0.004), but not by pre-gestational exercise (PGE+MS: P=0.053). Similar results were found in the SR test. All groups not submitted to MS consolidated memory, exploring the new animal for a longer time (CT+NI: P=0.04; PGE+NI: P=0.009; ME+NI: P=0.001). MS caused memory deficit (CT+MS: P= 0.05). The physical exercise started and performed during pregnancy was able to prevent this deficit (ME+MS: P=0.01). Regarding spatial memory, in the learning curve of the test days, both the CT group and the MS group learned the location of the escape in the third session (CT+NI: P=0.007; CT+MS: P=0.018), not denoting memory deficit. In the preference test, the ME+MS group showed better learning than the PGE+MS group, requiring less time to find the escape (P=0.021).

Conclusions and Support: Physical exercise performed during pregnancy is able to prevent object and social recognition of offspring submitted to MS. Furthermore, MS pups from the mothers that performed the exercise only during pregnancy presented better results than the pups from the mothers that performed the exercise continuously before and during pregnancy in spatial memory. support: CNPq.

ID: 3380

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: MINOCYCLINE TREATMENT IMPROVED COGNITION, BUT NOT RESPIRATORY, MOLECULAR AND SLEEP-WAKE DEFICITS IN A SPORADIC MODEL FOR ALZHEIMER'S DISEASE.

Introduction: Neuroinflammation in Alzheimer's disease (AD) is postulated as a result of the accumulation of amyloid beta-peptide (Aβ) in the brain of patients with AD. Preclinical studies have shown that treatment with minocycline (microglia inhibitor) is capable to prevent the accumulation or to reduce beta-amyloid (Aβ) and cytokines.

Objective: Thus, we tested the hypothesis that minocycline treatment could reverse/minimize the cognitive, respiratory, and sleep deficits of our sporadic AD model a result of increased expression of beta-amyloid protein in the Locus coeruleus region.

Methods: AD was induced in rats by intracerebroventricular injection of streptozotocin (STZ; 2 mg/kg). All experiments were conducted according to the guidelines of the Brazilian College of the National Council for the Control of Animal Experimentation (CONCEA, MCT, Brazil) and with the approval of the Faculty of Agricultural and Veterinary Sciences and Animal Care, Use Committee (CEUA, FACV-UNESP, Jaboticabal campus; Protocol no. nº 05796/19). After five consecutive days of daily treatment with minocycline (30 mg/kg, i.p), the animals were submitted to the experiments. We evaluated memory and learning by Barnes'maze (n=12), ventilatory parameters during sleep and wakefulness by whole-body plethysmography and sleep time using electroencephalography.

Results: Minocycline treatment improved learning and memory of the STZ-AD model (n=12, $p<0.05$), but did not restore CO2 sensitivity during wakefulness (VE mean ± standard deviation: Placebo: STZ-AD= 2479.07 ± 125.2 mL. Kg-1. min-1 vs VE Minocycline-STZ-AD = 2581.3 ± 92.2 mL. Kg-1. min-1) ($P >0.05$ test Two-Way ANOVA) in the AD model. Similarly, the treatment had no effect on the reversal of wakefulness increase in the STZ-AD model (% Time spent in the awake state mean ± standard deviation: Placebo-STZ= 72.9 ± 5.27 vs Minocycline-STZ= 64.5 ± 4.14) ($P >0.05$ test Two-Way ANOVA). In addition, there was no change in the expression of Aβ peptide in the LC region after treatment (% peptide expression Placebo: STZ-AD= 70.6 ± 20.8 vs Minocycline-STZ-AD = 78.5 ± 25.4). No difference was observed in the body temperature of the animals during the experiments, but hypoxia promoted a regulated fall in body temperature.

Conclusions and Support: Minocycline is a promising drug to minimize cognitive dysfunctions in the AD model without changing the respiratory, temperature, and sleep-wake cycle parameters. Support: FAPESP and CNPq

ID: 3381

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: ROLE OF THE RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM ON SODIUM INTAKE INDUCED BY WATER DEPRIVATION IN RENOVASCULAR HYPERTENSIVE RATS

Introduction: Water deprivation (WD) followed partial rehydration (PR) with only water to ingest induces sodium appetite due to activation of the renin angiotensin system (RAS). Renovascular 2-kidney, 1-clip (2K1C) hypertensive rats present an overactive RAS. Indeed, data from our laboratory have shown that sodium intake induced by WD-PR is increased in 2K1C rats, suggesting that 2K1C rats are more sensitive to the natriorexigenic effects of angiotensin II (ANG II). Although aldosterone (ALDO) levels appear not to rise significantly with WD, it levels are increased in 2K1C hypertension.

Objective: To verify the role of the renin-angiotensin-aldosterone system in the increase of sodium intake in 2K1C rats after 24 hours of water deprivation + partial rehydration.

Methods: CEUA: 12/2018; Male Holtzman rats (initial weight 150 – 180 g) received a silver clip around the left renal artery to induce 2K1C hypertension (n = 8). Sham rats (n = 8) underwent similar surgery, but no clip was placed around the renal artery. Six weeks after the renal surgery, both groups received a guide-cannula implant directed to the lateral ventricle (LV) and were let to recover for 5-7 days. The 2K1C and sham rats were submitted to 24 h of WD and thereafter received either an injection of vehicle (1% of ethanol in saline; 2 µl) or RU28318 (100 ng/2 µl, mineralocorticoid antagonist) into the LV. Ten min latter animals received a second injection of saline (0.15 M NaCl) or losartan (66 µg/1 µl, AT1 antagonist) into the LV. Fifteen min latter animals had access to only water and the intake was recorded for 2 h. After this period, 0.3 M NaCl was also available and the intake of both 0.3 M NaCl or water was recorded for an additional 2 h (salt appetite test). After 3 days the test was counterbalanced.

Results: In WD 2K1C rats treated with the combined central blockade of AT1 and MR receptors, the intake of water reduced during the PR compared to treatment with vehicle + saline (11 ± 2 vs: vehicle + saline: 17.7 ± 1.8 ml/ 2h; $p < 0.05$). In addition, WD 2K1C rats, in the salt appetite test, had the water (0.0 ± 0.0 vs. vehicle + saline: 3.6 ± 1.7 ml/ 2h; $p > 0.05$) and 0.3 M NaCl intake (0.7 ± 0.4 vs. vehicle + saline: 8.9 ± 1.6 ml/ 2h; $p < 0.05$) completely suppressed after the concurrent central blocked of AT1 and MR receptors. The central combined blockade of AT1 and MR receptors produced no change in mean arterial pressure (MAP) throughout the 4 hours of the protocol WD-PR in normohydrated 2K1C rats (ΔMAP/min: 5 ± 1 versus. ΔMAP final: 4 ± 7 mmHg; $p > 0.05$).

Conclusions and Support: The present results suggest that ALDO or ANG II or both are involved in sodium intake in water deprived 2K1C animals. Support: FAPESP, CNPq, CAPES (Financial Code: 001).

ID: 3638

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR EFFECTS OF DEPRESSIVE-LIKE BEHAVIOR INDUCED BY THE EARLY MATERNAL SEPARATION PROTOCOL AND THE EFFECTS OF TREATMENT WITH ESCITALOPRAM IN RATS

Introduction: Depression is a disease that affects a large part of the world's population and drastically interferes with the individual's quality of life. Studies show a connection between depression and cardiovascular disease (CVD) in which depression can increase its incidence. Therefore, the use of antidepressant drugs could be beneficial in depressive patients who present cardiovascular risk, and selective serotonin reuptake inhibitors are the most used in this case. Among them, escitalopram (ESC) stands out for its better effectiveness and safety.

Objective: This study aims to evaluate the cardiovascular response of early maternal separation protocol in rats and the effect of ESC treatment in depressive-like rats.

Methods: This project was approved by CEUA/UEL (203/2015). Two experimental protocols were performed: I - Evaluation of cardiovascular effects caused by early maternal separation protocol (EMS group). II - Evaluation of cardiovascular effects caused by treatment with ESC. Then, depressive-like animals were treated with ESC (5 mg/kg; ESC group) or vehicle. All the animals had catheter implantation in the femoral artery and vein and the cardiovascular parameters were analyzed. Only the results that showed a statistical difference were detailed.

Results: The EMS group showed an increased response to phenylephrine (Curve: Interaction: $p= 0.4087$, $F(10, 165)= 1.044$; Dose: $p= < 0.0001$, $F(10, 165)= 33,35$; Manipulation: $p= < 0.0001$, $F(1, 165)= 21.89$; n= EMS: 9, UH: 8), observed by increase of Emax (EMS= 50.36 ± 2.997 mmHg, n= 9; UH= 39.51 ± 3.328 mmHg, n= 8; $p= 0.0281$; $t= 2.430$) and EC50 (EMS= 0.6203 ± 0.03005 µg/kg, n=97; UH= 0.7320 ± 0.03519 µg/kg, n= 8; $p= 0.0282$; $t= 2.429$) compared to unhandled group (UH). The hemodynamic response to sodium nitroprusside and de others cardiovascular parameters showed no difference. In the depressive-like rats, the ESC treatment decreased intrinsic heart rate (Time: $p= 0.0005$, $F (1, 107) = 12.79$; Treatment: $p= 0.0063$, $F (1, 107) = 7.773$; Interaction: $p= 0.0546$, $F (1, 107) = 3.776$) and increased value of low plateau (P1) of sigmoid curve of baroreflex (CTL= -97.81 ± 8.3 bpm; n=8; ESC= -137.1 ± 12.31 bpm; n= 10; $p= 0.0236$; $t= 2.502$), however, the others parameters of sigmoid curve and cardiovascular parameters were not changed by ESC treatment. In order to evaluate the cardiac autonomic influence in the P1 response, the animals were pretreated with atropine or atenolol before baroreflex evaluation and was observed an increase of parasympathetic modulation on that response (ESC: -144,8 ± 32,05 bpm, n= 10; ESC + ATROP: -61,38 ± 27,59 bpm, n= 4; ESC + ATEN: -187,0 ± 10,94 bpm, n= 4; $p= 0,0008$).

Conclusions and Support: The present work showed that EMS protocol caused change on hemodynamic response of rats and that ESC pretreatment increased the parasympathetic cardiac modulation suggesting that ESC could counteract to CVD effects. This work was supported by CAPES and Fundação Araucária.

ID: 3130

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: 8 WEEKS AEROBIC TRAINING REDUCES THE TRIGLYCERIDEMIA OF DYSLIPIDEMIC MICE BY APOCIII OVEREXPRESSION

Introduction: Transgenic mice for human ApoCIII overexpression become hypertriglyceridemic and with high concentrations of fatty acids in the blood. Such dyslipidemias are capable of making the animal atherosclerotic, obese, among other pathologies related to its metabolism. Physical exercises, as well as running exercises, are a condition of physical stress that can modify the metabolic picture of those who practice it, and can cause positive alterations against several pathologies and dyslipidemias.

Objective: To verify if the aerobic physical exercise, systematized in 8 weeks of training is capable to modify the triglyceridemia of this animal model, dyslipidemic by super-expression of human ApoCIII.

Methods: All procedures described were approved by CIBio and CEUA from Universidade Estadual de Maringá. We used C57Bl/6 mice, males between 12 and 14 months of life. The animals had a capillary blood sample collected before training, in which the group's basal triglyceridemia was analyzed. Later, they underwent a process of adaptation to the mat, one week walking at a constant speed of 16 cm/s. After the adaptation the animals were submitted to an incremental stress test, with heating of five minutes, followed by an addition of 9 cm/s every 3 minutes until the exhaustion of the animal. This test served as the main variable for prescribing the intensity of training applied. Therefore, the animals underwent a protocol of 8 weeks of training, with three sections of 44 minutes per week, in a relative intensity of 60% of the maximum capacity of the animal.

Results: The baseline values of triglyceridemia of the animals had a mean of (571±147 mg/dL), and when the same animals were analyzed after the training the values fell to (362±58 mg/dL), difference whose significance was demonstrated $p^*<0.05$, for the decrease of triglyceride after the training.

Conclusions and Support: We concluded, therefore, that the aerobic training of 8 weeks was able to decrease triglyceridemia in C57Bl/6 dyslipidemic mice by human ApoCIII overexpression.

ID: 3387

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: EXPANDED LITTER SIZE-INDUCED NEONATAL UNDERNUTRITION DOES NOT AFFECT HYPOPHAGIC RESPONSES OF CHOLECYSTOKININ AND LIPOPOLYSACCHARIDE IN MALE ADULT RATS

Introduction: Undernutrition is one of the most prevalent conditions affecting humans in the world and it prevents the normal growth and development of children. Changes in nutritional supply during perinatal period can contribute to development of metabolic disorders in adulthood. Therefore, nutrition can be highlighted as an important stimulus in the context of metabolic programming, as it plays important role in the development of hypothalamic circuits that regulate food intake and energy expenditure. The manipulation of the litter size is one of the methods to neonatally alter nutritional supply in early life, such as expansion of litter sizes, which results in malnutrition. Such nutritional and, consequently, metabolic changes, may challenge some regulatory processes, among them the hypophagic effect of cholecystokinin (CCK) and lipopolysaccharide (LPS). This gut hormone and bacterial endotoxin, respectively, are known to act in the hypothalamus and to stimulate anorexigenic neurons, thus decreasing food intake. However, adult rats subjected to neonatal overnutrition presented reduction of hypothalamic CCK-neurons and increased response to LPS, but there is no evidence, so far, about the anorexigenic effects of these agents in adult rats subjected to neonatal undernutrition.

Objective: To evaluate the effects of CCK and LPS on food intake of male adult Wistar rats from normal (NL) and expanded litters (LL).

Methods: To induce normal- or undernutrition, on day of birth, litter size was adjusted to 10 pups (normal litter - NL) and 16 pups (large litter – LL), respectively. After weaning, NL and LL rats received unrestricted control chow. On postnatal day 60, animals were intraperitoneally treated, after 16 hours fasting, with CCK, LPS or saline. After 15 minutes, animals were refed and food intake was measured after 1, 2 and 24 hours. Only male rats were evaluated in the study. All procedures performed were approved by Ethics Committee for Animal Use of the State University of Londrina (UEL) (Protocol 18310.2019.03).

Results: CCK reduced food intake in NL and LL rats 1 hour after treatment. There were no effects of CCK after 2 and 24 hours, both in NL and LL animals. However, 2 hours after treatment, LL rats, treated with CCK and saline, showed increased food intake compared with their respective NL groups. No differences were observed 24 hours after treatment in CCK protocol. LPS reduced food intake in NL and LL 1, 2 and 24 hours after treatment. In addition, 24 hours after treatment, LL rats treated with saline showed lower food intake than their respective NL group.

Conclusions and Support: Expanded litter size-induced underfeeding does not modify CCK and LPS hypophagic responses. These results suggest that the mechanisms underlying the anorexigenic actions of CCK and LPS were not disrupted by neonatal undernutrition, however further experiments are necessary to confirm this hypothesis. Support: CAPES

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Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: NEONATAL SEROTONIN DEPLETION INCREASE PLAY BEHAVIOR AND ALTER SEROTONIN RECEPTORS EXPRESSION IN ADOLESCENT RATS

Introduction: The serotoninergic system plays an important role in the ontogeny of the mammalian central nervous system, and changes in serotonin production during development may lead to permanent changes in brain cytoarchitecture and function.

Objective: The present study investigated the programming effects induced by neonatal serotonin depletion on behavior and molecular components of the serotoninergic system in adolescent male and female rats.

Methods: Experimental procedures were approved by the Ethics Committee on Animal Use of Universidade Federal de São Paulo (CEUA/UNIFESP), protocol #6751130919 (ID 009317). Between postnatal days 8 and 16, serotonin depletion was achieved by daily subcutaneous administration of para-chlorophenylalanine (pCPA; 100 mg.kg−1), an irreversible inhibitor of the enzyme tryptophan hydroxylase (TPH; responsible for the first step and the rate-limiting of serotonin biosynthesis). At postnatal day 33, offspring were evaluated in the social play behavior test and 48 h after that they were submitted to euthanasia. Relative expression of Tph1 and Tph2, serotonin transporter (Slc6a4) and serotonin receptor Htr1a were determined by qPCR in dorsal raphe nucleus. We also investigated the expression of the serotonin receptors Htr1a and Htr2c in the basolateral amygdala and paraventricular nuclei. Additionally, we assessed the mRNA expression of neuropeptides in the paraventricular nucleus.

Results: Neonatal 5-HT depleted rats performed more of all the play behaviors recorded (pouncing, pinning, wrestling, evasion, following and social exploration) in both male and females. At the gene expression level, mRNA Htr1a of serotonin depleted rats were lower than controls in the dorsal raphe nucleus. In the basolateral amygdala, serotonin depletion decreased Htr1a and increased Htr2c expression. While, in paraventricular nucleus, Htr1a, Htr2c, Oxt, Avp, Crh and Trh were not different in any treatment or sex.

Conclusions and Support: The results indicate that neonatal serotonin depletion has long-term consequences on social play behavior associated with long-lasting molecular changes in the brain serotoninergic receptors in adolescent rats. Also, the consequences of neonatal serotonin depletion are similar in male and female adolescent rats. Support: RR was supported by grant 2016/17968-6, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP). LCR was supported by grant of Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) 308893/2018-2 and 010239/2016-2. ASM and VT were supported by Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) under the program CAPES-Print (Process number 88887.374200/2019-00).

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Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EXPOSURE TO NOVELTY MODULATES RECOGNITION MEMORY BY D1 DOPAMINERGIC RECEPTORS ACTIVATION.

Introduction: The exposure to a novelty facilitates the recognition memory persistence and involves the activation of dopaminergic neurons. However, little is known about the involvement of different dopaminergic receptors.

Objective: To investigate the involvement of D1/D5 dopaminergic receptors on the novelty exposure modulatory effects on object recognition memory.

Methods: The experiments were approved by the Institutional Animal Care and Use Committee (033/2019). Adult Wistar male rats were divided into groups: (i) Control; (ii) SKF38393 (D1/D5 dopaminergic agonist); (iii) Novelty (novel environment exposure); (iv) Novelty + SCH23390 (D1/D5 dopaminergic antagonist); (v) Novelty + Rp-cAMPS (PKA inhibitor; PKA is the second messenger of D1 receptors); (vi) Novelty + Go6976 (PKC inhibitor, PKC is the second messenger of D5 receptors); (vii) Novelty + SCH23390 + Sp-cAMP (PKA stimulator) and (viii) Novelty + SCH23390 + PMA (PKC stimulator). The object recognition (OR) task was used. Immediately after the OR training session, some animals were exposed to novelty (a novel environment) for 5min and/or received CA1 intrahippocampal infusion of vehicle or drug(s), according to the experimental groups. The OR test was performed 24h, 7, 14, and 21 days after training, to evaluate memory consolidation and persistence. The one-sample t-test was used to compare the percentage of the total exploration time spent in each object with a theoretical mean (50%). The differences were considered significant when $P < 0.05$.

Results: In the 24h OR test all animals explored significantly more than 50% of the total exploration time the new object, demonstrating preserved memory. In the memory persistence tests, the control group explored similarly both objects ($P = 0.3485$/7th day), suggesting physiological forgetfulness. The SKF38393 group explored the new object significantly more than the familiar ($P = 0.0446$/21st day), therefore, the pharmacological activation of D1/D5 receptors promoted memory persistence. The animals exposed to novelty showed memory persistence until the 14th day ($P = 0.0001$). Still, we observed that the blocker of D1/D5 receptors (by SCH23390) inhibited the novelty effect, once the Novelty+SCH23390 group explored similarly both objects ($P = 0.0796$/7th day). However, when this same drug was associated with Sp-cAMP, memory persistence is observed until the 14th day ($P = 0.0001$), demonstrating the involvement of D1 receptors in the novelty modulatory effects. The animals of Novelty+Rp-cAMPS group explored similarly both objects ($P = 0.5240$/7th day), demonstrating that the inactivation of D1 second messenger hinders the novelty modulation of memory. Moreover, we demonstrated that the inhibition of D5 second messenger did not affect memory persistence ($P < 0.0001$/14th day). In the same way, novelty exposure associated with D1/D5 blocker and PKC stimulation did not promote memory persistence ($P = 0.9897$/7th day).

Conclusions and Support: Our results demonstrated the involvement of dopaminergic receptor D1 in the modulation of OR memory persistence induced by the novelty. This study was financed in part by the Coordination for the Improvement of Higher Education Personnel - Brazil (CAPES), Brazilian National Council of Research of (CNPq/Brazil) and Research Support Foundation of the State of Rio Grande do Sul (FAPERGS/RS/Brazil).

ID: 3133

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de São Carlos - São Carlos - Sao Paulo - Brasil

Title: EFFECTS OF ATMOSPHERIC PARTICULATE MATTER ON CARDIAC FUNCTION OF NILE TILAPIA, OREOCHROMIS NILOTICUS

Introduction: Introduction: Mining-steel industries located in Metropolitan Region of Vitória, Espírito Santo, emit a smoke with atmospheric particulate matter (APM) called “black powder”. This material consists of a mixture of solid particles and nanoparticles containing several metals and it may reach water bodies and exert toxicity toward non-target species. However, the literature about the toxicity of APM is still scarce, especially for animals. Teleost fish have proved to be good models to evaluate the toxicity and effects of contaminants on animals, since their biochemical responses are similar to those of mammals and of other vertebrates.

Objective: Objectives: The aim of this study was to evaluate the effects of APM sampled from Metropolitan Region of Vitória on myocardial contractility of the freshwater fish Nile tilapia, Oreochromis niloticus. Then, isometric cardiac muscle preparations were used to determine the force-frequency relationship (FFR) after APM exposure.

Methods: Methods: This study was performed under the approval of the Animal Ethics Committee at the Federal University of São Carlos (CEUA/UFSCar, #8105110718). Fish were divided in two experimental groups: control (n = 10) and APM group, fish exposed to 1 g of the APM per liter of water for 96 h (n = 10). Fish of both experimental groups were euthanized, the hearts were carefully excised and placed into an oxygenated bathing medium containing (mM): 100.0 NaCl; 5,0 KCl; 1.2 $MgCl_2$; 1.5 $NaH_2PO_4$; 27.0 $NaHCO_3$; 2.5 $CaCl_2$; 10.0 $C_6H_{12}O_6$. Strips (mean length 1.3 ± 0.25 mm and mean mass 1.4 ± 0.15 mg) were excised from the ventricle and their ends were tied in two metal rings. One ring was connected to an isometric force transducer through a stainless steel wire and other was tied around platinum electrodes connected to a stimulator, which delivered electrical square pulses of 8 ms and a voltage 50% above that eliciting maximal twitch force. These preparations were immersed in bath containing physiological solution kept at 25°C and continuously bubbled with a mixture of 98% $O_2$ and 2% $CO_2$.

Results: Results: Both groups showed a negative FFR, mainly at high frequencies (Ct: 4.46 mN/mm² at 0.2 Hz to 1.39 mN/mm² at 3.2 Hz; APM: 9.47 mN/mm² at 0.2 Hz to 3.44 mN/mm² at 3.2 Hz). In APM-exposed group, the twitch force values were significantly higher (117%, $p<0.05$) compared to control, in all frequencies. High concentrations of metals were detected in water samples from APM group, exceeding the maximum allowed value established by national legislation (CONAMA): Al (640%), Fe (200%), Cu (100%) and Zn (514%).

Conclusions and Support: Conclusions: The increased FFR in response to APM exposure could be attributed to a stress-induced catecholamine release due to high concentrations of toxic metals. Nile tilapia is able to develop adaptive strategies to survive during APM exposure. However, our results were obtained after 96 h exposure and longer exposure periods could exacerbate these responses and lead a negative impact on fish performance. Support: CAPES Scholarship (PPGCAm/UFSCar).

ID: 3389

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: UFSCar - Sao Carlos - Sao Paulo - Brasil

Title: THE ESTIMATION OF THE TIME CONSTANT FOR PRESSURE DECAY IS AFFECTED BY THE CRITICAL CLOSING PRESSURE: A METHODOLOGICAL ANALYSIS

Introduction: The vascular branch of the baroreflex regulates arterial blood pressure through adjustments of the peripheral resistance (R) and arterial compliance (C). The viscoelastic properties of large arteries allow them to act as an energy reservoir during the ventricular ejection phase. And also, as a pumping mechanism when the aortic valve closes during diastole (i.e., the Windkessel effect). The rate of pressure decay after the valve closes is governed by the action of both R and C, and the product from both variables is the time constant of arterial pressure decay ($\tau = R \times C$), which indicates the time required for pressure (P) to fall approximately 63% of the total pressure gradient. For practical purposes of R calculation, it is common to assume that P falls to zero ($R = P / Q$; Q = blood flow). However, when calculation assumes P tends to an asymptote (known as the critical closing pressure - CCP), the gradient P-CCP reduces. Therefore, simple multiplication of R and C may overestimate $\tau$. We addressed that supposed overestimation comparing multiples methods to calculate $\tau$, considering P decays either to zero or CCP.

Objective: We examined how the P-CCP pressure gradient affects $\tau$ calculations and the limitations of different methods to estimate pressure decay in the South American decerebrate rattlesnake, Crotalus durissus.

Methods: The data were collected in previous experimental protocols. Preparations were cannulated through the vertebral artery, and a perivascular flow probe was placed around the left aortic artery, allowing for instantaneous systemic P and Q recordings. We analyzed 50 pressure waves from 8 resting animals at room temperature (~25oC). The first calculation method (W1) fitted the second half of the diastolic pressure wave to a modified version of the two-element Windkessel equation, which considers that P decays towards CCP [P(t) = (P0 – CCP) e-t/τ + CCP; t = time]. The first half was removed to ensure that the pre-dicrotic notch pressure signal was not used. The second calculation (W2) was similar, but we sectioned the first and last quarter of the diastolic pressure wave to remove the pre-dicrotic notch pressure and the effect of later influencing factors. In the third method (RC), τ was estimated as R × C (C = stroke volume/pulse pressure). Finally, we used the CCP value estimated from W1 method as a correction factor to calculate resistance [Rccp = (P – CCP) / Q] and used this new value to estimate τ (RCccp = Rccp × C). The same pressure waves were analyzed in each method. Zero was the imputed final value whenever data did not fit to the Windkessel equation. Mean results were compared using a one-way ANOVA and Tukey test ($P<0.05$).

Results: The four calculation methods resulted in different (mean ± S.D.) values for τ ($F = 4.5$; $P = 0.01$): W1 = 1.33 ± 0.47 s; W2 = 0.96 ± 1.15 s; RC = 2.11 ± 0.98 s; and, RCccp = 0.96 ± 0.63 s. RC calculation resulted in higher τ values, whereas W1, W2, and RCccp resulted in a similar estimation. However, RC calculation was the only method able to process all the waves.

Conclusions and Support: The assumption that pressure decays to zero tends to overestimate τ. That was corroborated by similar values from W1, W2, and the corrected RCccp. Despite the need to correct decay magnitude, the RC model was more versatile due to the diversity of pressure waves that this method was able to analyze. CNPq #168061/2017-1; FAPESP #2018/05035-0; CEUA-UFSCar. #4568110917

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Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: STRENGTH TRAINING WITH RESTRICTED BLOOD FLOW DECREASES OXIDATIVE STRESS IN RATS

Introduction: Practice of physical exercise is one of the main lifestyle changes that can significantly reduce cardiovascular events, and strength training (TF), performed alone or combined with aerobic training are widely used, even in populations already affected by cardiovascular and/or metabolic diseases. When performed at high intensity (greater than 70% of 1 maximum voluntary contraction -MVC-), it produces muscular, morphological and functional adaptations as a result of metabolic stress. However, training sessions with the use of high intensities are impeditive for certain populations. As an alternative, studies have indicated that low inteisity (20 - 50% of 1MVC) strength training with blood flow restriction (TFRF) may produce beneficial adaptations, similar to strength training with intensity equal to or greater than 70% 1MVC . However, until now, the vast majority of studies have been dedicated to the effects of TFRF related to muscle adaptations and, to date, there are few studies in which the effects of TFRF on endothelial function have been investigated.

Objective: In this sense, the objective of the present study was to evaluate the effects of a low intensity strength training program (50% of 1MVC), on endothelial function of rats subjected to blood flow restriction. All procedures were reviewed and approved by the Ethics Committee on the Use of Animals in Research (protocol CEUA / EEFERP number 2016.5.80.90.4), in accordance with the "Principles of care for laboratory animals" (NIH publication No. 86- 23, revised in 1985) and the national law (CONCEA publication No. 11,794, 2008).

Methods: 52 Wistar Hannover rats aging 8 weeks were divided in 4 groups: sedentary sham (SD, n= 16), sedentary with blood flow restriction (SDRF, n= 8)), trained sham (TF, n= 8), and trained with blood flow restriction (TFRF, n= 8). Training protocol consisted of four weeks of strength training with 50% of 1MVC. Training was initiated 14 days after arteriovenous restriction surgery. Body composition (BC) and blood pressure (BP) were analyzed. The maximal response (Emax) was obtained from concentration-response curves to acetylcholine (ACh) and phenylephrine (PHE) in the abdominal aorta, as well as production of nitric oxide (NO) and reactive oxygen species (ROS). Blood analyzes of the antioxidant profile (SOD), nitrite/nitrate and tumor necrosis factor alpha (TNF-α) were also investigated.

Results: TF prevented final weight gain. BP and vessel reactivity weren´t altered, as well as NO concentration. However, the TFRF group showed a decrease in ROS, but also increased blood TNF- α concentration and no changes in SOD and nitrite/nitrate.

Conclusions and Support: In conclusion, these results are promising and suggest that TFRF should also be considered as an alternative clinical intervention to decrease oxidative stress and, therefore, endothelial health, but should be prescribed with caution. Financial support: CAPES (finance code 001) and FAPESP (#2017/13348-6).

ID: 3390

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: UFSCar - Sao Carlos - Sao Paulo - Brasil

Title: VASCULAR MODULATION AFTER HEMODYNAMIC DISTURBANCES IN DECEREBRATE RATTLESNAKES

Introduction: The vascular branch of the baroreflex is usually neglected in studies regarding blood pressure modulation. Despite that, it has an enormous impact on pressure adjustments. Diverse vascular characteristics, such as peripheral resistance (R), arterial compliance (C), and the elastic components present in the structure of the large arteries, are responsible for the arterial blood pressure decay during ventricular diastole. Orthostasis may impact homeostasis in terrestrial vertebrates due to the gravity effect over hemodynamics. Several cardiovascular mechanisms were described to compensate for it. Apparently, the relevance of each possible compensation is a species-specific trait. It relates to the use of the environment and the range of behavioral patterns. The effect of postural alterations can be especially relevant for cylindrically shaped animals like snakes. Therefore, the compensatory adjustments performed by the vascular system might be especially prominent in that vertebrate group. We investigated the action of the vascular branch of the baroreflex to compensate for the hemodynamic alterations caused by postural shifts.

Objective: We have addressed the relevance of the vascular branch of the baroreflex to compensate for the hemodynamic alterations caused by typical postural positioning in South American rattlesnakes, Crotalus durissus.

Methods: The present data were collected in previous experimental protocols with the use of decerebrate rattlesnake preparations (n=3, partial data). For the hemodynamic recordings, we performed occlusive cannulations in both the vertebral artery and in a branch of the pulmonary artery. That allowed for pressure recording from systemic and pulmonary circuits. Besides, perivascular flow probes were placed around the pulmonary artery and left aortic arch, allowing for blood flow recordings. For the protocol, the preparation was decerebrated, instrumented, and recovered from anesthesia. The cardiovascular variables were stable at 25oC before the experimental protocol commenced. We used simple mechanic maneuvers to trigger hemodynamic alterations due to gravity. We lifted its tail (⅓ - caudal part of the body - TL) for 3 min. The tail was released, and recordings followed until cardiovascular stability. Subsequently, we raised its head (with the rostral part of the body - HL) for 3 min. We analyzed the vascular response accessing TAU by the use of the RC-method ($\tau = R \times C$). We estimated C as the ratio between stroke volume/pulse pressure. For calculations, we used 300 cardiac cycles before, during, and also after each maneuver.

Results: The maneuvers triggered alterations in both systemic and pulmonary circuits. Both TL and HL responses peaked after about 20s. TL increased C (mL x mmHg-1) in the systemic (from 0.0034 to 0.0039) and pulmonary (from 0.0073 to 0.0086) circulation. While $\tau$ was increased to 1.5s and 1s in the systemic and pulmonary circulation, respectively. In contrast, HL decreased C in the systemic (from 0.0034 to 0.0025) and pulmonary circuits (from 0.0073 to 0.0061). $\tau$ was not significant altered in the systemic circulation but increase to 0.5s in the pulmonary circuit.

Conclusions and Support: These preliminary results indicate that an active and relatively fast vascular response was present. Furthermore, it is possible that the vascular adjustments in the pulmonary circuit play a significant role in the hemodynamic adjustments in animals with vascular shunts. CNPq #168061/2017-1; FAPESP #2018/05035-0 CEUA-UFSCar. # 4568110917

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Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de São Carlos - São Carlos - Sao Paulo - Brasil

Title: LONG-TERM VIABILITY OF AUTONOMOUS MODULATION IN DECEREBRATE RATTLESNAKE

Introduction: Despite the high interest in reptile cardiovascular system, the experimental investigations of several questions remain justifiably limited by the obvious and indispensable ethic aspects regarding in vivo animal experimentation and the development of instrumentation techniques. As a response, some cardiovascular mechanisms had their functional description based on anesthetized animals. Decerebrate rattlesnake preparation is a prospective experimental model to study squamate cardiovascular physiology, once the decerebration process was developed to inactivate thalamus and cortical structures including the areas responsible for processing pain and stress while maintaining the integrity of autonomic structures that allows for cardiovascular reflex mechanisms.

Objective: We aimed to assay the long-lasting viability and how decerebration process affects the dynamic of post-mortem preparation for in situ experiments in South American rattlesnakes (Crotalus durissus) analyzing: the presence and alterations of autonomic modulation of heart rate variability (HRV), the maintenance of resting cardiovascular parameters and the presence and magnitude of baroreflex.

Methods: On the first surgery, snakes (863.0±146.3g, n=10) were decerebrated by cauterization, and electrodes were implanted to ECG records for HRV analyses. After 15 days of recovery, a second surgery was made to record cardiovascular parameters such as: (heart rate fH, systemic mean arterial pressure MAPsys, pulmonary mean arterial pressure MAPpul, systemic blood flow $\dot{Q}$sys, pulmonary blood flow $\dot{Q}$pul, cardiac output CO, total stroke volume Vstot, systemic conductance Gsys, pulmonary conductance Gpul, and shunt direction $\dot{Q}$pul·$\dot{Q}$sys-1). Vertebral artery and a branch of the pulmonary artery were occlusive cannulated and flow probes were placed around the left aortic arch and pulmonary artery for pressure and blood flow recordings, respectively. All the cardiovascular parameters at rest were compared with both, previously reported data at the same preparation - 24h after decerebration and previously published cardiovascular data reporting non-anesthetized snakes. The sequence method was used to analyze the baroreflex. CEUA #4568110917.

Results: Mean fH decreased during first 24h after surgery and stabilized over the remaining 15 days. However, cardiac modulation denoted by PSD was low or absent and increased on the 7th day remaining higher and stable between 1.0·105 and 3.0·105 ms2. Mean values of all cardiovascular parameters were MAPsys (kPa) 5.02 ± 0.39; $\dot{Q}$sys (ml·min-1·kg-1) 18.82 ± 2.96; Gsys (ml·min-1·kg-1·kPa-1) 5.46 ± 0.99; MAPpul (kPa) 2.73 ± 0.29; $\dot{Q}$pul (ml·min-1·kg-1) 17.04 ± 2.99; Gpul (ml·min-1·kg-1·kPa-1) 6.69 ± 1.33; Vstot (ml·kg-1) 1.00 ± 0.14; fH (beats·min-1) 35.1 ± 2.02; CO (ml·min-1·kg-1) 34.23 ± 5.90; $\dot{Q}$pul ·$\dot{Q}$sys-1 1.16 ± 0.28 and presented values similar to the 24h preparation and literature data. The preparation presented baroreflex sequences and the adjustment remained functional and equivalent to the intact resting snake.

Conclusions and Support: The preparation is able to make precise adjustments to the cardiovascular system, being useful for cardiovascular studies in squamate reptiles since it makes it possible to simultaneously recording multiple variables allowing proper parameter correlation, reducing the number of animals used, it also allows escaping from anesthetic bias effect, and allows investigation of processes inaccessible on in vivo preparations. CNPq 168061/2017-1; FAPESP 2018/05035-0.

ID: 2880

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: ASSOCIATION OF BODY MASS INDEX WITH THE CONCENTRATIONS OF TAMOXIFEN AND ITS METABOLITES IN PATIENTS WITH BREAST CANCER

Introduction: Tamoxifen is a nonsteroidal agent used in adjuvant hormonal therapy of primary breast cancer. Overall, patients under hormonal therapy with the drug has an increased of weight, which can modify the blood levels of tamoxifen and its metabolites.

Objective: The aim of the present study was to associate the body mass index with the plasma concentrations of tamoxifen, endoxifen and 4-OH tamoxifen.

Methods: An observational study of cases was performed in patients with breast cancer using tamoxifen. The drug and its metabolites were determined by reversed-phase high-performance liquid chromatography. The body mass index was based on the height and weight of the patients. Kruskal-Wallis was used to compare the levels of the drug and its metabolites among groups. A total of 20 female patients were admitted to the study. The median age was 43 years (range; 32 to 50 years). A total of eight was in the pre-menopausal phase. All patients are under radiotherapy. The median time of treatment with tamoxifen was 25 months (range; 13 to 50 months). All the participants gave the written and informed consent term and all the procedures were evaluated and approved by the Ethical Committee in Research with Human of the Health Science Institute of the Federal University of Pará (report 3.015.710) and of the Ophyr Loyola Hospital (report 3.119.456).

Results: The median body mass index was 36.43 (range; 21.2 to 35.25). A total of 20% of patients were eutrophic, 65% overweight, and 15% obese ($p<0.0001$). The median plasma level of tamoxifen was 62 ng/mL (range; 38-140 ng/mL).The metabolite 4-OH-tamoxifen presented a median value of 1.04 ng/mL (range; 0.8 to 2.67 ng/mL) and endoxifen has a medium plasma concentration of 8.79 ng/mL (range; 6.5 to 16.8 ng/mL). The plasma concentrations of tamoxifen were similar among normal weight, overweight and obese patients ($p=0.4435$). A similar result was found for endoxifen ($p=0.7913$) and for 4-OH tamoxifen ($p=0.9789$).

Conclusions and Support: These results suggest the lack of influence of body mass index in the plasma concentrations of tamoxifen and its metabolites. Support: Federal University of Pará

ID: 3392

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: HIGH-INTENSITY INTERVAL TRAINING IS MORE EFFECTIVE THAN LOW INTENSITY TRAINING TO REDUCE NF-κB EXPRESSION AND INFILTRATION OF IMMUNE CELLS IN RATS WITH CISPLATIN-INDUCED NEPHROTOXICITY

Introduction: Inflammation contributes to acute renal injury (ARI) induced by the antineoplastic cisplatin (CP). The activation of the nuclear transcription factor kappa B (NF-κB) by CP is associated with the production of several pro-inflammatory mediators, which act together with infiltrated immune cells, amplifying the inflammatory response and intensifying tissue injuries. Aerobic exercise has been reported to be renoprotective, however the intensity more effective to provide renoprotection is still unclear.

Objective: Thus, the aim of this study is to compare the impact of high intensity interval training (HIIT) with continuous low intensity training (LIT) on the expression of NF-κB and infiltration of macrophages and lymphocytes in the kidneys of wistar female rats with CP-

induced AKI.

Methods: For this, 28 rats were randomly divided into 4 groups (n=7): C +S, sedentary control; CP+S, treated with CP and sedentary; CP+LIT, treated with CP and submitted to a LIT (45 to 55% of the maximum capacity); CP+HIIT, treated with CP and submitted to HIIT (85% of the maximum capacity). The training protocols consisted of running on a motorized treadmill, 5 days / week, for a period of 8 weeks. The CP+S, CP+LIT and CP+HIIT groups received a single dose of CP (5 mg/kg, i.p.), and 07 days later they were euthanized by decapitation. The kidney tissue was fixed, paraffinized, cut in 4 μm sections and submitted to immunohistochemical for evaluating the expression of NF-κB, ED-1 and CD43 (macrophage and lymphocyte marker, respectively). The quantification of the immunoreactivity for NF-κB was performed in 20 fields (original magnification x200) of the renal outer medulla by means of the Image-J software, whose result was expressed in percentage, whereas the number of ED-1 and CD43 positive cells was quantified in 30 microscopic fields (original magnification x400) of the tubulointerstitial compartment. This study was approved by the Ethics Committee in Animal Experimentation of the UFBA/IMS (protocol 056.2018). Data are presented as mean±SEM. Statistical differences were defined when $p<0.05$.

Results: The results demonstrate that all groups treated with CP showed an increase in NF-κB expression compared to C+S (2.5±0.3) ($p<0.05$). Although both training protocols were able to mitigate the increase in this expression in CP+LIT (8.3±1.04) and CP+HIIT (5.7±0.69) compared to the group CP+S (14.6±1.15) ($p<0.001$), HIIT demonstrated a greater regulation of this factor in relation to LIT ($p<0.001$). Concerning the infiltration of macrophages, there was an increase in these cells in all groups treated with CP compared to the control (1.76±0.48) ($p<0.05$), however, only CP+HIIT (9.43±0.6) showed an attenuation of this effect in relation to CP+S (20.9±3.76) ($p<0.05$). Regarding lymphocytes, CP+S (25.48±1.12) and CP+LIT (14.91±2.18) showed increased infiltration of these cells compared to control (7.56±0.64) ($p<0.01$), and although the LIT was able to reduce this effect in relation to the CP+S group ($p<0.001$), this effect was more pronounced in the CP+HIIT group (7.78±0.36) compared to CP+TL ($p<0.001$).

Conclusions and Support: In conclusion, although both training protocols brought renoprotective actions, these benefits were more pronounced in HIIT, suggesting that this type of training is more effective in preventing CP-induced AKI.

ID: 3138

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF SUSTAINED HYPOXIA ON THE CARDIOVASCULAR AND RESPIRATORY FUNCTIONS OF DIFFERENT RAT STRAINS

Introduction: Short-term sustained hypoxia (SH) produces active expiration, increased late-expiratory (late-E) sympathetic activity, hypertension, augmented ventilation, and amplified sympathetic and abdominal expiratory responses to chemoreflex activation in rats from the Wistar-Ribeirão Preto (WRP) strain. However, evidence suggests that different rat strains display distinct response patterns to hypoxia.

Objective: Herein, we tested the hypothesis the SH exposure elicits distinct responsiveness and patterns of cardiovascular and respiratory responses in different rat strains.

Methods: Sprague Dawley (SD) and Wistar Hannover (WH) rats (~80 g) were exposed to SH ($FiO2 = 0.1$) for 24 h and arterial pressure, sympathetic activity, and respiratory pattern were evaluated. Results were compared to previously obtained data using the WRP strain. All procedures were approved by the institutional Ethics Committee on Animal Use (CEUA, 51/2018).

Results: SD rats presented increased mean arterial pressure (92 ± 5 vs. 85 ± 4 mmHg), respiratory rate (200 ± 11 vs. 163 ± 21 breaths min-1) and tidal volume (12.38 ± 1.32 vs. 8.98 ± 1.58 ml kg-1) compared with control rats. SH also elicited augmented late-E expiratory motor output (19.20 ± 8.11 vs. 1.66 ± 1.86 %) and increased sympathetic outflow (16.98 ± 5.83 vs. 10.07 ± 3.1 %) due to post-inspiratory (41.32 ± 5.36 vs. 26.73 ± 8.17 %) and late-E (37.79 ± 10.5 vs. 12.75 ± 4.73 %) sympathetic overactivity in this rat strain in relation to controls. WH rats presented reduced changes, suggesting lower responsiveness of this strain to this SH protocol. The magnitudes of changes in sympathetic (75.68 ± 16.56 vs. 182.6 ± 76.58 %) and abdominal (137.5 ± 31.31 vs. 256 ± 88.89 %) expiratory motor activities to chemoreflex activation in SD rats were reduced by SH when compared to control. Pressor responses to chemoreflex activation were shown to be blunted in SD (44 ± 12 vs. 60 ± 9 mmHg) and WH rats (41 ± 8 vs. 56 ± 10 mmHg) after SH when compared to control.

Conclusions and Support: SD, WH and WRP rats exhibit different patterns of alterations in baseline cardiovascular, autonomic and respiratory profiles and in chemoreflex responses after SH. It is important to note that WH rats exhibited lower responsiveness to SH. Our results indicate that studies evaluating the impact of SH on the cardiovascular and respiratory functions require careful attention to the responsiveness of different rat strains to this experimental protocol of hypoxia. Support: FAPESP, CNPq, CAPES

ID: 3394

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Oswaldo Cruz Foundation - RIO DE JANEIRO - Rio de Janeiro - Brasil

Title: CHOLESTEROL EXACERBATES MICROCIRCULATORY DISTURBANCES IN A DIET INDUCED ANIMAL MODEL OF NON-ALCOHOLIC FATTY LIVER DISEASE

Introduction: Nonalcoholic fatty liver disease (NAFLD) is the most prevalent liver disease worldwide. Among 25% of NAFLD patients develop nonalcoholic steatohepatitis (NASH), the inflammatory form of the disease that leads to progressive liver damage, cirrhosis, and hepatocellular carcinoma, therefore, there is a significant need to better understand the pathophysiological mechanisms in the NAFLD progression.

Objective: The aim of this study was to evaluate the effects of cholesterol on NAFLD complications and progression.

Methods: C57BL6 mice were fed a high-fat and high-carbohydrate diet (HFHC), during 31 weeks. The CTL group received normocaloric diet during the same period. During the weeks 31 to 39, a subgroup of animals on HFCH diet received 2% cholesterol (HFHC+Col), while the other groups remained in the same diet. Leukocyte recruitment was assessed by intravital microscopy. Laser Speckle Contrast Imaging flowmetry was used to assess in vivo microcirculatory liver perfusion and endothelial function.

Results: At 31 weeks, the HFHC group showed hepatomegaly, cardiomegaly, increase in body weight, visceral, subcutaneous and brown fat content, fasting blood glucose levels and impairment of glucose metabolism when compared to the CTL group. The HFHC group had a decreased number of total blood leukocytes, with increase in monocyte and neutrophil counts. HFHC group showed a significant decrease in the hepatic, renal and visceral adipose tissue microvascular blood flow. In addition, HFHC group showed endothelial dysfunction, marked by the deficient microcirculation vasodilatory responses to acetylcholine in the adipose tissue. HCHF had increased endothelial-leukocyte interactions both in the hepatic and adipose microvascular bed. At 39 weeks, HFHC and HFHC+Col group had increased body weight, visceral, subcutaneous and brown fat deposits, when compared to the control group. HFHC+Col group had liver enlargement and pale yellow discoloring, indicating hepatic steatosis. The leukocyte count in peripheral blood of HFHC+Col revealed an increase in the number of total leukocytes, including lymphocytes, monocytes and neutrophils when compared to the HFHC group. Microcirculatory analysis showed that the HFHC+Col and HFHC group had similar impairment of the hepatic basal microvascular blood flow. HFHC and HFHC+Col groups demonstrate a similar reduction in the basal microvascular perfusion of the adipose tissue, however; the HFHC+Col group had higher levels of endothelial dysfunction. Cholesterol supplementation also led to superior leukocyte recruitment in the microcirculation of liver and adipose tissue when compared to HFHC group.

Conclusions and Support: Based on these results, we conclude that the addition of cholesterol to the diet can lead to an aggravation of NAFLD, seen by the exacerbation of hepatomegaly and microcirculatory disturbances, i.e. leukocyte recruitment, tissue perfusion and endothelial dysfunction. Supported by CNPQ, FAPERJ and FIOCRUZ. Experimental procedures were approved by the Oswaldo Cruz Foundation Animal Welfare Committee (CEUA license L-012/2018 A1).

ID: 3141

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: UNIFESP - São Paulo - Sao Paulo - Brasil

Title: GINKGO BILOBA EXTRACT INDUCED THE IMPROVEMENT OF ENDOGENOUS ANTIOXIDANT DEFENSES AND ENHANCED THE 5-HT1A AND 5-HT1B SEROTONIN RECEPTORS IN HIPPOCAMPUS OF OVARIECTOMIZED RATS

Introduction: Ginkgo biloba extract (GbE) is recognized by its beneficial effects such as antioxidant, anti-inflammatory and antiapoptotic activities, reactive oxygen species scavenger, and improvement of the endogenous antioxidant defense system. Moreover, previous studies from our group demonstrated that GbE exerts important effects on serotonergic system activity. In ovariectomized rats, a prolonged treatment (14 days) with GbE reduced the hypothalamic serotonin transporter protein levels and restored serotonin levels in the lateral hypothalamus. Furthermore, the mRNA levels of 5-HT2C serotonin receptor were enhanced after a single acute dose (500mg*kg-1) of GbE in eutrophic rats. Thus, these findings suggest that GbE may promote a modulatory action on serotonergic signaling in the central nervous system (CNS). Additionally, it is possible that GbE might promote a neuroprotective effect, minimizing the damages generated by oxidative stress.

Objective: This study aimed to investigate the GbE effects on protein expression of serotonin receptors and on the activity of endogenous antioxidant enzymes in the hippocampus of ovariectomized rats.

Methods: The ovaries of 2-month-old female Wistar rats were surgically removed (OVX) or not (SHAM), and then, sixty days after surgery, OVX rats were daily gavaged with 500mg*kg-1 of GbE (OVX+GbE) while SHAM and OVX groups received saline 0.9% (vehicle) for 14 days. Concluded the treatment period, rats were euthanized, and hippocampi were collected. SOD, Catalase and GPx activity were mensured by colorimetric assays. 5-HT1A and 5-HT1B protein levels were evaluated by Western Blotting. The Ethics Committee on Animal Research of Federal University of São Paulo (protocol number 7159090317) approved all procedures.

Results: An increased activity of Superoxide dismutase (SOD) was observed in OVX rats in comparison to SHAM rats ($p=0.046$), while GbE restored SOD activity to similar levels to SHAM rats. Glutathione peroxidase activity was also improved by GbE in comparison to SHAM rats ($p=0.036$). No differences were observed in Catalase activity ($p=0.087$). Both 5-HT1A ($p<0.001$) and 5-HT1B ($p=0.044$) protein levels were reduced in OVX rats in comparison to SHAM rats while 5-HT1A was significantly increased in OVX+GbE rats in relation to OVX rats.

Conclusions and Support: In summary, these findings revealed that GbE promoted an improvement in the impaired endogenous antioxidant system suggesting a protective effect, and an enhancement in response to oxidative stress, as well as reestablished the protein levels of

the serotonin receptors analyzed. Therefore, GbE presents a therapeutic potential to improve menopausal-related hippocampal disorders and might be particularly interesting as an alternative approach for those women that cannot use hormone replacement therapy. Support: Fundação de Amparo à Pesquisa do Estado de São Paulo - FAPESP[2014/18929-9] and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - CAPES [Finance code 001].

ID: 3142

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF CANABINOID AGONIST ON Ca2+-HANDLING PROTEINS IN THE HEART OF FISH, Brycon amazonicus

Introduction: The endocannabinoid system (ECS) is a complex lipid signaling system composed of the two known subtypes of receptors, cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2), which are widely distributed in the central nervous system and peripheral nervous system, including cardiac tissue. The endocannabinoid-receptor interaction generates responses that directly or indirectly affect physiological functions. During the last decades, the remarkable increase in the understanding of the molecular basis of cannabinoid activity has encouraged many pharmaceutical companies to develop more potent synthetic cannabinoid analogues and antagonists, leading to an explosion of basic research and clinical trials. However, the mechanisms of the cardiovascular effects of cannabinoids is not yet fully understood. The distribution of receptors, predominantly CB1 in this tissue, together with the results obtained in studies with rats, indicate that there is an important role to be explored. A progress in the understanding of the effects of cannabinoids on cardiac function can lead to the consideration of cannabinoids as possible therapeutic agents in cardiovascular diseases.

Objective: The study aimed to evaluate the effects of the activation of CB1 and CB2 receptors on expression of key proteins involved in regulating Ca2+ signaling in the heart of Brycon amazonicus, a freshwater Neotropical fish, popularly known as matrinxã.

Methods: This study was performed under the approval of the Animal Ethics Committee at the Federal University of São Carlos (CEUA – #4997170718). Fish were divided in two experimental groups: control (Ct), fish treated with vehicle (5% DMSO in sterile saline with a drop of Tween 80, i.p.) and cannabinoid group (WIN), fish treated with a single dose (1 mg.kg-1, i.p.) of the WIN55,212-2, a potent synthetic agonist of cannabinoid receptors type 1 (CB1) and cannabinoid receptor type 2 (CB2). After 24 hours, the hearts of 6 animals from each group were collected and, after extraction of total proteins, the analysis of the expression of the Sarcoplasmic Reticulum Ca2+ -ATPase (SERCA), the sodium/calcium exchangers (NCX) and phospholambam (PLB) was performed using Western Blotting.

Results: The WIN treatment caused significant ($P< 0.05$) increases in both PLB (168% - Ct: $0.82 \pm 0.02$; WIN: $2.20 \pm 0.06$, mean ± SEM in arbitrary units) and NCX expression (139% - Ct: $0.73 \pm 0.02$; WIN: $1.75 \pm 0.02$, mean ± SEM in arbitrary units). There was none significant difference ($P> 0.05$) in the expression of SERCA protein. Furthermore, WIN group showed a variation of the expression of the two NCX isoforms.

Conclusions and Support: The results obtained in this work allow us to conclude that the activation of CB1 and CB2 receptors can play an important role in heart function, since it has been shown to up regulated the expression of proteins that play a key role in the cardiac excitation-contraction coupling. CNPq Proc. 404688/2018-7

ID: 3400

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: UNICAMP - Campinas - Sao Paulo - Brasil

Title: EFFECTS OF PROTEIN RESTRICTION ON GENERAL NUTRITIONAL PARAMETERS AND PANCREAS AND GUT WEIGHTS IN MALE MICE

Introduction: The excess and the lack of nutrients can trigger morphofunctional damages in the gastrointestinal system. These changes have been correlated with the development of diseases such as obesity and type 2 diabetes mellitus. It has been reported that protein restriction alters endocrine pancreatic morphofunction and insulin action. However, there is little information regarding protein undernutrition effects on intestine morphofunction, and whether the gut in undernutritoncontributes to the impairments in glucose homeostasis observed in malnourished subjects.

Objective: To evaluate glucose tolerance, insulin sensitivity, pancreas and gut weight of protein-restricted mice.

Methods: C57Bl/6 male mice from 30 to 120 days-old were randomly distributed into: control (CT) group, which fed ona diet containing 14% protein; or protein-restricted group (RP), which fed on a diet containing 6% protein. Data were analyzed by Shapiro Wilk, following comparisons with Student t or Mann-Whitney U test ($P <0.05$; CEUA UNICAMP approval nº 5564-1/2020).

Results: RP mice displayed hyperphagia ($364.2 \pm 2.1$ g.weeks-1) and higher kilocalories intake ($96.5 \pm 0.5$ kcal/week) during the experimental period, when compared to CT ($298.8 \pm 7.1$ g.weeks-1 and $79.3 \pm 1.9$ kcal/week, respectively). However, RP mice exhibited

lower body weight (BW; 24.6 ± 0.6 g), feed efficiency (29.3 ± 0.3%), Lee Index (304.6) and mesenteric fat pads (6.9 ± 0.9 mg/g BW)at the end of experimental period, when compared to CT (27.2 ± 0.5 g, 41.4 ± 0.2% and 312.6 ± 1.5, 12.0 ± 2.0 mg/g BW; respectively). In addition, RP mice displayed higher total cholesterol levels (92.1 ± 5.2 mg/dL), without modifications in triglyceridemia (55.91 ± 2.5 mg/dL) or glycemia (70.3 ± 2.1 mg/dL), than CT mice (66.2 ± 7.5, 55.2 ± 4.0 and 72.4 ± 3.0 mg/dL, respectively). Protein restriction significantly increased in 30% the insulin sensitivity (5.7 ± 0.2%min) in RP group, when compared to CT (4.4 ± 0.2%min). Furthermore, RP mice exhibited reductions of 22%, 23.3%, 12.1% and 16.5% in pancreas (8.0 ± 0.3 mg/g BW), cecum (12.3 ± 1.3 mg/g BW), small (45.8 ± 3.0 mg/g BW) and large intestines (26.8 ± 2.2 mg/g BW) weights, respectively, when compared to CT (10.4 ± 0.7 16.0 ± 0.5; 52.1 ± 1.8 and 32.1 ± 0.8 mg/g BW, respectively). But, only the length of the small intestine (31.5 ± 0.3 cm) was reduced in RP mice, when compared to CT (35.3 ± 1.7 cm).

Conclusions and Support: Protein restriction induced hypotrophy both in pancreas and gut.Despite diminished pancreas weight, RP mice displayed normoglycemia due to augmented insulin sensitivity. Further investigations are necessary to clarify the correlation between intestine morphofunction and the impaired glucose homeostasis in protein restriction. Support: FAPESP.

ID: 3401

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: PREVENTIVE AND THERAPEUTIC EFFECTS OF EXERCISE ON MUSCLE REDOX PARAMETERS AND MITOCHONDRIAL FUNCTION IN AGING AND OBESE MALE RATS

Introduction: The practice of physical exercise provides beneficial changes to the general metabolism, including regulation of the redox balance. However, no studies were found that evaluated the preventive and therapeutic effects of physical training on muscle changes caused by the association between aging and obesity.

Objective: To evaluate the preventive and therapeutic effects of physical training on redox balance and mitochondrial function in the gastrocnemius of aging rats in a in a model of diet-induced obesity.

Methods: 32 male Wistar rats (initial age=4 months, final age=14 months) were randomly distributed into four aged groups: aged sedentary (ASed), aged sedentary fed a high-fat diet (ASed+HFD), aged therapeutically trained and fed a high-fat diet (ATT+HFD) and aged preventively trained and fed a high-fat diet (APT+HFD). The training was performed on a treadmill, moderate intensity, alternate days for 60 minutes. All animals were euthanized 24 hours after the last training session. The adiposity index, gastrocnemius weight, levels of thiobarbituric acid reactive substances (TBARS), carbonylated proteins, and the activity of catalase, glutathione peroxidase (GPx) and citrate synthase (CS) were evaluated. This study was approved by the IMS-UFBA Ethics Committee on the Use of Animals (protocol: 011/2014). Data were expressed as mean ± standard deviation and analyzed by one-way ANOVA and Tukey's post-test.

Results: The high-fat diet increased the adiposity index in the ASed+HFD compared to ASed (8.85±1.62 vs 3.72±1.20, $p<0.05$), and reduced the average weight of the gastrocnemius muscle (0.51±0.04 vs 0.57±0.04, $p<0.05$). ASed+HFD showed an increase in the muscular levels of TBARS (1.56±0.14 vs 0.54±0.06, $p<0.05$) and carbonylated proteins (5.50±0.37 vs 3.88±0.63, $p<0.05$), in addition to higher activity of catalase (0.44±0.03 vs 0.25±0.03, p<0. 5), GPx (0.026±0.001 vs 0.022±0.001, $p<0.05$), and reduced activity of the CS in relation to the ASed (1.42±0.32 vs 2.30±0.20, $p<0.05$). Only preventive training reduced adiposity (APT+HFD: 5.09±2.09 vs ASed+HFD:8.85±1.62, $p<0.05$) and increased muscle weight (0.62±0.03 vs 0.51±0.04, 0.05). Both trained groups showed a reduction of TBARS (APT+HFD: 0.76±0.10 / ATT+HFD: 0.81±0.13 vs ASed+HFD: 1.56±0.14, $p<0.05$) and carbonylated proteins (APT+HFD: 3.74±0.69 / ATT+HFD: 4.12±0.63 vs ASed+HFD: 5.50±0.37, $p<0.05$), and increase in the activity of the enzymes GPx (APT+HFD: 0.033±0.001 / ATT+HFD: 0.028±0.001 vs ASed+HFD: 0.026±0.001, $p<0.05$) and CS (APT+HFD: 4.51±0.25 / ATT+HFD: 2.64±0.12 vs ASed+HFD: 1.42±0.32, $p<0.05$). Additionally, APT+HFD showed the highest enzyme activity compared to the other groups ($p <0.05$). Only APT+HFD showed increased activity of the catalase enzyme compared to ASed+HFD (0.59±0.07 vs 0.44±0.03, $p<0.05$).

Conclusions and Support: Conclusions: High-fat diet led to compromised parameters of body composition, redox balance, and mitochondrial function. On the other hand, preventive exercise was able to protect against changes in adiposity and muscle weight. Both trainings were effective in protecting against the effects of obesity on the parameters of redox balance and mitochondrial function in aged animals, however the best results were associated with preventive training. Support: This work was supported by the National Counsel of Technological and Scientific Development [481268/2013- 8]; and the Foundation of Support for Research of the State of Bahia [RED009/2014].

ID: 3402

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR AND OXIDATIVE PROFILE OF THE ROSTRAL VENTROLATERAL MEDULLA IN OBESE RATS: EFFECTS OF TREATMENT WITH VITAMIN C

Introduction: The rostral ventrolateral medulla (RVLM) is the main sympathetic output of the central nervous system for control of blood pressure. Studies show that reactive oxygen species (ROS) can contribute to the increase of arterial pressure and lead to hypertension. Obese animals present an increased oxidative profile in organs of the cardiovascular system.

Objective: Considering that ROS contribute to the increase in sympathetic tone in RVLM and that obese animals present greater oxidative stress, our aim was to assess neurotransmission by glutamate (L-glu) and vitamin C (Vit C) in RVLM of awake obese rats, to verify the oxidative balance, and the effects of chronic treatment with vitamin C.

Methods: Wistar rats received 4 mg/g body weight of monosodium glutamate or equimolar saline within the first 5 days of life. The chronic treatment was distributed into 4 groups: control (CTR) and obese (MSG) group treated with water and CTR and MSG treated with Vit C (50 mg / kg) orally for 21 consecutive days from the 69th day until 90th day of life. The RVLM area was collected from punch technique and was designate to tests ABTS, NBT, FRAP and TBARS oxidative stress protocol. The acute treatment in CTR and MSG groups were performed by the microinjection of L-glutamate (5nmol/100nl), vit C (10nmol/100nl) or sterile saline (100nl) unilaterally in the RVLM rats. At 90 days of life a catheterization of artery and femoral vein was performed as central guide-cannula implantation directed to RVLM. After 48 hours, mean arterial pressure (MAP) and heart rate (HR) were evaluated in rats with free movement and unanesthetized. Statistical analyses were performed using GraphPad Prism and the variables analyzed by ANOVA one way or test t, being results presented as mean ± SEM. Differences were considered statistically significant if *$p<0.05$.

Results: Our study showed that obese rats were hypertensive and tachycardic compared to control rats (CTR). Obese rats show a higher blood pressure response after L-glu microinjection, and a lower response to vit C in RVLM compared to the CTR group. Biochemical analysis of oxidative stress showed that obese rats presented an increase in NBT and T-BARS in RVLM and after treatment with vitamin C, the oxidative profile was lower. Our data suggest that due to the antioxidant capacity of vit C, the amount of ROS in the RVLM area may have been reduced and this may lead to a lower increase in blood pressure.

Conclusions and Support: Our data indicate a possible beneficial effect of antioxidants in the treatment of hypertension due to obesity. Financial support: CAPES (fellowship) and CNPq (Edital Universal 2016/ process number: 408474/2016-5).

ID: 3405

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de São Paulo - SAO PAULO - Sao Paulo - Brasil

Title: EFFECT OF POINT MUTATIONS ON WATER TRANSPORT BY UREA TRANSPORTERS, EXPRESSED IN LITHOBATES CATESBEIANUS OOCYTES

Introduction: In the kidney, urea transporters (UTs) facilitate the diffusion of urea across plasma membranes, consequently contributing to the concentration of urine. It has been shown that UT isoforms are expressed in specific renal regions. UT-A1 and UT-A3 are expressed on the apical membrane and basolateral membranes of the inner medullar collecting duct, respectively, UT-A2 is expressed in the thin descending limb of the Loop of Henle and UT-B is expressed in the descending vasa recta. The X-ray crystal structure of bovine UT-B (bUT-B) shows that this protein is a homotrimer, and each monomer contains a selectivity filter that transports urea down its concentration gradient. In the narrowest region of each pore, two highly conserved threonine (T) residues form the urea binding site. Previous studies with bUT-B demonstrated that mutating both T residues to Valine (V) reduces urea transport. Recent studies in our laboratory showed that Lithobates catesbeianus oocytes can heterologously express wild type (WT) mouse UT-A2, mUT-A3 or mUT-B on the cell surface. Additionally, oocytes expressing mUT-A2WT, mUT-A3WT or mUT-BWT can transport water in addition to urea.

Objective: Investigate the effect of mutating the two conserved T residues in the selectivity filter of the monomeric pore of mUT-A2WT, mUT-A3WT and mUT-BWT has on membrane protein expression and the osmotic water permeability (Pf).

Methods: Oocytes were injected with cRNA encoding for c-Myc tagged mUT- A2WT, mUT- A2T176V, mUT- A2T338V, mUT-A3WT, mUT-A3T246V, mUT-A3T408V, mUT-BWT, mUT-BT172V or mUT-BT334V. Control oocytes were injected with H2O. UT cell surface expression was evaluated by biotinylation, followed by immunoblotting with an anti-c-Myc antibody. The Pf of the oocytes was assessed by placing the oocytes in a hypotonic solution (70 mOsm/L) and recording cell swelling via video microscopy. Subsequent changes in cell volume were used to calculate the Pf (cm/s). All experimental procedures were approved by the Committee on Ethics in the Use of Animals (nr 7971160519).

Results: Western blot analyses of biotynaled samples from H2O-injected control oocytes had no detectable signal, whereas samples from oocytes expressing mUT-A2WT, mUT-A3WT and mUT-BWT and their respective T to V mutations revealed immunoreactive bands at around 45 kDa. This value is consistent with the molecular weight of glycosylated UT monomers. Additionally, our results demonstrated that the mutant proteins could be expressed on the surface of the oocytes. Notably, oocytes expressing mUT-A2WT, mUT-A3WT or mUT-BWT had significantly higher Pf values when compared to oocytes expressing their respective T to V mutants, as well as H2O-injected controls.

Conclusions and Support: Our results demonstrate that the conserved T residues in the monomeric pore of mUT-A2, mUT-A3 and mUT-B are essential for UT-mediated water transport. We hypothesize that the hydroxyl groups present on the T side-chain of the pore surface interact with water molecules and help guide them through the urea channel. The findings of this study provide a better understanding of the molecular mechanisms underlying UT-mediated water transport and how the kidney produce concentrated urine and suggest that UT inhibitors could function as effective diuretics by blocking both urea and water transport. This work has been supported by FAPESP and CNPq.

ID: 3406

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: Instituto de Biociêncas da Universidade de São Paulo - São Paulo - Sao Paulo - Brasil

Title: PHYSIOLOGICAL AND MOLECULAR ALTERATIONS IN TOADS FOLLOWING AN IMMUNE CHALLENGE

Introduction: Glucocorticoids, melatonin, and androgens are hormones with integrated and complex immunomodulatory effects with temporal dynamics better explored during an inflammatory response in mammals. Available data suggest that these functional elements are conserved during vertebrate evolution, but the temporal pattern of the inflammatory response is yet underexplored in other vertebrates, mainly in ectotherms. In this context, studies integrating information on molecular and endocrine mediators across a timeline of the inflammatory response in ectothermic vertebrates, such as amphibians, are imperative to a broader understanding of comparative aspects of inflammatory response.

Objective: Our study aims to investigate the temporal dynamics of the inflammatory response in anurans by assessing physiological and molecular data of Rhinella diptycha toads submitted to an immune challenge.

Methods: Captive male toads (N = 32) were kept in a 13:11 LD at 21 ± 2ºC. The animals received an LPS (2mg/kg) or saline injection at 7pm. Blood samples were collected 1 and 6h post-injection to measure: corticosterone (CORT), melatonin (MEL), and testosterone (T) plasma levels, neutrophil to lymphocyte ratio (NLR), and plasma bacterial killing ability (BKA). Following blood sampling, toads were euthanized, peritoneal lavage fluid and spleens were collected to quantify phagocytosis of peritoneal leukocytes (PP) and gene expression of cytokines (IL-1β, IL-6, IL-10) respectively. CORT, T, and MEL levels were quantified using ELISA kits. NLR through optical microscopy and BKA by spectrophotometry. PP was measured by imaging flow cytometry and cytokines gene expression through RT-PCR. Animals were collected under the license (ICMBio, 29896-1) and ethics permission (CEUA 242/2016).

Results: Our preliminary results for physiological measures showed increased CORT and decreased MEL levels in LPS-treated toads compared to saline-treated 6h post-injection. T levels and PP were affected by time post-injection, with toads showing lower T levels and higher PP 6h post-injection compared with 1h, independently of the treatment. BKA was higher in LPS-treated toads independently of the time, and NLR was not affected by treatment nor time. For molecular data, our preliminary results showed IL-1β and IL-6 upregulation in both 1h and 6h post-injection for the LPS group compared to saline, with higher values for both cytokines in the LPS-treated toads 1h post-injection. Interestingly, IL-10 mRNA was only expressed in the LPS-treated toads 6h post-injection.

Conclusions and Support: Toads were responsive to LPS, exhibiting an increase in CORT, implying activation of the hypothalamic-hypophysis-adrenal/interrenal axis. At the same time, the decrease in MEL suggests the activation of the immune-pineal axis, represented by a reduction in central MEL production. The upregulation of the proinflammatory cytokines IL-1β and IL-6 was observed in both time-points, while the anti-inflammatory cytokine IL-10 was only present 6h post-injection, showing the progression of the inflammatory response. This research was supported by FAPESP: regular grants (2014/16320-7 and 2019/24950-4), master (2020/00370-6 to FRF) and postdoctoral fellowships (2016/01782-0 to BTJ and 2015/23801-4 to VRA). By CAPES: master fellowship to FRF; and by CNPq: undergrad fellowship (PIBIC 120086/2019-0 to LFF).

ID: 3408

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: INVOLVEMENT OF N-GLYCOSYLATION IN UREA TRANSPORTER A2-MEDIATED NH3 TRANSPORT

Introduction: Urea transporters (UTs) are transmembrane glycoproteins that facilitate urea diffusion across cell membranes and play an essential role in the urinary concentration mechanism. Renal UTs include UT-A1 and UT-A3, expressed in the apical and basolateral membranes of the inner medullary CD, respectively; UT-A2, expressed in the thin descending limb of the inner and outer renal medulla;

and UT-B, expressed in the descending vasa recta. The X-ray crystal structure of the bovine UT-B revealed that UT is a homotrimer. Each monomer contains ten transmembrane helices that fold together to form an independent urea channel. Between helices 5 and 6, there is a long extracellular loop that has a highly conserved asparagine (N) residue that serves as an N-glycosylation site. Previous work from our laboratory has shown that UT-A2, UT-A3 and UT-B can transport both urea and water and likely play an important role for optimal concentrated urine production. Moreover, it has been shown that UT-B expressed in Xenopus oocytes can transport urea, water and NH3; however, it is not known if other UT proteins are also permeable to NH3.

Objective: Herein, we sought to determine if UT-A2 is capable of conducting NH3 and if N-glycosylation regulates its NH3 transport activity.

Methods: To achieve this goal we injected Lithobates catesbeianus oocytes with cRNA encoding for wild-type mouse UT-A2 (mUT-A2WT), the N210Q mutant of mUT-A2 (mUT-A2N210Q) or H2O (control) and evaluated the expression on the oocyte surface and monitored surface-pH (pHS) transients caused by NH3 influx. Membrane expression was assessed by western blot analyses of biotinylated surface proteins probed with anti-c-Myc antibody. To visualize the molecular weight of the unglycosylated monomer, we treated mUT-A2WT surface samples with PNGaseF to remove the glycosylation of the protein. NH3 transport was assessed using a microelectrode with a blunt tip to record the maximum transient change in pH at the oocyte surface [ΔpHS(NH3)] caused by exposing the oocytes to a 0.5 mM NH3/NH4+ solution.

Results: We found that H2O controls had no detectable signal, whereas mUT-A2WT exhibited immunoreactive bands at 45 and 55 kDa, values consistent with the molecular weights of the glycosylated forms of the protein. Additionally, mUT-A2WT treated with PNGase F generated a band at 34 kDa, which is the approximate molecular weight of the unglycosylated monomer. Interestingly, no immunoreactive bands were observed with mUT-A2N210Q, thus demonstrating that N-glycosylation is necessary for UT-A2 protein insertion into the oocyte membrane. Furthermore, oocytes expressing mUT-A2WT had significantly greater ΔpHS(NH3) values when compared to UT-A2N210Q and H2O-injected control oocytes.

Conclusions and Support: The results of the present study show that the membrane expression of UT-A2 is dependent on N-glycosylation at the N210 and that in addition to transporting urea and water, mUT-A2 can also transport NH3. Our observations provide valuable insights into the role of N-glycosylation in the UT-A2 protein expression, which could have direct implications in renal cell function. Understanding the mechanisms involved in the role of UTs on urea, water and ammonia transport provides insights into an integration of nitrogenous waste, water and acid excretion by the kidney. Animal studies were approved by the Committee on Ethics in the Use of Animals (nr 7971160519). FAPESP and CAPES supported this study.

ID: 3153

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: SELECTIVE ATTENTION TASK IN DOGS WITH HYPERADRENOCORTICISM

Introduction: Hyperadrenocorticism (HAC) is an endocrinopathy with clinical manifestations resulting from chronically elevated circulating cortisol. In dogs, the most common form occurs when a pituitary tumor secretes adrenocorticotropic hormone (ACTH) autonomously, which stimulates cortisol secretion by the adrenal glands. Hypercortisolism may be related to cognitive impairment because cortisol changes hippocampus structure and functions. Attention is the cognitive process and a decline in selective attention can be observed in dogs with the cognitive dysfunction syndrome (CDS). This syndrome is common in elderly dogs, but little is known about the effects of hypercortisolism resulting from HAC on cognitive processes in dogs.

Objective: The aim of this study was to evaluate the performance of dogs with HAC in a selective attention task and thus the possible effects of hypercortisolism on cognition.

Methods: A total of 30 elderly dogs were recruited for this study: 10 with HAC (HAC group), 7 cognitively impaired (CDS group) and 13 cognitively unimpaired (control group). Diagnosis of HAC was based on history, physical examination findings and routine laboratory abnormalities and confirmed by the low-dose dexamethasone suppression test or ACTH stimulation test. Diagnosis of CDS was made by recognition of behavioral signs and exclusion of concomitant disease. Serum cortisol was measured by radioimmunoassay and dogs were tested measuring selective attention by finding palatable food hidden in an object. According to the dog's response (ability and latency to search and locate the food), a score of 1 to 4 was given, where 1 represented the best answer and 4 the worst. The statistical analysis was done by ANOVA and Tukey's test and Pearson's coefficient was used to correlation analysis ($p<0.05$). CEUA protocol: 8411250518.

Results: The mean value of age was higher in the CDS group (14.6±0.61 years) compared to HAC group (10.0±0.79 years) and control group (11.2±0.44 years) ($p<0.01$). Despite age and diagnoses of HAC and CDS, in the respective groups, all dogs showed good general condition at the time of selective attention task. No dog had neurological or locomotor impairment. Baseline cortisol concentration was higher in HAC group compared to control group (6.44±0.83 µg/dL vs. 2.14±0.45 µg/dL) ($p<0.001$). In the CDS group, the mean value of baseline cortisol concentration was 4.01±1.21 µg/dL and did not differ from HAC and control groups. There was no difference in the mean score of the selective attention task between the groups; however, the performance was considered good in the control group (2.31±0.40) and bad in both HAC (3.00±0.49) and CDS (and 3.00±0.42) groups. In addition, a positive (+0.34) and significant ($p=0.035$) correlation was found between baseline serum cortisol concentration and selective attention test score.

Conclusions and Support: The performance of HAC group in the selective attention task was similar to CDS group. Preliminary results indicate a possible relationship between sustained serum cortisol elevation and a worse cognitive performance in dogs. Support: FAPESP grant 2018/10554-7.

ID: 3409

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

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Title: ANALYSIS OF HEART RATE AND HEART RATE VARIABILITY IN INDIVIDUALS INDUCED TO ACUTE PSYCHOLOGICAL STRESS

Introduction: The heart is an organ able to contract voluntarily and independently. The hart's impulse originates from myocardial cells called auto-rhythmic cells, regulated by the Autonomic Nervous System (ANS). Changes in Heart Rate (HR) and Heart Rate Variability (HRV) are due to reactions interpreted by the organism in the face of physiological and psychological stimuli, such as stress, when HR tend to higher and HRV lower. HRV refers to the oscillations in the intervals between consecutive heartbeats (R-R interval).

Objective: In view of this, the present study aimed to analyze the HR and HRV of individuals during an experiment for the induction of acute psychological stress.

Methods: This is pre-experimental study that included subjects who did not have heart disease, psychiatric disorders, moderate or severe pain and who did not experience any stressor in the 120 days prior to data collection. The Trier Social Stress Test (TSST) experiment was used to induce acute psychological stress, which consists of two consecutive tasks: a) a Free Speech activity (FS) before an examination board composed of three evaluators trained for this role and; b) Arithmetic Activity (AA) in which a difficult mental subtraction series is requested. The HR and HRV variables were obtained by the polar cardiofrequency meter obtaining the averages in four moments: during five minutes of baseline (pre-TSST); during the TSST and; post-TSST at 15 minutes and during 30 minutes of the recovery. Thirty three individuals participated in the study, 18 women and 15 men aged between 18 and 34 years old. Among them, most were undergraduates (78.8%; N=26), were working or were trainees (66.7%; N=22) were single (84.8%; N=28), had a per capita family income of more than 4 minimum wages (45.5%; N=15). Among the various HRV parameters, the RMSSD was selected, which is the Root-Mean Square of Differences between adjacent normal RR intervals in a time interval, expressed in milliseconds.

Results: The results obtained showed an increase in HR in both the FS and AA tasks in relation to the baseline level (95 bpm), with an average of 125 bpm and 118 bpm, respectively. After TSST, HR decreased to 99 bpm (15 minutes later) and to 98 bpm (30 minutes later). HRV showed synchronous results with HR, with a decrease during the stress induction considering the baseline level (39.385ms). During the FS and AA tasks the RMSSD was 25.242ms and 22.318ms respectively. After TSST, the averages decreased to 37.013ms at 15 minutes and 36.919ms at 30 minutes.

Conclusions and Support: It can be concluded the effectiveness of the TSST as a methodology to induce stress and, likewise, the effectiveness of HR and HRV as measures to assess acute psychological stress.

ID: 3410

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: PROTECTIVE EFFECTS OF Lactobacillus rhamnosus AND Lactobacillus reuteri ON BEHAVIORAL AND METABOLIC DYSFUNCTION INDUCED BY CHRONIC STRESS IN RATS

Introduction: Chronic stress is associated with metabolic alterations, increased oxidative stress, cardiovascular complications and behavioral changes, such as anhedonia. The animal model of Chronic Unpredictable Mild Stress (CUMS) consists of the random, intermittent, and unpredictable exposure of laboratory animals to a variety of stressors during consecutive weeks, resulting on metabolic, cardiovascular and behavioral complications. Probiotics, dietetic supplements containing live bacteria, have been studied as a therapeutic alternative to minimize the damage resulting from several diseases.

Objective: This study aimed to investigate the effects of probiotics Lactobacillus rhamnosus and Lactobacillus reuteri (1 billion of Colony-forming units/probiotic) on body weight gain, liver weight, liver damage and anhedonia, in rats submitted to CUMS protocol.

Methods: Male Wistar rats were randomly assigned into four groups (n= 11-12/group): Control (C), Stress (S), Control+Probiotic (CP), and Stress+P (SP). Probiotic was administrated for 8 weeks, and during weeks 3, 4 and 5, CUMS was applied. On week 6, animals were

submitted to the Sucrose Preference Test (1% sucrose solution for 1 hour, calculated as sucrose intake/total fluid intake x 100). The rats were euthanized 15 days after CUMS exposure (week 8), and blood and liver samples were collected. Results were evaluated by Two-Way ANOVA and Tukey's post-test ($p<0.05$). The Ethics Committee of the Federal University of São Paulo approved the experimental procedures (n° 9678230719). Serum transaminases (aspartate and alanine aminotransferases, AST and ALT) were measured using commercial tests.

Results: Stressed animals showed lower body weight gain during the experimental period (S= 98 ± 4; SP = 124 ± 16%), compared to C and CP (C= 147 ± 10; CP = 149 ± 10%, $p<0.05$). Probiotics significantly increased the weight gain of the animals submitted to CUMS (SP= 124 ± 6 vs. S= 98 ± 4%, $p<0.05$). Animals submitted to CUMS presented anhedonia, evidenced by the reduction of preference for sucrose in the SPT (S= 15 ± 1.7%) compared to the other experimental groups (C= 25 ± 1.3; CP= 26 ± 1.3; SP= 20 ± 0.1%). Liver weight corrected by tibia length(g/mm) was decreased in CMSU groups, with no effect of probiotics (S= 2.48 ± 0.07; SP= 2.5 vs. C= 2.83 ± 0.04; CP= 2.7 ± 0.1; ± 0.5g/cm, $p<0.05$). We did not observe statistical differences in AST among experimental groups (C= 212.9 ± 9.3; CP= 219.8 ±. 8.5; S= 220.5 ± 12.2; SP= 230.453 ± 9.6U/L). S group presented higher levels of ALT compared with C and SP (C = 116.8 ± 1.9; SP= 131.60 ± 4.22 vs. S= 147.56 ± 3U/L, $p<0.05$), showing a therapeutic effect of probiotics on mild liver damage induced by CUMS.

Conclusions and Support: Thus, the data presented here show up a novel potential therapeutic role of Lactobacillus rhamnosus and Lactobacillus reuteri body weight, anhedonia, and liver injury induced by CUMS. Financial Support: CAPES.

ID: 3157

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Instituto de Ciências Biomédicas (ICB/USP) - São Paulo - Sao Paulo - Brasil

Title: GLUTAMINE SUPPLEMENTATION ACCELERATES SKELETAL MUSCLE REPAIR AFTER FREEZING DAMAGE

Introduction: The skeletal muscle has a great capacity of regeneration after injury and non-pharmacological approaches to attenuate morbidity of freezing muscle injuries are under continuous investigation. A viable strategy would be to use a supplementation with the amino acid glutamine, since evidences have shown that glutamine is capable of inducing an increase in protein synthesis. However, the mechanisms by which glutamine regulates skeletal muscle's protein metabolism are still not well known and the effect of supplementation with glutamine on skeletal muscle regeneration is still to be determined.

Objective: This study investigated the effects of glutamine supplementation immediately after freezing injury on morphological and functional repair of soleus and extensor digitorum longus (EDL) muscles from young rats

Methods: Two-months old male Wistar rats were randomly divided into two groups (without or with glutamine supplementation) and were subjected to cryolesion of soleus and EDL muscles. Immediately after the cryolesion, the supplemented group received daily doses of glutamine (1g/kg/day) for 3 or 10 days. Afterwards, the muscles were submitted to histological, immunofluorescence, Western Blotting and contractile function analyzes. This project was approved by the Committee on Ethics in the Use of Animals (CEUA, ICB/ USP) registered under protocol No. 71/2017.

Results: Glutamine supplementation markedly increased the size of regenerating myofibers of soleus and EDL muscles (43% and 53.1%, respectively), reduced the inflammatory area (60.9% and 66.71%, respectively) and prevented the decline in maximum tetanic force of these muscles evaluated on post-cryolesion day 10. In addition, soleus and EDL muscles from the glutamine-supplemented injured group evaluated on post-cryolesion day 10 presented a higher increase in the phosphorylation of 70-kDa ribosomal protein S6 kinase, a downstream component of the mechanistic target of rapamycin complex 1 (mTORC1) pathway, compared to those from the cryolesioned group (Soleus: 8.4 vs 5.1 fold-increases, respectively; EDL: 12.8 vs 4.8 fold-increases, respectively). Additionally, glutamine-supplemented regenerating soleus and EDL muscles had marked decrease in the number of CD11b positive macrophages (39.7% and 50.6%, respectively), TCF4 positive fibroblasts (74.5% and 56.1%, respectively) and the expression of the collagen specific molecular chaperone HSP47 (52.9% and 51.74%, respectively) on post-cryolesion day 10.

Conclusions and Support: Glutamine supplementation accelerates recovery of soleus and EDL contractile function after freezing injury by increasing the size of regenerating myofibers via activation of mTORC1 signaling pathway and accelerating the remodeling of some extracellular matrix components. These results could serve as a guide for future non-pharmacological rehabilitation studies to test the application of glutamine supplementation for better outcome of skeletal muscles in patients with frostbite injuries. Support: CAPES, FAPESP (14/23391-8; 17/09069-4; 18/24946-4), CNPq (312142/2018-8).

ID: 3413

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: ANALYSIS OF OXIDATIVE LIPID DAMAGE AND NON-ENZYMATIC ANTIOXIDANT DEFENSE IN THE SUBLINGUAL GLANDS OF WISTAR RATS AFTER ORCHIECTOMY

Introduction: There are many factors that influence the oral health of men, such as variations of serum testosterone concentration. In men, the hypogonadism is associated with several clinical signs. For example, loss of density mineral bone, decreases muscle strength, signs contributing to more prevalence periodontal disease and gum inflammation, and decreasing quality of life. However, studies have shown that the influence of testosterone on oral health are limited to contextualizing its effect on periodontist. It neglects the importance of salivary glands and saliva in oral homeostasis.

Objective: The objective of the study was to evaluate lipid oxidative damage and non-enzymatic antioxidant of sublingual glands of castrated Wistar rats compared to animals in the SHAM group.

Methods: Twenty male Wistar rats (three-month-old) underwent surgical orchiectomy or sham surgery and were randomly assigned to two experimental groups: SHAM and ORX. Water and food were available ad libitum throughout the experiment. The protocol was approved by the Ethics Committee on the Use of Animals of School of Dentistry, São Paulo State University-UNESP, Araçatuba (Protocol FOA nº 00956-2018). At the end of treatment, the rats were euthanized, blood samples were collected and plasma testosterone was measured and the sublingual glands were removed, weighed, and stored at -80 °C. Sublingual gland homogenate supernatants were used for spectrophotometric assays: total protein concentration (TP), oxidative damage to lipids was analyzed TBARS method (reactive substances to thiobarbituric acid), protein oxidative damage was determined by the Carbonyl Protein method (CP). Non-enzymatic antioxidant capacity was evaluated by the antioxidant power of total ferric reduction (FRAP), total glutathione (tGSH), and uric acid (UA). Enzymatic antioxidant capacity was determined by the activity of the enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Data were analyzed by Student's t-test, considering a significance level of 5% ($P < 0.05$).

Results: The ORX group, presented serum concentrations of testosterone below the sensitivity of the test ($P < 0.0001$). ORX group dramatically decreased the prostate mass ($P < 0.001$) and the final body mass ($P < 0.01$) compared to SHAM. The calculated relative glandular weight showed a difference that is not statistically significant between ORX and SHAM. In addition, the ORX group increased lipid oxidative ($P < 0.05$) and protein ($P < 0.05$). Oxidative damage decreased non-enzymatic antioxidant defense, FRAP levels ($P < 0.01$), UA ($P < 0.05$) and tGSH ($P < 0.05$) and enzymatic antioxidant defense SOD ($P < 0.01$), CAT ($P < 0.05$) and GPx ($P < 0.05$) compared to SHAM.

Conclusions and Support: These findings suggest that the increased oxidative damage induced by OQX was associated with a reduction in enzymatic and non-enzymatic antioxidant defense. PIBIC ENSINO MÉDIO/CNPQ/UNESP - EDITAL 05/2019 - PROPe (Processo 1384465/2019-3).

ID: 2903

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: Ê-POSTER

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Title: NPARM PHOX2B MUTATION IN THE RETROTRAPEZOID NUCLEUS IMPAIRED BREATHING IN CONSCIOUS MICE

Introduction: Retrotrapezoid nucleus (RTN) neurons modulate central chemoreception and respiratory automaticity. Phox2b and Atoh-1 expression characterizes these neurons. Germline Phox2b mutations result in congenital central hypoventilation syndrome, producing an impaired respiratory response to hypercapnia and hypoxia.

Objective: Our goal was to investigate whether a conditional mutation of Phox2b driven during Atoh-1 expression in RTN neurons might affect a) respiratory rhythm; b) ventilatory responses to hypercapnia (HCVR) or hypoxia (HVR) and c) number of RTN neurons during developmental stages.

Methods: Here, we used a transgenic mouse line carrying a conditionally expressed, humanized PHOX2BΔ8 mutation (CEUA-3618221019). We crossed them with Atoh-1-cre mice. Thus, experimental group was selected based in the presence of both phenotypes: Atoh-1-cre+ and PHOX2BΔ8+ (neonates n=8; adults n=8, male/female). Cre-negative mice were used as control (neonates: n=9; adults: n=8; male/female). Ventilation recordings performed by whole body plethysmograph occurred in neonatal (P1-3) and adult life (P45-50). Basal recordings were done in room air. To test respiratory chemoreflex responses, mice were submitted to hypercapnia (7%CO2) or hypoxia (8%O2) with duration of 5 min in neonates and 10 min in adults. Anatomically, RTN neurons can be defined by Phox2b expression and absence of tyrosine hydroxylase (TH). These studies were followed by Phox2b+/TH- neuron immunohistochemical quantification.

Results: Respiratory rhythm was analyzed by Poincare plot and showed an increase of breath irregularity during both neonatal and adults after Phox2b mutation. In relation to chemoreflex, the peak change of respiratory responses to both hypercapnia and hypoxia were impaired in neonates. In contrast, adult animals recovered the HCVR. Curiously, fos-activated neurons in the RTN in response to hypercapnia were reduced in adult mice with PHOX2B mutation ($35 \pm 9$ vs. control: $87 \pm 19$; $p<0.03$). HVR maintained reduced during adult life. Anatomical

results showed that Phox2b mutation induced a reduction of total Phox2b+/TH- neurons (143 ± 41 vs. control: 263 ± 20; $p<0.04$).

Conclusions and Support: Our data indicates that NPARM mutation in Atoh-1 expressing cells compromised respiratory rhythm, respiratory response to hypercapnia and hypoxia during neonatal phase. But, in adults ventilatory responses to hypercapnia were recovered despite reduction of the number of Phox2b and Fos activated neurons in the RTN. Financial Support: FAPESP, CAPES, CNPq, NIH.

ID: 3415

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CONTRACTIONWAVE: OPEN SOFTWARE TO PROCESS, ANALYZE AND VISUALIZE CELLULAR CONTRACTILITY

Introduction: Evaluation of cardiomyocyte contractility can be achieved using several methods that capture cellular movement, which obtain important information about contraction- relaxation dynamics. Yet despite the progress in this area, no existing computational framework provides a fast and accessible analysis of cellular contractility in a single platform. Here, we present CONTRACTIONWAVE (CW), a robust computational framework, with a built-in user-friendly interface, that provides a single platform to acquire visualize, analyze and quantify contractility parameters of cardiac cells at different developmental stages through image capture and optical flow.

Objective: This study goal was to develop non-invasive software for acquiring data regarding membrane kinetics of cardiac cells during contraction-relaxation cycles through image capture

Methods: To validate the system, we used adult and neonatal cardiomyocytes, and human-induced pluripotent stem cell-derived cardiomyocytes (hiPSC-CM). Cardiomyocytes were exposed to 100 nM of Isoproterenol (ISO), or Verapamil (VERA) in order to validate the system efficiency to detect differences in contraction/relaxation. We also used cardiomyocytes from a rat hypertension model (TGR-mREN2-27). Images were obtained by bright field microscopy and processed by CW optical flow algorithm. Statistical analysis was performed using ANOVA and Test t student, using $p<0.05$*.

Results: CW can automatically process large data image files, finding contraction-relaxation average speed parameters and frequency, detecting membrane displacement throughout the whole cellular area, with sarcomere sensitivity (0.0625 μm²). Moreover, CW presents to the user speed vectors on a scale of visual and numerical intensity. By applying CW to adult, Neonate, and hiPSC cardiomyocytes we could detect a significant decrease in Contraction Time, Relaxation, and Total Contraction-Relaxation (ms) between cell groups treated with ISO or VERA. Additionally, cells treated with VERA showed a decrease in the Maximum Contraction Speed (μm/s) and Maximum Relaxation Speed (μm/s) while ISO induced an increase in these parameters. Likewise, ISO and VERA induced opposite effects in the shortening area (μm²). Cardiomyocytes from hypertensive rats showed a significant increase in Contraction and Total Contraction-Relaxation time, showing no differences between the other contractility parameters. CW also allows contouring some usual experimental issues related to smoothing/denoising algorithms and separating waves from noise. Another innovation introduced in CW is a visualization window that permits simultaneous viewing of the cell image and the contraction waves during real-time acquisition.

Conclusions and Support: CW is a robust computational framework, that in a single platform is capable of visualizing, analyze, and quantify contractility parameters of cardiac cells from different developmental stages through image capture and optical flow. Its use to acquire contractility parameters in hIPSC-CM is crucial for determining the phenotypic maturity of the cardiac cell, and to allow its application in clinical research. Support: CNPq;FAPEMIG;CAPES

ID: 3161

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF FRUCTOSE OVERLOAD DURING PREGNANCY AND LACTATION ON THE MORPHO-FUNCTIONAL ASPECTS OF MATERNAL KIDNEYS.

Introduction: In the latest decades, there was an important increase in the consumption of foods that have fructose in their composition. This sugar has been widely used in the preparation of soft drinks, jellies, cakes, puddings, etc; due the fact that it is sweeter than sucrose. However, the consumption of high levels of fructose in humans and in experimental animals has been associated with metabolic changes, hypertension and renal dysfunction. During pregnancy and breastfeeding, there are multiple physiological adjustments in the maternal organism including in kidney function, and the consumption of fructose overload may change these alterations. Therefore, it is important to evaluate the repercussion of excessive consumption of fructose during pregnancy and lactation on maternal blood pressure and renal function.

Objective: To evaluate changes in blood pressure and renal morphology and function in rats subjected to fructose overload during pregnancy and lactation.

Methods: Female Wistar rats were divided into 4 experimental groups: Non-Pregnant Control group (NP-C); PC - Pregnant Control group (PC); Non-Pregnant Fructose group (NP-F) and Pregnant Fructose group (PF). PC and NP-C received food and water "ad libitum" during all the experimental period. PF and NP-F received food and a solution of fructose (20%) "ad libitum". The offer of fructose (20%) begun 1 week before mating for the PF group and continued during pregnancy and lactation until the experimental evaluations one week after weaning. The NP-F group received fructose for the equivalent period of group PF. After birth, the litters were reduced to eight offspring. Lactation period was 21 days. After weaning, the progenitor rats had their blood pressure (BP) measured, using plethysmography, and then their renal function and morphology were assessed. The blood pressure of non-pregnant groups was measured throughout the experimental period. The results are presented as medium ± standard error, statistic analyses was performed using two-way ANOVA followed by Tukey - GraphPad Prism program (version 6.0). Values of $p \leq 0.05$ were considered significant. Approved by CEUA/UNIFESP nº: 2757270117.

Results: Increased BP was observed in rats treated with fructose both pregnant and non-pregnant compared to control rats (BP, mmHg: NP-C: 116±1.3; PC: 119±1.7; NP-F:134±3.2*; PF:131±1.1*). Regarding the renal function, we observed in the PF group reduction in: creatinine clearance (CLcr, ml/min/kg: NP-C: 7.07 ± 0.70; PC: 6.58 ± 0.45; NP-F: 6.73 ± 0.59; PF: 4.52 ± 0.50*), excreted load of sodium (Na+EL, mEq/24h: NP-C: 1.50 ± 0.14; PC: 1.42 ± 0.12; NP-F: 0.72 ± 0.094*; PF: 0.96± 0.10*), excreted load of potassium (K+EL, mEq/24h: NP-C: 4.17 ± 0.15; PC: 3.97 ± 0.21; NP-F: 2.09 ± 0.27*; PF:2.44 ± 0.36*), excreted load of urea (Urea EL, mEq/24h: NP-C: 80.23 ± 2.72; PC: 84.59 ± 2.62; NP-F: 36.83 ± 4.94 *; PF: 47.39 ± 7.84 *), and urinary osmolarity (Uosm, mOsm/kg: PC: 1553 ± 73; PF: 1124 ± 112*). Although only group PF had reduced values of CLcr, both groups treated with fructose (NP-F and PF) had reduced Na+ and K+ excretions and increased blood pressure.

Conclusions and Support: The data suggest that fructose overload during pregnancy increases the risk of development of hypertension and renal dysfunction in female Wistar rats after weaning. Financial support: FAPESP (2018 / 03511-0).

ID: 3417

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: LOW DOSES OF CYCLOSPORIN A DO NOT CAUSE HISTOPATHOLOGICAL DAMAGE TO THE SPLEEN OF MALE MICE

Introduction: Cyclosporin A (CsA) is a drug widely used to prevent transplant rejection. CsA inhibit calcineurin protein gene expression, involved in T lymphocyte activation and spermatogenesis, but has recently been studied as a potential male contraceptive. As CsA is an immunosuppressant and the spleen is one of the main lymphoid organs.

Objective: The present study aims to evaluate the possible morphometric and histochemical alterations of the spleen after the administration of low-dose CsA in the short term.

Methods: For this, male Swiss mice were distributed into 3 groups (n = 6): C10 (received filtered water for 10 days); CsA10I (received 10 days diluted CsA); CsA10R (received diluted CsA for 10 days, and underwent a 10-day recovery period). In this study, a dose of 10 mg/kg of CsA was used in a final volume of 0.2 ml. After euthanasia, the spleen of the animals was processed by routine histological techniques. In the histological sections stained with hematoxylin and eosin the area of the splenic pulps, lymphoid nodules and periarterial sheaths were determined at light microscopy. The histological sections stained with Picrossirius red were observed in polarized light to determine the percentage of collagen types I and III. And the histological sections stained by the periodic acid schiff (PAS) technique, the proportion of neutral glycoconjugates in the white and red pulp of each animal has analyzed. The experimental protocol followed the Ethical Principles in Animal Research adopted by Brazillian Council for Control of Animal Experimentation and it were approved by the Ethics Committee on Animal Use of State University of Londrina (OF. CIRC CEUA N° 94/2018). Two-way ANOVA was used to compare the mean area of the splenic pulps, percentage of collagen types and proportion of neutral glycoconjugates. And the one-way ANOVA was used to compare the area of nodules and sheaths between groups. Both with Tukey post-test ($P < 0.05$).

Results: No structural changes were observed in the area of the splenic pulps or in the area of the main splenic histological structures. The histochemical characteristics, also did not have statistically significant alteration between the groups. It was possible to observe a greater presence of type I collagen in the groups, thus indicating that there was no change in the constitution of the tissue, this type of fiber being predominant in healthy tissues.

Conclusions and Support: In conclusion, low-dose CsA treatment did not cause alterations in spleen of the mouse, indicating that the dose used in a short time is not toxic to the spleen in the conditions evaluated. Support: CAPES-PROEX - AUXILIO 690/2018 PATOLOGIA EXPERIMENTAL. Keywords: Histology. Calcineurin. Toxicity. Spleen.

ID: 3418

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF MELATONIN SUPPLEMENTATION ON ANHEDONIA BEHAVIOR IN Drosophila melanogaster EXPOSED TO HYDROGENATED VEGETABLE FAT

Introduction: The nutritional transition that occurred in the last decades has reflected changes in food quality. An increase in the consumption of ultra-processed foods is observed, which are generally rich in trans fats. The health impact of the population on the consumption of ultra-processed products is demonstrated in several studies associated with mental illnesses such as depression. Depression is a common disease that affects the social and physical function of individuals. One of its main symptoms is anhedonia, characterized by the loss of the ability to feel pleasure. Drug treatments for this disease are limited, provide remission for only half of the individuals, and cause undesirable side effects. New compounds are researched, such as melatonin. Studies show a potential antidepressant effect associated with melatonin supplementation; it modulates neuroinflammation, neuroplasticity, and performing a neuroprotective function.

Objective: To verify the effects of melatonin supplementation on anhedonia behavior, food consumption and mortality in Drosophila melanogaster exposed to hydrogenated vegetable fat.

Methods: 50 flies, of both sexes, per group, were used. The treatment consisted of 4 groups: Group 1: regular diet (RD); Group 2: diet with 10% hydrogenated vegetable fat (HVF10%); Group 3: diet with melatonin (MEL) and; Group 4: diet with HVF and melatonin (MEL + HVF10%). The mortality percentage was verified, counting was evaluated by a daily count of the number of living flies until the end of treatment. Food consumption was assessed using a blue dye to the diet to check the flies' acceptance of different diets. After seven days, the anhedonia behavior was verified by the mating test: a male fly from each group was placed together with a virgin female on a coupling wheel to perform the test. Latency until the first copulation and the number of courtships it was evaluated. The results were assessed by one-way ANOVA, followed by Tukey's post hoc. The percentage of mortality was determined using the Mantel-Cox log-rank test. Differences between groups were considered significant when $p < 0.05$.

Results: The food consumption of flies exposed to the different experimental diets did not significantly differ between the experimental groups (One-way ANOVA, $F3, 16 = 0.8223$, $p = 0.5005$). HVF significantly increased the mortality rate of flies exposed to HVF compared to the RD and MEL groups ($p < 0.05$). Besides, MEL avoided reducing life expectancy caused by HVF in the MEL + HVF10% group. In the mating test, HVF increased copulation latency compared to the RD group; already, the MEL supplementation prevented this increase caused by HVF (One-way ANOVA, $F3, 12 = 10.94$, $p = 0.0009$). HVF caused a reduction in the number of the courtship concerning the RD, and supplementation with melatonin partially protected this decrease (One-way ANOVA, $F3, 12 = 4.477$, $p = 0.0249$).

Conclusions and Support: The supplementation with melatonin in the diet did not alter food consumption and protected the increase in mortality generated by HVF. Besides, it was effective to prevent anhedonia caused by HVF in Drosophila melanogaster. Support: CNPq, PDA.

ID: 3420

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF ADRENALINE IN CARDIAC MUSCLE PROTEIN METABOLISM OF FASTED RATS.

Introduction: Skeletal and cardiac muscle mass are regulated by a fine balance between the processes of protein synthesis and degradation. The main processes of muscle protein degradation are lysosomal-autophagic and ubiquitin-proteasoma and both are regulated by neural and hormonal factors. Previous studies in our laboratory have demonstrated the physiological role of adrenaline in the regulation of skeletal muscle mass and its function in preventing muscle atrophy in catabolic situations. However, the role of this hormone in the regulation of cardiac muscle mass during fasting is still not well known.

Objective: The purpose of this study is to evaluate the role of adrenaline in the regulation of cardiac muscle protein metabolism during fasting and the signaling pathways envolved in these responses.

Methods: Male Hannover rats (180-200g) were submitted to bilateral adrenodemedulation surgery (ADMX) and 8 days after, the animals were fasted for 48h. On the tenth day, the animals were anesthetized, blood was collected and the heart was excised for biochemical and molecular biology analysis (western blot) (CETEA n087/2010). The results were expressed as mean ± SEM, the ANOVA test was used for statistical analysis and the level of significance was 5%.

Results: The ADMX decreased plasma levels of adrenaline in fed and fasted animals (~90%) and noradrenaline levels just in fasted rats (~40%). The ADMX did not alter the glycemia and corticosterone levels in both groups ( fed and fasted ). The ADMX increased the protein content of LC3-II in fasted animals (~30%) in comparison to control, without changes in fed group. The surgery did not alter the protein content of Atrogin and MurF in both groups. In addition, ADMX increased S6 phosphorylation in fed animals (~40%), but no significant difference was found in fasted groups.

Conclusions and Support: These data suggest that adrenaline may regulate the cardiac muscle protein metabolism by decreasing lysosomal-autophagic proteolytic activity, which could help preserve heart mass. Further experiments will be necessary to understand the effects of adrenaline in cardiac muscle protein synthesis. Support: Fapesp (2019/22446-7)

ID: 3165

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CB1 AND CB2 CANNABINOID RECEPTOR AGONIST MODULATES MYOCARDIAL CONTRACTILITY IN FISH HEART CONTRATILITY

Introduction: Cannabinoids have been increasingly gaining attention for their therapeutic potential in treating various cardiovascular disorders. Endocannabinoids and their synthetic analogs have positive and negative effects on the cardiovascular system, activating both subtypes of receptors, cannabinoid receptor type 1 (CB1) and cannabinoid receptor type 2 (CB2). Thus, the role of cannabinoid receptors in the heart remains extremely controversial.

Objective: The aim of this study was to evaluate the effects of the activation of CB1 and CB2 receptors on myocardial contractility of the freshwater Neotropical fish matrinxã, Brycon amazonicus.

Methods: This study was performed under the approval of the Animal Ethics Committee at the Federal University of São Carlos (CEUA – #4997170718). Fish were divided in two experimental groups: control (Ct, n = 10), fish treated with vehicle (5% DMSO in sterile saline with a drop of Tween 80, i.p.) and cannabinoid group (WIN, n = 10), fish treated with a single dose (1 mg.kg-1, i.p.) of the WIN55,212-2, a potent synthetic agonist of CB1 and CB2. After 24 hours, fish of both experimental groups were euthanized and the hearts were carefully removed. Strips were excised from the ventricle and their ends were tied in two metal rings. One ring was connected through a stainless steel wire to an isometric force transducer coupled to a data acquisition/analysis system (BIOPAC). Other ring was tied around platinum electrodes connected to a stimulator. The preparations were immersed in bath containing oxygenated physiological solution kept at 25°C. The contraction force (Fc) at different stimulation frequencies (force-frequency relationship - FFR), the post-rest contraction obtained after pause of 300 s, and the cardiac pumping capacity (CPC) were evaluated.

Results: The WIN treatment caused significant increases in the Fc and CPC values (~53%, $P< 0.05$) above 0.8 Hz. In the Ct group, increments in the stimulation frequency resulted in decreases in the Fc values between 1.4 Hz and 2.0 Hz, whereas WIN group maintained a constant higher Fc over the range between 0.2 and 1.8 Hz. In the Ct group, a potentiation (~25%, $P< 0.05$) of post-rest contraction was evidenced, but WIN treatment completely abolished this post-rest potentiation.

Conclusions and Support: The activation of cannabinoid receptors was able to improve the cardiac performance of matrinxã leading to a positive inotropism. The increased CPC curve and abolished post-rest potentiation suggest that NCX plays an essential role on excitation contraction coupling, after WIN treatment. CNPq Proc. 404688/2018-7

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Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: ALUMINIUM CHLORIDE EXPOSURE DURING THE PERIPUBERTAL PERIOD ALTERS EPIDIDYMAL HISTOPATHOLOGY AND SPERM MOTILITY IN PUBERTAL MALE RATS QUADRELI, D.H.; LEAL, F.A.V.D.; FERRARI, L.S.; FATTORI, V.; FRIGOLI, G.F.; VERRI, W.A.; FERNANDES, G.S.A

Introduction: Aluminium (Al) is an important metal, but it can be toxic to the reproductive system including the epididymal tissue and sperm parameters.

Objective: This study aims to evaluate whether exposure to aluminium chloride (AlCl3) during the peripubertal period affects spermatic parameters and post natal development of the epididymis in rats.

Methods: For that, male Wistar rats (30 days old) were distributed in three experimental groups: control (sterile 0.9% saline solution), AL7 (7 mg AlCl3/kg) and AL34 (34 mg AlCl3/kg). Animals were treated intraperitoneally from postnatal day (PND) 36 to 66 (peripubertal period). At PND67, the epididymis were colleted, weighed and used for histological and determination of myeloperoxidase (MPO) and N-acetyl glycosidase (NAG) activity. In addition, sperm from the vas deferens were used to sperm motility analysis. This experimental protocol followed the Ethical Principles in Animal Research adopted by Brazillian Council for Control of Animal Experimentation and it was approved by the Ethics Committee on Animal Use of State University of Londrina (OF. CIRC CEUA/UEL 059/2015).

Results: Aluminium did not induce changes in epididymal weight, but decreased the final body weight. In AL7 and AL34 groups, the histopathological analysis showed an increase on the diffuse inflammation in the stromal compartment. However, there was no significant difference in epididymis and vas deferens weighs, sperm count and MPO and NAG activity. The percentage of immobile sperm increased in AL34 group compared to Control group.

Conclusions and Support: In conclusion, the exposure to aluminium chloride during the peripubertal period alters the epididymal histopathology and sperm motility in pubescent rats. Keywords: Aluminium chloride, epididymis, inflammation. Financial Support: CNPq (process nº 406189/2016-1).

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Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: HIGH SUCROSE INTAKE INDUCES TESTICULAR AND SPERM DAMAGE BY OXIDATIVE STRESS IN ADULT MALE RATS: CAN PTEROSTILBENE NORMALIZE THAT?

Introduction: The higher consumption of sugar in the last decades has been associated with increased prevalence of metabolic diseases but it has been little related to damage to the male reproductive system. It is well stablished that sucrose consumption can lead to oxidative damage and dietary antioxidants such as pterostilbene may can play a protective role against oxidative stress. Pterostilbene is an antioxidant component of blueberries and has demonstrated to exert therapeutic benefits in several diseases.

Objective: The aim of present study was to evaluate whether the high sucrose intake by adult Wistar rats could impair testicular parameters and verify if the antioxidant potential of pterostilbene can ameliorate eventual tissue damage caused by sugar consumption.

Methods: Twenty-four adult male Wistar rats were distributed into four experimental groups (n=6 animals/group): control group (CG); Control + Pterostilvene (CP); Sucrose Group (SG) and Sucrose + Pterostilbene (SP) group. The animals were exposed to sucrose solution (40%) or vehicle between postnatal day (PND) 67 and 217 and treated with pterostilbene (40mg/kg) 45 days after the end of the sugar treatment (PND 217 – 262). At PND 262, the rats were anesthetized and euthanized. The protocol was approved by the Ethics Committee on Animal Use of State University of Northern Paraná (OF CIRC CEUA nº 05/2017). The right testis was collected and submitted to morphometrical and histopathological analysis. The left testis was stored in a freezer -80º C for later evaluation of oxidative profile. The sperm was collected from vas deferens for following sperm morphology analysis. The data was submitted to the normality Bartlett test and homogeneity Shapiro-Wilk test. Then, the data was compared using ANOVA followed by Dunnet's post-hoc test. Differences were considered significant for $p<0.05$. Statistical analyses were performed using GraphPad InStat (version 3.02).

Results: In the testis, the sucrose consumption induced oxidative stress, increased number of abnormal seminiferous tubules and abnormal sperm and reduced Leydig and Sertoli cells number. Pterostilbene treatment normalized the number of Sertoli and Leydig cells and increased the number of normal seminiferous tubules. On the other hand, the pterostilbene did not prevent the elevation of malondialdehyde (MDA) levels in testis caused by sucrose ingestion.

Conclusions and Support: In conclusion, although some testicular damages in testis caused by high ingestion of sucrose has been normalized by treatment with pterostilbene in adult male rats, the lipid peroxidation and sperm morphology were not reversed. Key-words sugar, pterostilbene, oxidative stress, male reproduction Support: CAPES-PROEX - AUXILIO 690/2018 PATOLOGIA EXPERIMENTAL

ID: 3422

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: RENAL HISTOLOGY, INFLAMMATORY AND REDOX CHANGES CAUSED BY DIET-INDUCED OBESITY IN AGING WISTAR RATS

Introduction: Previous studies have evaluated the isolated connection between aging or obesity and impairments in renal parameters. In this perspective, we justified the proposed animal model that links aging to diet-induced obesity as a helpful tool for elucidate the renal changes resulting of this association and its pathophysiological mechanisms.

Objective: This study aimed to determine the implications of diet-induced obesity on renal histology, inflammatory and redox parameters of aged Wistar rats.

Methods: 16 male Wistar rats (initial age=9 months, final age=14 months) were randomly divided into two groups: fed with control diet (aging control - AC) and fed with high-fat diet (aging obese - AO). Both groups were fed with respective diets for five months. Adipose tissue deposits were collected and weighed to determine visceral adipose tissue (VAT). The left and right kidneys were used for histological, morphometric and immunohistochemistry studies, as well as for biochemical analyzes of thiobarbituric acid reactive substances (TBARS), carbonylated proteins, and the activity of catalase, glutathione peroxidase (GPx). This study was approved by the IMS-UFBA Ethics Committee on the Use of Animals (protocol: 011/2014). Data were expressed as mean ± standard deviation and comparisons between groups were performed using the Student's t test. The statistical significance level was set at $P < 0.05$.

Results: Aging obese rats exhibited significantly higher VAT when compared to aging control (AC: 3.25 ± 1.08 vs AO: 7.38 ± 1.84, $P < 0.05$). Regarding the parameters of glomerular injury, the aging obese group showed a reduction in the glomerular tuft area (AC: 12841 ± 649 vs AO: 11719 ± 1036, $P < 0.05$), in addition to the greater glomerulosclerotic index (AC: 2.74 ± 0.18 vs AO: 2.97 ± 0.21, $P < 0.05$). The analysis of tubulointerstitial histology showed that the high-fat diet determined an increase in tubular cast (AC: 7.20 ± 3.26 vs AO: 15.41 ± 8.05, $P < 0.05$), tubular necrosis (AC: 2.01 ± 1.11 vs AO: 6.40 ± 2.50, $P < 0.05$), loss of brush border (AC: 45.47 ± 17.46 vs AO: 57.33 ± 15.08, $P < 0.05$), tubular dilatation (AC: 1.52 ± 2.00 vs AO: 5.79 ± 4.96, $P < 0.05$), tubular atrophy (AC: 1.87 ± 1.14 vs AO: 3.26 ± 1.34, $P < 0.05$) and interstitial fibrotic area (AC: 2.75 ± 1.21 vs AO: 14.85 ± 5.00, $P < 0.05$) in aging obese compared to aging control. The count of immunoreactive cells showed that the number of macrophages in the renal cortex was greater in the aging obese when compared to aging control (AC: 2.72 ± 1.04 vs AO: 4.67 ± 1.74, $P < 0.05$). The high-fat diet caused increased levels of TBARS (AC: 0.25 ± 0.07 vs AO: 0.39 ± 0.08, $P < 0.05$) and carbonylated proteins (AC: 2.86 ± 0.95 vs AO: 5.00 ± 1.72, $P < 0.05$) in renal tissue from aging obese rats. At the same time, the aging obese group showed a reduction in the activity of antioxidant enzymes catalase (AC: 0.54 ± 0. 11 vs AO: 0.32 ± 0.02, $P < 0.05$) and GPx (AC: 0.07 ± 0.01 vs AO: 0.04 ± 0.01, $P < 0.05$) when compared to aging control.

Conclusions and Support: The results provide evidences that the association between aging and a high-fat induced obesity determined harmful outcomes in renal pro-inflammatory, pro-oxidative profile and consequent structural renal damage, which represent an unfavorable prognosis, since it indicates an accelerated progression of age-associated renal impairment. Support: National Counsel of Technological and Scientific Development [481268/2013- 8]; and the Foundation of Support for Research of the State of Bahia [RED009/2014].

ID: 3423

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF EXERCISE ON MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE PANCREAS IN AN ANIMAL MODEL OF AGING AND OBESITY

Introduction: Obesity and aging are factors that interfere with pancreatic functional parameters, causing inflammatory, oxidative and morphological changes, which can result in metabolic disorders compromising vital organ functions. The preventive and therapeutic modalities of physical exercise have been related to a decrease in body adiposity and prevention or reversal of diseases associated with obesity, by improving the inflammatory and oxidative profile in tissues.

Objective: To evaluate the effects of preventive or therapeutic exercises on morphological and functional parameters in the pancreas of Wistar rats in a model of aging and obesity, induced by a high-fat diet.

Methods: Twenty-four male Wistar rats (initial age = 4 months and final age = 14 months) were used and were randomly assigned to three aged (A) and obese (O) experimental groups (n = 8 / group): sedentary (S), therapeutic exercise (T) and preventive exercise (P). Parameters of body adiposity, plasma concentration and pancreatic immunostaining of insulin, markers of tissue inflammation, lipid peroxidation, activity and immunostaining of antioxidant enzymes and parameters of pancreatic morphology were evaluated.

Results: Preventive exercise improved the parameters of body adiposity (AOS: 13,11±2,45 vs AOP: 9,06±1,14; $p<0,05$) and plasma insulin concentration (AOS: 2,31 ± 0,54 vs AOP: 1,26 ± 0,61, $P<0,05$). Therapeutic and preventive exercises increased the density of pancreatic islets (AOS: 0,12 ± 0,03 vs AOT: 0,25 ± 0,04 and AOP: 0,18 ± 0,03, $p<0,05$). The infiltration of macrophages in the pancreas was reduced only in animals submitted to preventive exercise (AOS: 2,33 ± 0,29 vs AOP: 1,21 ± 0,34, $p<0,05$). In addition, animals submitted to preventive and therapeutic exercises showed lowest percentage of insulin immunomarked area (AOS: 44,13 ± 6,05 vs AOT: 35,77 ± 4,98 and AOP: 27,57 ± 1,86, $p<0,05$), and lower optical density for insulin (AOS: 1,21 ± 0,003 vs AOT: 1,13 ± 0,008 and AOP: 1,07

± 0,03, p<0,05), Nuclear Factor Kappa B (NF-kB) (AOS: 8.99 ± 7,75 vs AOT: 0,15 ± 0,13 and AOP: 0,00 ± 0,00, p<0,05) and Growth Transformation Factor b (TGF-b) (AOS: 0,87 ± 0,48 vs AOT: 0,09 ± 0,15 and AOP: 0,00 ± 0,00, p<0,05) in the pancreatic parenchyma, as well as, lower tissue lipid peroxidation (AOS: 10,80 ± 1,36 vs AOT: 5,26 ± 5,44 and AOP: 1,12 ± 1,31, p<0,05), with the effect being greater in preventive exercise group. Both exercise protocols promoted a smaller area of fibrosis (AOS: 9,56 ± 6,20 vs AOT: 3,53 ± 4,26 and AOP: 1,20 ± 1,38, p<0,05), increased activity of antioxidant enzymes, such catalase (AOS: 0,45 ± 0,07 vs AOT: 0,89 ± 0,42 and AOP: 1,12 ± 0,08, p<0,05) and Glutathione Peroxidase (GPx) (AOS: 0,06 ± 0,03 vs AOT: 0,09 ± 0,01 and AOP: 0,19 ± 0,02, p<0,05) and increased immunostaining for Hemeoxygenase-1 (HO-1) (AOS: 0,15 ± 0,16 vs AOT: 0,79 ± 0,89 and AOP: 2,18 ± 1,46, p<0,05), and preventive exercise also had a greater effect on these variables.

Conclusions and Support: The beneficial effects of physical exercise, mainly preventive, on body adiposity, insulinemia, morphology, inflammation and oxidative stress in the pancreatic parenchyma under combined conditions of aging and obesity are promising in the prevention of degenerative processes in this organ under both conditions. Support: Cappes, Fapesb and CNPq.

ID: 3424

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR PROTECTION BY OVARIAN HORMONES IN FEMALE RATS WITH 6-OHDA-INDUCED PARKINSONISM

Introduction: Parkinson's disease (PD) is a neurological disorder caused by environmental and genetic factors, characterized by the death of dopaminergic neurons of the substantia nigra pars compacta (SNpc), leading to a decrease of dopamine in the striatum. In addition to motor symptoms, PD has several abnormalities, among which are cardiovascular changes, such as orthostatic and postprandial hypotension, and blood pressure lability. Studies demonstrate gender differences in PD pathogenesis, indicating that female hormones have a protective role against disease development. However, no studies examining cardiovascular changes in a female rat model of parkinsonism exist.

Objective: To evaluate cardiovascular parameters, autonomic modulation, and peripheral NO concentration in ovariectomized or Sham Wistar rats, induced to parkinsonism by bilateral 6-OHDA infusion in SNpc. To evaluate cardiovascular parameters, autonomic modulation, and peripheral NO concentration in ovariectomized or Sham Wistar rats, induced to parkinsonism by bilateral 6-OHDA infusion in SNpc.

Methods: The study was approved by the ethics committee of the State University of Londrina, process number: 175/2018. Wistar female rats were subjected to ovariectomy (OVX) or sham surgery. After seven days, these animals were submitted to stereotatic surgery for bilateral infusion of 6-hydroxydopamine (6 mg/mL in 0.2% ascorbic acid in sterile saline) or vehicle solution in their SNpc. On the 14th experimental day, catheterization of the femoral artery was performed and after 24 hours they were submitted to the recording of cardiovascular parameters. After registration, euthanasia was performed to collect organs. Analysis of cardiovascular variability and spontaneous baroreflex were performed. The nitrite concentration in the heart, thoracic aorta, abdominal aorta, and plasma was measured by the Griess method.

Results: The injury induced by 6-OHDA was confirmed by the decrease in the levels of DA in the striatum in the 6-OHDA groups compared to their control groups (p<0.0001). The effectiveness of ovariectomy surgery was confirmed by the decrease in uterine weight in the OVX groups compared to sham groups (p<0.0001). The sham-6-OHDA group had no decrease in the mean arterial pressure compared to sham-saline group, whereas the OVX-6-OHDA group presented a baseline decrease in comparison to sham-6-OHDA (p<0.05). The OVX-6-OHDA group showed a nitric oxide increase in the heart and abdominal aorta (p<0.001), whereas the sham-6-OHDA group did not. The VLF variability component decreased in the sham-6-OHDA and the OVX-6-OHDA group, when compared to sham-saline (p<0.001).

Conclusions and Support: We suggest a cardiovascular protection by ovarian hormones in PD with a possible NO involvement. Further studies are needed to assess the mechanisms involved in these changes. Financial support: CAPES.

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Área: FISIOLOGIA DO EXERCÍCIO

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Title: EFFECTS OF EXERCISE ON MORPHOLOGICAL AND FUNCTIONAL CHANGES IN THE LIVER IN AN ANIMAL MODEL OF AGING AND OBESITY

Introduction: Aging and obesity are associated with the development of metabolic disorders resulting from morphological and inflammatory changes and oxidative stress in organs. These changes can cause damage to the liver parenchyma, such as tissue fibrosis and hepatic steatosis, compromising organ function. Physical exercise performed in a therapeutic and preventive manner has demonstrated beneficial effects in the prevention or reversal of diseases associated with obesity, by improving the inflammatory and oxidative profile in tissues.

Objective: To evaluate the effects of preventive and therapeutic exercises on morphological and functional parameters in the liver of Wistar rats in a model of aging and obesity induced by a high-fat diet.

Methods: Twenty-four male Wistar rats (initial age = 4 months and final age = 14 months) were used and were randomly assigned to three aged (A) and obese (O) experimental groups (n = 8 / group): sedentary (S), therapeutic exercise (T) and preventive exercise (P). Immunomarking was performed for macrophages, lipid peroxidation was assessed by measuring thiobarbituric acid reactive substances (TBARS). The activity and immunostaining of the antioxidant enzymes catalase, Glutathione Peroxidase (GPx) and Hemeoxygenase 1 (HO-1), as well as the parameters of macrovesicular and microvesicular steatosis were evaluated in the liver.

Results: Animals submitted to preventive and therapeutic exercises showed lower immunostaining for macrophages (AOS: 41.60 ± 11.25 vs AOT: 15.95 ± 2.28 and AOP: 10.28 ± 2.20; p<0,05), less tissue lipid peroxidation hepatic (AOS: 0.78 ± 6.63 vs AOT: 2.72 ± 0.75 and AOP: 1.51 ± 0.70, p<0,05), smaller area of fibrosis (AOS: 0.87 ± 0.24 vs AOT: 0.13 ± 0.16 and AOP: 0.05 ± 0.03, p<0,05), increased activity of catalase antioxidant enzymes (AOS: 0.78 ± 0.09 vs AOT: 1.55 ± 0.029 and AOP: 1.85 ± 0.020, p<0,05), GPx (AOS: 0.08 ± 0.03 vs AOT: 0.12 ± 0.02 and AOP: 0.21 ± 0.06, p<0,05) and increased immunostaining for HO-1 (AOS: 0.08 ± 0.03 vs AOT: 0.23 ± 0.04 and AOP: 0.39 ± 0.15, p<0,05), with the effect being greater in the preventive exercise group. The macrovesicular hepatic steatosis was lower in animals submitted to the two exercise protocols (AOS: 48.19 ± 22.30 vs AOT: 15.38 ± 9.88 and AOP: 9.90 ± 7.02, p<0,05), however, the microvesicular steatosis (AOS: 51.33 ± 22.20; AOT: 41.99 ± 9.41; AOP: 33.83 ± 7.89, p=0,109) did not differ between experimental groups.

Conclusions and Support: The beneficial effects of physical exercise, mainly preventive, on inflammation, oxidative stress and steatosis in the liver tissue, in combined conditions of aging and obesity, are promising in the prevention or treatment of pathological degenerative conditions in this organ in both conditions. Support: Cappes, Fapesb and CNPq

ID: 3426

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: PARTICIPATION OF THE INOS ISOFORM IN CARDIOVASCULAR AND AUTONOMIC DYSFUNCTION IN MALE RATS SUBMITTED TO PARKINSONISM BY 6-OHDA

Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disease. In addition to motor symptoms, there are non-motor symptoms, more specifically in the cardiovascular system: blood pressure lability, postural and postprandial hypotension. Several studies have shown the involvement of nitric oxide (NO) in the processes that lead to neurodegeneration in PD. Administration of inducible nitric oxide synthase (iNOS) inhibitors promoted neuroprotection in rats with unilateral injection of 6-OHDA, as well as providing protection for neurotoxic effects of the MPTP injury. NO appears to be involved in cardiovascular changes in 6-OHDA parkinsonism.

Objective: To evaluate the participation of the iNOS isoform in cardiovascular and autonomic function in animals submitted to parkinsonism by 6-OHDA in SNpc, as well as the mechanisms involved in phenylephrine hyporeactivity in rings with endothelium in these animals.

Methods: The study was approved by the ethics committee of the State University of Londrina, process number: 14605.2018.88. Wistar male rats (280-320g) were submitted to stereotactic surgery for bilateral microinfusion of neurotoxin 6-OHDA (6 mg/mL in 0.2% ascorbic acid in sterile saline) or vehicle solution for the Sham group. On the day of stereotaxy until the day of femoral artery catheterization, the animals were treated with an iNOS inhibitor, S-methylisothiourea (SMT - 10 mg / kg - ip) or saline solution (0.9% - ip). The animals were divided into 4 groups: Sham-Salina; Sham-SMT; 6-OHDA-Saline, 6-OHDA-SMT. After 6 days, they underwent catheterization of the femoral artery and, 24 hours later, the recording of mean arterial pressure (MAP) and heart rate (HR). Another groups of animals (6-OHDA and Sham), were submitted to vascular reactivity of the aorta for phenylephrine in the presence of L-NAME (10-5 M), SMT (10-6 M) and indomethacin (10-5 M).

Results: The efficacy of the lesion was confirmed by the decrease in the concentration of dopamine in the 6-OHDA-Saline and 6-OHDA-SMT groups in relation to their controls (p <0.001). There was no difference in MAP and HR between the 4 groups. For spectral analysis of systolic blood pressure (SBP), there was no statistical difference in variance and in the LF component. For the VLF component, there was a difference between the Sham-SMT group in relation to the 6-OHDA-Saline (p <0.05). The pulse interval (PI), we did not observed differences in the variances and in LF and HF components. However, there was a difference in the LF/HF ratio, in which interaction between treatment and surgery was observed and the 6-OHDA SMT group showed higher values than the 6-OHDA-Saline and Sham-SMT groups (p <0.05). Vascular reactivity data show that indomethacin did not alter Rmax to Phenyl in 6-OHDA rings; while the incubation with L-NAME increased Rmax to Phenyl in 6-OHDA rings (p = 0.00), as well as S-MT (p = 0.40), demonstrating that the pathway involved in

the hyporeactivity of these animals is through iNOS. In relation to pD2, there was an increase only with L-NAME in the 6-OHDA rings. For the Sham group, indomethacin and SMT (0.625) did not interfere with Rmax, however, incubation with L-NAME (p = 0.00) increased Rmax in SHAM rings. Regarding pD2, there was an increase only with the incubation with L-NAME in the SHAM rings.

Conclusions and Support: Our data suggest a participation of the iNOS isoform in the cardiovascular changes of animals submitted to parkinsonism by 6-OHDA. Financial support: CAPES.

ID: 3171

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EXERCISE DURING PREGNANCY PREVENTS MEMORY DEFICITS CAUSED BY MATERNAL SEPARATION IN PRE-PUBERTAL FEMALES

Introduction: Maternal separation (MS) causes harm changes linked to stress and is a lead risk factor to mental disorders such as depression, anxiety, and Alzheimer's disease (AD). Its effects include learning and memory deficits related to oxidative stress increase and alterations in neurotransmitters systems. Physical exercise reverses memory deficits caused by MS through the restoration of neurotransmitters levels and redox balance. In addition, maternal exercise prevents AD-related memory deficits. However, the effects of maternal exercise on offspring female rats submitted to MS have not been elucidated.

Objective: To investigate the effects of physical exercise (PE) performed before and/or during pregnancy on the memory of maternal separated prepubertal female offspring.

Methods: This study was approved by the Institutional Committee of Animals Use (protocol 042/2018). 24 adult female rats were divided into 3 groups: I. Pre-gestational and Maternal exercise (PGE); II. Maternal Exercise (ME) and; III. Control (CT). The group I underwent to a 60-70% VO2max treadmill running PE for 4 weeks. After, this group continued the PE during all pregnancy (3 weeks; 8m/min until pregnancy day 14; 6m/min until delivery). The group II only performed the PE during the pregnancy. The group III did not perform PE. After birth, the offspring of each group were separated into two subgroups of 8 rats per dam: no intervention (NI) or MS. MS offspring were separated from their mothers 3h per day during the first 10 days of life. Only female offspring were evaluated in this study. In the postnatal day 22, the females were submitted to recognition and spatial memory tests: object recognition (OR), social recognition (SR) and Barnes Maze (BM). Data from OR and SR was converted in percentage of time and analyzed by one-sample t-test (theoretical mean = 50%). Data from BM by repeated measures ANOVA and two-way ANOVA followed by Fisher's LSD post-hoc.

Results: In the OR test, CT+NI group explored for more time the novel object (P = 0.02), as well PGE and ME non-submitted to MS groups (PGE+NI: P = 0.02; ME+NI: P = 0.01), demonstrating memory consolidation. MS caused memory deficit since exploration time was about 50% in both objects (CT+MS: P = 0.06). ME was able to prevent this deficit (ME+MS: P = 0.01). Surprisingly, PGE did not prevent the memory deficit caused by MS (PGE+MS: P = 0.28). In the SR test, CT and non-MS groups explored for more time the non-familiar animal (CT: P = 0.01; CE: P = 0.04; ME: P = 0.04). MS caused memory deficit (P = 0.051) and only ME was able to prevent MS effect (ME+MS: P = 0.04; CE+MS: P = 0.99). During the BM training, ME was the only group that learned and was able to find the escape on the first day of training (Trial 1 vs Trial 3 P = 0.02). In the BM test, ME+NI needed less errors compared to PGE+NI offspring to find the escape (P = 0.024). Additionally, the PGE+MS group spent a lower time than CT+NI group on the target quadrant of BM, which means memory deficit (P = 0.038). Still, ME+MS group performed better than the PGE+MS group (P = .01), spending more time in the target quadrant.

Conclusions and Support: The practice of physical exercise initiated during pregnancy enhances spatial learning and avoids deficits in recognition memory caused by maternal separation. CNPq. The autors recognize the intention to participate of Prêmio Branca de Almeida Fialho - 2020.

ID: 3427

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: Ê-POSTER

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Title: AUTONOMIC AND RESPIRATORY PROFILES OF MICE SUBMITTED TO SHORT-TERM SUSTAINED HYPOXIA

Introduction: Previous studies from our laboratory described changes in the coupling between sympathetic and respiratory activities in rats submitted to sustained hypoxia (SH), resulting in increased sympathetic activity and hypertension. Current studies in our laboratory are showing that the same protocol of hypoxia in mice does not induce hypertension. However, studies about possible changes in the sympathetic and respiratory coupling in mice submitted to SH are lacking in the literature.

Objective: To characterize the sympathetic and respiratory activities of mice submitted to SH using the in situ working heart-brainstem preparation (WHBP).

Methods: C57BL/6J mice (7-8 weeks old, ~25g) were submitted to normoxic or SH protocol (24h, FiO2 0.1). At the end of SH or normoxic protocol, mice were deeply anesthetized with Isoflurane, sectioned sub-diaphragmatically, exsanguinated, eviscerated and decerebrated precollicularly. Mice were then placed into a recording chamber for the WHBP, the descending aorta was catheterized and perfused with ACSF. This catheter was also used to record the perfusion pressure. In addition, phrenic (PN), abdominal, (AbN), cervical vagus (cVN) and thoracic sympathetic (tSN) nerves were dissected and their activities were recorded using bipolar glass electrode. All experimental protocols were approved by the institutional Ethics Committee on Animal Use (CEUA #163/2019).

Results: The frequency of the baseline PN discharge (PND) was significantly reduced in the SH (n=11) in relation to control (n=26) group (0.69 ± 0.06 vs 1.13 ± 0.10 Hz, P=0,0154). The incidence of Late-E bursts in the abdominal nerve AbN activity (AbN) in the SH group (n=10) was significantly increased in relation to control (n=20) group (83.3 ± 7.7 vs 24.3 ± 8.0%, P<0,0001). The duration of the total expiratory phase in SH (n=11) was longer than in control (n=22) group (1.13 ± 0.16 vs 0.67 ± 0.07s, P= 0,0002) as well as the duration of post-inspiration (0.78 ± 0.12 vs 0.35 ± 0.04s, P= 0,0032). The tSNA in the SH group (n=10) presented a significant reduction in comparison to the control group (n=16) in the final expiration phase (E2, 19.0 ± 4.3 vs 39.7 ± 4.2%, P= 0,0203).

Conclusions and Support: The data are showing that SH mice presented active expiration and longer expiratory phase in the WHBP. The changes in the respiratory pattern were associated with reduction in the sympathetic activity in the E2 phase of the respiratory cycle. We conclude that changes in SH mice's respiratory pattern reduce the baseline sympathetic activity, which may explain why these animals are not hypertensive after SH. Support: FAPESP, FAEPA, CAPES, CNPq

ID: 3174

Área: NEUROFISIOLOGIA

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Title: TRANS FAT DURING THE DEVELOPMENT PERIOD CAUSES DEPRESSIVE AND ANXIOUS BEHAVIOR IN A MODEL OF Drosophila melanogaster

Introduction: Trans fatty acids can be easily found in processed foods, being present in the diet of a large part of the world population. Its consumption is associated with neurological changes, since it can be incorporated into neural membranes, resulting in neurophysiological changes. Also, it can increase susceptibility to neurological diseases, for example, depression and anxiety. The formation of neural membranes occurs with greater intensity during the developmental period. Therefore, the type of fatty acid offered during this period is of great importance for neural development. Given the search for alternative models that enable a better understanding of human diseases, in this work, we use the model of Drosophila melanogaster, which has demonstrated great homology with human systems.

Objective: The objective of the work is to evaluate the exposure to a diet rich in trans-fatty during the development period on depressive and anxiety-like behavior in Drosophila melanogaster.

Methods: Parents were divided into 4 groups, containing 50 flies of both sexes in each: (1) RD (corn flour, sugar, wheat germ, salt, powdered milk, and agar), (2) SHVF (HVF replaced fat values of RD in the same proportion), (3) HVF 10% (RD with 10% HVF) and (4) HVF 20% (RD with 20% HVF). After 7 days of exposure, the parents were removed from the medium, leaving the larvae and eggs. The flies born from this environment (1-3 days) were used to perform forced swimming behavioral tests: to assess depressive-like behavior and; Light/dark: to assess anxiety-like behavior, and open field: to assess locomotor ability. Statistics: For the normality of data, the Shapiro – Wilk test was used for homogeneity, Bartlett's test. Normal and homogeneous data were assessed by one-way ANOVA, followed by Tukey, whereas abnormal and/or heterogeneous data were assessed using Kruskal-Wallis, followed by Dunn's. It was considered significant when $p < 0.05$.

Results: In the forced swim test, there was a reduction in the first immobility time and in the total swimming time in flies exposed to all HVF concentrations, compared to the RD (One-way ANOVA, $F_{3, 16} = 24.42$, $p < 0.0001$; $F_{3, 16} = 25.17$, $p < 0.0001$). There was an increase in the total immobility time in flies exposed to all concentrations of HVF, when compared to RD (One-way ANOVA, $F_{3, 16} = 25.17$, $p < 0.0001$). The number of swimming attempts was similar between groups (One-way Kruskal-Wallis, $p = 0.0472$). In the light/dark test, there was a significant increase in the total time on the dark side of the box in flies exposed to all concentrations of HVF, compared to RD. Besides, the group exposed to 20% HVF remained on the dark side longer, when compared to SHVF (One-way ANOVA, $F_{3, 20} = 90.96$, $p < 0.0001$). The locomotor capacity of the flies was not affected (One-way ANOVA, $F_{3, 16} = 0.99$, $p = 0.42$).

Conclusions and Support: We demonstrated that exposure to trans fatty acid during the development period could lead to behavioral changes associated with depression and anxiety, with no influence of locomotor damage. In addition, Drosophila proved to be a promising model, bringing positive results in assessing disorders related to psychological changes. Support: CAPES, CNPq.

ID: 3430

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: MUSCULAR FITNESS AND HEALTH INDICATORS IN YOUTH

Introduction: Children and adolescents have shown a secular decrease in physical fitness levels and an increase in the incidence of chronic diseases such as obesity, diabetes, hypertension and their associated cardiometabolic risk factors (blood pressure, % fat mass, lipemia, glycaemia and insulin resistance). In contrast, high levels of physical fitness might be associated with a protective effect on cardiometabolic healthy.

Objective: To verify whether different levels of muscle strength affect health indicators in children and adolescents.

Methods: The study was approved by the University Research Ethics Board (CAAE: 40235214.4.0000.5347). Forty-eight children and adolescents aged between 10 to 17 years old of both sexes participated in the present study. They were allocated into three groups according to their percentile (P) of handgrip force, measured by an analogical hand dynamometer: Low-Fit group (<P30%, n=11; 17.5±6.2 kgf), Moderate-Fit group (P>30% to P<80%, n=27; 26.3±10.0 kgf) and High-Fit group (P>80%, n=9; 35.6±13.1 kgf). Health indicators were considered as anthropometric characteristics as body mass index (BMI), percentage of fat mass (%FM), fat-free-mass (FFM), ratio waist to height (W/S), and cardiometabolic variables as systolic (SBP) and diastolic blood pressure (DBP), and mean arterial pressure (MAP). The %FM and FFM mass were measured by skinfolds. Hemodynamic variables were measured using electronic automatic-measurement arterial blood pressure device. The mean ± standard deviation values were used in the descriptive analysis. Differences among groups were tested with analysis of variance (ANOVA One-way). Bonferroni adjustments were done for post hoc comparisons. The level of statistical significance was set at a<0.05.

Results: No differences were found among groups according to their anthropometric characteristics. BMI (kg.m-2), W/S ratio (cm), FM (%) and FFM (kg) were, respectively: 20.3±5.5, 0.43±0.07, 24.9±14.0 and 32.9±7.4 for Low-Fit; 19.7±3.1, 0.41±0.04, 22.1±9.8 and 37.6±11.0 for Moderate-Fit; and 21.5±3.9, 0.41±0.03, 21.3±10.6 and 41.6±8.3 for High-Fit. In addition, no differences were established among groups for hemodynamic variables (p>0.05). SBP, DBP and MAP (mmHg) were, respectively: 109±11, 62±6 and 78±7 for Low-Fit; 111±13, 61±5 and 78±7 for Moderate-Fit; and 119±14, 63±9 and 82±8 for High-Fit.

Conclusions and Support: Conclusions: Different levels of muscle fitness did not affect health indicators in children and adolescents. Financial Support: The authors CDFP and NCB were supported by a scholarship from CAPES.

ID: 2923

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: THE UNIPODAL FLEXION EVOKES AN ADAPTIVE MICROCIRCULATORY REFLEX IN THE CONTRALATERAL FOOT

Introduction: The study of movement related adaptive microcirculatory physiology has been focused in provocation tests or quasi-static position changes, specially in the lower limb. It is the case of the reactive hiperemia procedure or the passive modification of the limb related with the body – the leg elevation test or the pending leg test. Recent studies drawn our attention to the cross-talk established between different sensors and effectors in the foot microcirculation when only one limb is stimulated such as in the veno-arterial reflex.

Objective: This study aimed to explore the perfusion variations in a unipodal support activity between the support and the unsupported limb with no joint load, a strategy that might be interesting for rehabilitation.

Methods: This exploratory protocol was previously approved by the institutional Ethical Commission (code reference: CE03/2013.12). Five healthy participants (26.0 ± 6.5 years old) of both sexes were selected after informed written consent. All participants had normal vascular function evaluated by the ankle-arm index. The protocol involved changing the orthostatic position to unipodal support and later recovery, returning to the standing position. Perfusion variations were assessed on the dorsal aspect of both feet using Laser Doppler flowmetry (LDF) as the reference method and Polarized Light Spectroscopy (TiVi system) which allowed to obtain the red blood cell concentration in the measured region of interest.

Results: Significant differences were detected during unipodal support for LDF perfusion in the support member (p = 0.043) and in the member without associated load (p = 0.043) with significant increase in the perfusion. Concentration of Red Blood Cells (CRBC) also detected an increase in both limbs, but it was not statistically significant (support member p = 0.345; unloaded member p = 0.500). Systolic and diastolic blood pressure increased slightly without statistical significance.

Conclusions and Support: The present results, although preliminary, are inline with previous studies exposing a similar microcirculatory reflex which seems to indicate a complex adaptive mechanism with systemic haemodinamical impact that should be further investigated. Support: Fundação de Ciência e Tecnologia (FCT) UIDB/04567/2020 and UIDP/04567/2020 Keywords: Microcirculation; Laser Doppler flowmetry; Polarized spectroscopy; Unipodal support; adaptive contralateral perfusion reflex.

ID: 3180

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: HUMAN PHYSIOLOGY TEACHING INVOLVING INTERDISCIPLINARY LEARNING WORKSHOPS

Introduction: Research on the formation of concepts has shown that students of basic as well as higher Education present difficulties in the construction of physiology thinking. Considering that biochemical studies allow the understanding of processes that guarantee the maintenance of life (that is, physiology), studying the contents of human physiology and biochemistry in an integrated manner is a pertinent and challenging proposal.

Objective: The goal of the presente work were to integrate physiology and biochemistry lessons by learning workshops related to the prevention of endocrine and cardiovascular diseases, mainly those related to hypertension and diabetes. In addition, to describe the experience in relation to this active teaching methodology as well as the student perception related to this didactic experience involving educational activities and health services by integration of school community and University.

Methods: The project was approved by the Research Ethics Committee with Human Beings of the State University of Feira de Santana (No. 1,524.897). The experimental design and application of this methodological approach were elaborated and conducted in two main stages, respectively, and involved students at all grade levels. First, high school students crafted panels, banners and didatic models of anatomical, biochemical and physiological sistems preferably using recycled materials and laboratory practices using easily accessible materials for biochemistry experiment. These activities are often implemented through university-school collaborations, involving teachers and students of universities and public schools. Second, interdisciplinary learning stations were created with the aim of working with students on the contents of physiology and biochemistry. To identify the level of student satisfaction was developed a structured questionnaire consisting of closed questions where all respondents are asked the same questions and alternatives of answers. The Likert scale was used.

Results: Eighty-one (81) students from the first grade of secondary education of the school were present in the ativities. Integrating physiology and biochemistry lessons, workshops teaching were aplicated as a tool that could help the student to contemplate the complexity of the concepts and mechanisms involved in maintaining the internal body environment. For this purpose, various educational activities and workshops were implemented, including dialogued lectures, demonstrations with didactic models, practical classes with cardiorespiratory and anthropometric measures. In the present study, the students were able to express their difficulties during this process, as well as to give their views about the interdisciplinary activities. In addition, 100% of the students reported interest in participating in new didactic experiences in the University.

Conclusions and Support: In the presente study, the immersion of students in the context of learning workshops contributed positively in the mediation of the teaching learning process, facilitating the absorption of the contents worked, especially for teaching physiology and health education. It's important to highlight, the need and relevance of this theme to be present at the university and at the basic school, with a view to learning significant impact that such methods can lead to. Support: Bahia State Research Support Foundation (FAPESB, 004/2018, PES 0008/2018), UEFS/Brazil.

ID: 2927

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: INVESTIGATION OF PLEIOTROPIC EFFECTS OF SIMVASTATIN IN A NON-ALCOHOLIC FATTY LIVER DISEASE MODEL

Introduction: Non-alcoholic fatty liver disease (NAFLD) is considered the hepatic manifestation of metabolic syndrome and is one of the most common chronic liver diseases, affecting about 30% of the adult population. NAFLD includes a wide liver disorder spectrum from simple steatosis to non-alcoholic steatohepatitis (NASH), in which steatosis progresses to hepatocellular injury, with lobular inflammation and fibrosis, increasing the risk of end-stage liver disease, liver cirrhosis and hepatocellular carcinoma, justifying the need to search for safe

therapeutic alternatives that minimize damage caused by NAFLD, especially vascular damage. Studies on the beneficial effects of statins on liver disease are still scarce, with most studies based on their lipid-lowering action, but recently there is growing interest in their pleiotropic action, regardless of their lipid-lowering effects.

Objective: Based on this, we aim to investigate the pathophysiology of liver dysfunction in NAFLD and the protective effects of simvastatin (SV) against metabolic and microcirculatory complications in NAFLD.

Methods: Non-alcoholic fatty liver disease was established by a high-fat and high-carbohydrate diet (HFHC) for 13 weeks. Oral treatment with SV was administered between weeks 6 and 13. Leukocyte recruitment was assessed by intravital microscopy. Laser Speckle Contrast Imaging flowmetry was used to assess microcirculatory liver perfusion. The measurement of thiobarbituric acid reactive substances, and activity of the anti-oxidative enzymes SOD and catalase were used to assess oxidative damage. The role of nitric oxide and inducible nitric oxide synthase in NAFLD was assessed by the Griess and western blot assay, respectively. The participation of the AGE-RAGE pathway was evaluated by fluorescence spectroscopy and western blot.

Results: NAFLD animals showed overweight and increase in fasting blood glucose, serum and hepatic triglycerides, serum cholesterol and fat deposition. Treatment with SV was able to decrease hyperglycemia and the increase in serum and liver triglycerides observed in animals with NAFLD. Liver histology confirmed the presence of severe steatosis and pronounced hepatocellular ballooning in animals fed with HFHC, which was markedly reduced by SV. Regarding the oxidative stress parameters, the NAFLD group showed a decrease in the activity of the catalase enzyme and an increase in the enzymatic activity of SOD and lipid peroxidation, however, the treated animal group with SV did not demonstrated these pathological changes. Concomitantly, the increase in iNOS expression, the greater bioavailability of NO, the increase in AGE content and the protein expression of RAGE in the liver, and changes in liver microcirculation (increased leukocyte recruitment and decreased perfusion) observed in mice fed a HFHC diet were not observed in SV treated animals, suggesting that microcirculation represents an important target for SV pleiotropic action.

Conclusions and Support: Therefore, the microvascular and metabolic effects of SV, regardless of cholesterol reduction, can contribute to the repositioning of statins with important therapeutic indications for NAFLD. Supported by CNPQ, FAPERJ and FIOCRUZ. Experimental procedures were approved by the Oswaldo Cruz Foundation Animal Welfare Committee (CEUA licence L-012/2018 A1).

ID: 3696

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

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Title: PHYSIOART: REINTERPRETING TARSILA DO AMARAL´S ARTWORK IN A PHYSIOLOGICAL CONTEXT.

Introduction: Recently we showed that the use of art in the classroom and direct participation in the artistic process, help students to enjoy and learn physiology (Flor et al., 2020). Here, in our physioart project we used reinterpretations of the Tarsila do Amaral´s artwork to arouse the interest of the undergraduate students to study physiology.

Objective: To motivate and help students to enjoy and understand physiology.

Methods: Biotechnology students from the Federal University of Paraíba/Brazil, enrolled in the human physiology course, participated in this project. The topic to be explored was the adrenal gland. The students were instructed to recreate an artwork from Tarsila do Amaral applying the physiological concepts of the adrenal gland. On a pre-established date, each group exposed their reinterpretations artwork in an event called “Physioart rediscovering Abaporu - Tarsila do Amaral tribute “. During the event, the students exposed their reinterpretations, as well as made a 10-15 minute presentation explaining the reason that led them to choose that specific artwork and which physiological conceptions of the adrenal gland were printed/ expressed in their reinterpretations.

Results: One of the reinterpretations was the painting “A boneca”, retitled as “Adrenaleca”, showing in the detail of the skirt the adrenal gland anatomy. Interestingly, “Adrenaleca” in opposition to the original artwork and against the sexism, was reinterpreted with a big head and a short skirt. The artwork “Estrada de Ferro Central do Brasil” was explored in the reinterpretation “Adrenal’s central regulation road” evidencing the phypothalamic-pituitary-adrenal axis. The artwork “La Tasse” was reinterpreted as “La Cushing” representing the original figure with symptoms of the Cushing’s syndrome (adrenal hyperplasia) which include; round face, abdominal fat, stretch marks, fragile skin and loss of the muscle mass. Another artwork reinterpreted was “A Negra”, which was repainted with Addison’s disease symptoms, where the low rates of the hormone cortisol promote weight loss, skin hyperpigmentation, mucosal sensitivity (reddish tone in the mouth) headache (hands on the head) and insomnia (expressive contoured eyes).

Conclusions and Support: Physioart helps us to show the physiology concepts in a more enjoyable and creative environment, which has motivated students to study and learn physiology.

ID: 3698

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: THE PERINATAL PROTEIN RESTRICTION AFFECT THE MALE AND FEMALE REPRODUCTIVE FUNCTION IN RATS OVERWEIGHT

Introduction: Some works has been showing the association with the low protein diet and some metabolic diseases, also the low birth weight is related with increased risk of cardiac diseases. The global number of infertility couples is approximately 15%, thus there is a elevated number of infertility people in countries with elevated number of famine people. The nutritional transition is the shift in the nutrients of the dietary that englobe changes in the economy, demographic and epidemiological. This way, our aim was evaluated the interference of perinatal low protein intake and a 'second-hit' by high fat diet in the male and female reproductive function.

Objective: Our aim was evaluated the interference of perinatal low protein intake and a 'second-hit' by high fat diet in the male and female reproductive function.

Methods: The dams were fed with 4% low protein diet (LP) or a 23% of protein chow diet (NP) during the first 12 days of sucking phase. During the PN 13 to 59 all the animals received a chow diet. To 60 until 90 days old, both LP and NP groups were divided, and half received a high fat diet (HF- 35% of fat) or a normal diet (NF-7%), the males and females were evaluated . The estrus cycle was assessed between the PN60 to 75. At PN90, the males and females were weighted, anesthetised, and euthanised and sexual organs, fat stoke, and hypothalamus were obtained and weight. The sperm in deferent duct was collected to motility and morphology analysis. The blood also collected and cholesterol and total protein were dosed.

Results: The female showed a reduction of estrus day in the LP/HF groups for 15 days. The LP males and females showed a resilience in the body gain by HF compared the NP/HF groups. Though both sexes showed an increase of fat stoke, although the LP groups had a low increase when received HF diet in relation to NP/HF groups. The reproductive organs were not affected by HF diet, however the perinatal LP intake caused a reduction in the testicles, epididymis and uterus weight, without any alteration in the ovaries weight. Also, the total cholesterol and protein in the blood was not affected in the NP/HF or LP/NF groups, controversy in the LP/HF groups there was an increase of total cholesterol and protein compared the LP/NF groups. The hypothalamus weight was similar between the groups, but there is an increase of weight in the females related to male. Only HF groups independently those received perinatal LP intake, showed a reduction in the mobile sperm and normal morphology sperm.

Conclusions and Support: Thus, the LP diet caused a permanent damage with reduction in the reproductive organs. However, the LP groups also showed a resilience in increase the body weight and fat stoke by HF diet. Together only HF diet induced sperm damages. Despite, the LP without the 'second hit' did not cause a huge damage in the reproductive organs weight or function, both male and female seems to be affected by HF diet. This way, these find may cause a reduction in the fertility of both male and female offspring. Also, the increase of the hypothalamus weight in female represents a sexual dimorphism which may explain why the males are more susceptible to diseases than females. But more studies are required to understand these findings.

ID: 3443

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: PHYSICAL VARIOLOGICAL VARIATIONS IN ENVIRONMENTAL GRADERS: IMPLICATIONS FOR VULNERABILITY EVALUATIONS TO CLIMATE CHANGE

Summary: Understanding the potential responses of organisms, populations and species to environmental change, including climate change, is one of the most urgent and interdisciplinary challenges facing contemporary science. In this context, the identification of patterns of variation, processes and underlying physiological mechanisms associated with the activity and occurrence/absence of organisms and their responses along environmental gradients (e.g., Janzen's, Brett's, Brattstrom's hypotheses) has shown promising character to indicate how different populations or species can (or cannot) cope with contemporary and future environmental/climatic changes. Several knowledge gaps still persist, but conceptual advances have occurred recently, largely due to the growing attempt to integrate different (i) areas of knowledge (physiology, ecology, biogeography, climatology), (ii) spatial (e.g., micro and macroenvironment) and temporal (present, past and future) scales and (iii) levels of biological organization (e.g., ontogenetic, organismic, population, species, etc.). Amphibians offer interesting opportunities for the development of such studies. From the organism's point of view, the warming of the climate does not imply an immediate increase in body temperature, but rather a decrease, which is intrinsically associated with water loss by evaporation due to highly permeable skin, thus showing the intricate interrelation between the thermal (i.e., energy) and hydric (i.e., mass) balances characteristic of this group of vertebrates. From the perspective of populations and species, amphibians encompass some of the most sensitive strains to environmental variation as well as some of the most resilient and successful invasive species; therefore, studies with anurofauna have the potential to improve our understanding of whether, and what, physiological parameters would be relevant in dealing with environmental/climatic changes in this diverse group - Brazil has the largest number of species in the world - and ecologically contrasting - aquatic, terrestrial and arboreal species occupy all continents except Antarctica . In this lecture, I will discuss the results of recent studies on patterns of intra- and interspecific physiological variation in amphibians along environmental gradients, highlighting the complexity of biotic and abiotic factors acting in synergy regarding responses of organisms, populations and amphibian species to environmental/climatic changes. Relationships between environmental factors beyond temperature and their impacts not only on physiological traits, but also on other biological parameters - body size, habitat use, phenological window, reproductive mode - need to be even better understood. An immediate consequence of this is that simplifications and/or generalizations of physiological variation patterns of organisms or populations (e.g., along

environmental gradients) for an entire species can be skewed and thus alter (or mask) estimates of local or regional vulnerability of fauna to impacts of environmental changes (e.g., climate forced extinctions).

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Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: ON THE SHORT-TERM CARDIOVASCULAR OSCILLATIONS OF A NEOTROPICAL TELEOST - THE TRAHIRA (HOPLIAS MALABARICUS)

Introduction: Short-term cardiovascular oscillations reflect the activity of essential reflex mechanisms involved in cardiovascular control, which are usually mediated by classic autonomic neurotransmitters and/or by nerve-secreted non-adrenergic non-cholinergic (NANC) factors. By understanding the patterns of cardiovascular oscillations and their mediators, it is possible to comprehend how animals thrive in their environments, unravel aspects of their evolutionary history, and pave the way for upcoming studies on the mechanisms of cardiovascular control in vertebrates. In this context, and given the lack of information on reflex cardiovascular control of teleosts, the present study sought to characterize the short-term cardiovascular oscillations and their mediators in the teleost Hoplias malabaricus.

Objective: Characterize the patterns of short-term heart rate (HR) and arterial blood pressure (BP) oscillations, and verify their autonomic mediation, in H. malabaricus.

Methods: H. malabaricus (N=4; 194±21g) were instrumented with a ventral aortic cannula to allow for the acquisition of HR (bpm) and mean BP (kPa). After 24 hours of recovery at 25°C, their cardiovascular variables were monitored for 1 hour. Then, the autonomic antagonists atropine and propranolol (1.5 mg kg−1 each) were jointly administered via intrarterial cannula, and after 1 hour for the drugs to exert their effects, cardiovascular variables were monitored for another hour. Later, the pulse interval (PI; ms; reciprocal of HR) and mean BP of 512 consecutive heartbeats were extracted from signals of each fish before and after autonomic blockade. These signal portions were used to analyze the animals' HR and BP variability, as well as their spontaneous baroreflex, on the CardioSeries v2.7 software using the following configuration: interpolation of 2 Hz, interpolated series of 256 data points, baroreflex sequences with a minimum length of 3 heartbeats, and a delay of 1 heartbeat between fluctuations in HR and BP. Data from fish under untreated condition and under autonomic blockade were compared using a two-tailed paired t test. The experiments were approved by the IBILCE/UNESP Animal Ethics Committee (#144/2016).

Results: Results are means±SEM. Under untreated condition, H. malabaricus exhibited a HR of 44.5±4.3 bpm (PI of 1403.0±148.8 ms), a mean BP of 4.6±0.3 kPa, a total HR variability of 215443.0±64319.0 ms2, a total BP variability of 0.036±0.007 kPa2, 23.0±8.2 baroreflex sequences, a baroreflex effectiveness index (BEI) of 0.18±0.05, and a baroreflex gain of 1637.0±339.5 ms/kPa. After autonomic blockade, the animals' HR increased to 82.0±6.6 bpm (PI decreased to 740.5±57.9 ms), mean BP remained at 4.8±0.1 kPa, total HR and BP variability were virtually eradicated (decreased to 41.3±11.0 ms2 and 0.001±0.001 kPa2, respectively), the number of baroreflex sequences and BEI remained unchanged (33.0±5.1 and 0.31±0.08, respectively), and baroreflex gain decreased to 212.7±64.3 ms/kPa.

Conclusions and Support: The tachycardia triggered by cardiac autonomic blockade is evidence that the parasympathetic nervous system plays the dominant role in short-term regulation of HR in H. malabaricus. The HR and BP variability patterns and baroreflex function of this species are similar to those documented for other ectotherms, being exclusively mediated by classic autonomic neurotransmitters, without the participation of NANC factors. This study was supported by São Paulo Research Foundation (FAPESP, Grant #2020/04335-0).

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Área: FISIOLOGIA COMPARADA

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Title: EVOLUÇÃO DA PLASTICIDADE, CÂMBIO DO CLIMA, E ATLÂNTICO SUL COMO REFÚGIO: APRENDENDO COM OS

CORAIS RECIFAIS

Introduction: Os recifes de coral estão fortemente ameaçados por mudanças climáticas. O aquecimento oceânico, e em menor grau a acidificação, promove a ruptura regulada da simbiose entre o coral hospedeiro e dinoflagelados fotossintéticos simbiontes (i.e. branqueamento), os quais são a fonte primária de radicais livres. Em holobiontes de águas oligotróficas, a fotossíntese provê até 98% da demanda energética do hospedeiro. Contudo, em águas com maiores níveis de sedimentação e nutrientes devido ao escoamento superficial do continente, tal contribuição cai para 40%, sendo o restante complementado heterotroficamente. Bermuda e Brasil ilustram tal oposta natureza físico-química das águas, manifestam corais de estreita relação filogenética, e hospedam, respectivamente, os recifes mais setentrional e austral do Atlântico.

Objective: Objetivou-se avaliar, como métricas indicadoras da fisiologia do branqueamento, a densidade de simbiontes, o conteúdo de clorofila a, a capacidade antioxidante e os danos em biomoléculas em diversas espécies de corais da costa do Brasil e do mar de Sargaços em Bermudas. Ainda, avaliou-se a taxa de calcificação como proxy de disponibilidade energética. Especificamente, testou-se a maior tolerância ao branqueamento dos representantes do Brasil devido ao também esperado maior potencial antioxidante, uma consequência da premissa de maior capacidade heterotrófica diante do tratamento induzido (amostras biológicas em análise).

Methods: Vinte espécies de corais, de ambas as localidades, foram avaliadas sob condições naturais e simuladas de mudanças climáticas (+2,5 oC, -0.3 pH; IPCC 2100). Uma filogenia com 65 espécies globalmente distribuídas foi aqui também proposta por verossimilhança usando-se marcadores moleculares (todo o DNA mitocondrial), sendo posteriormente utilizada para comparações via métodos filogenéticos.

Results: Contrariamente ao esperado, as espécies de Bermuda apresentaram maior densidade de simbiontes, conteúdo de clorofila e capacidade antioxidante, tanto em condições naturais quanto em simuladas. Contudo, as espécies brasileiras demonstram um expressivo efeito compensatório: mais clorofila por célula de simbionte, elevação no potencial antioxidante e menos danos em biomoléculas diante do aquecimento e acidificação. Ainda, os representantes do Atlântico Sul apresentaram uma maior taxa de calcificação em ambas as condições controle e tratamento simulado.

Conclusions and Support: Corroborou-se a hipótese de maior tolerância das espécies brasileiras, mas também se verificou uma co-evolucao das plasticidades simbiótica e antioxidante no Atlântico Sul, uma relação potencialmente dirigida pela emblemática natureza nutricional e luminosa das águas. Sugere-se, portanto, que políticas ambientais para conservação do seu potencial de refúgio para a vida marinha sejam imperativamente reforçadas e ampliadas.

ID: 3701

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: SHORT AND MODERATE PHYSICAL TRAINING ASSOCIATED WITH INTERMITTENT FASTING ATTENUATES METABOLIC DYSFUNCTION INDUCED BY EARLY OVERFEEDING

Introduction: The use of non-pharmacological strategies to improve metabolic syndrome in adulthood is necessary, since its prevalence is increasing worldwide. In addition, most experimental models have focused on preventing or treating metabolic dysfunctions early in life. Therefore, there is a demand to treat subjects already affected by metabolic diseases in adulthood, improving quality of life and extending lifespan. Several research shows that there is positive correlation between increasing individual's physical performance and metabolic improvements (e.g. increased glucose uptake, insulin sensitivity and oxidative metabolism). Similarly, it has been demonstrated that apart from its effects on body weight (BW) control, intermittent fasting (IF) improves glucose tolerance and insulin sensitivity in rodents. Moreover, IF has been shown to have comparable benefits to caloric restriction in improving metabolic health. Mechanistic insights from molecular biology have linked IF to the activation of peroxisome proliferator-activated receptor alpha (PPARα), which is a key factor involved in the regulation of energy homeostasis. In addition, the IF has shown to regulate both the thermogenesis of brown adipose tissue and adaptive thermogenesis of white adipose tissue.

Objective: To evaluate whether the combination of physical training with IF can improve the metabolic dysfunctions of overfed rats in early life.

Methods: At postnatal day 3 (PN3), litter size was standardized either with 9 pups per mother (NL - normal litter) or 3 male pups per litter (SL - small litter). At PN90, the litters were randomly split into five groups: NL; SL; SL-EX (small litter combined with exercise); SL-IF (small litter combined with intermittent fasting) and SL-EXIF (the combination of small litter with exercise and intermittent fasting). From PN90 to PN120 the groups were subjected to EX, IF or both. Moderate-intensity training protocol was performed on a treadmill for rodents, 3 times a week, with a workload corresponding from 55% to 65% of VO2max, with sessions of 44 minutes per day. IF protocol was 2:1 regimen, 2 days feeding followed by 1 day fasting; having food removed at 8:00 am and provided 24h later (8:00 am in the following day). In the SL-EXIF group EX and IF were never carried out at the same time.

Results: As expected, at 120 days old SL group presented hyperphagia, increased BW and fat pads, glucose intolerance and insulin resistance as previously described by our group and others. Regarding caloric intake, no differences were observed among SL-EX, SL-IF and SL-EXIF groups. Therefore, short and moderate exercise training initiated in adult life did not cause feeding changes. The SL-IF group showed a compensation in caloric intake after the fasting day, however 2:1 IF regimen leads to isocaloric IF. SL-IF and SL-EXIF exhibited a decrease in BW and fat pads. Interestingly, SL-IF had the lowest fat stores, comparable to those presented by NL group. On the other hand, SL-EX, SL-IF and SL-EXIF showed an increase in muscle mass, however, SL-EX presented the larger muscle mass relative to BW. Ongoing tests have shown that SL-IF and SL-EXIF have improvements in glucose tolerance.

Conclusions and Support: Initiating physical training and IF in adult life can lead to metabolic improvements in early-overfed rats. The evidence so far has shown that no synergistic effects between EX and IF have occurred. Further investigations are nedeed to determine the possible effects related to thermogenesis.

ID: 3702

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: HRV AS A TOOL TO ASSESS PROCEDURE RECOVERY THROUGH AUTONOMIC MODULATION

Introduction: Regarding animal use, analyzing the animal state is paramount. Different studies used a variety of parameters to verify it: behavior, mean heart rate, ventilation pattern, metabolism, etc. Analysis of Heart Rate Variability (HRV) is a well-known tool to provide information about autonomic modulation. Resting healthy vertebrates present diverse autonomic influences over instantaneous inter-beat intervals (RRi) and so it modulates fast and constant RRi alteration. Active, alarmed, or distressed vertebrates, on the other hand, have a less variable RRi. Hence, once resting HRV is described for a species, such information can be analyzed and checked to address resting reestablishment after a disturbance.

Objective: We aimed to verify if HRV reestablishment after disturbance would correlate to the procedure invasiveness degree and thus test the effectiveness of HRV as a tool to analyze the autonomic recovery of resting.

Methods: After we established their resting HRV, tegu lizards (Salvator merianae) underwent a series of procedures used in experimental biology protocols (each disturbance was followed by resting recovery): (1) handling for inspection; (2) intraperitoneal saline injection; (3) intraperitoneal injection of anti-inflammatory and antibiotic; (4) pre-anesthetic $CO_2$ sedation; (5) sedation followed by 30min isoflurane anesthesia; (6) and sedation followed by 2h isoflurane anesthesia (Ethics Committee approval code: 7382270916).

Results: After each disturbance, total HRV (analyzed as the Power Spectral Density of the frequency domain analysis) was reduced and later recovered, validating expected autonomic response after disturbance. Time for HRV recovery correlated with the disturbance level of invasiveness

Conclusions and Support: Considering the results, we suggest HRV can be an interesting alternative to contribute to the quality of experimental biology protocols. Support: CNPq.

ID: 3703

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Pampa - Uruguaiana - Rio Grande do Sul - Brasil

Title: PRETREATMENT WITH EGG WHITE HYDROLYSATE PREVENTS CARDIOVASCULAR DAMAGE IN RATS EXPOSED TO HIGH CADMIUM CONTENT

Introduction: The increase in heavy metal contamination has stimulated the investigation of therapeutic alternatives with antioxidant and chelating properties such as the hydrolyzate of egg white, a functional food with a high antioxidant capacity against metals.

Objective: To investigate the effects of pretreatment with egg white hydrolysate on cardiovascular damage induced by exposure to cadmium chloride ($CaCl_2$) in rats.

Methods: Three-month-old male Wistar rats (± 300 g) were divided into four groups and treated for 28 days: a) Untreated (Control - distilled water ip), b) Cd (First 14 days: distilled water ip; Next 14 days: Cadmium Chloride - $CdCl_2$ - 1mg/kg ip) c) EWH (egg white hydrolysate, 1 g/ kg/day per gavage), d) EWHCd (egg white hydrolysate, 1 g/ kg/day per gavage and last 14 days: Cadmium Chloride - $CdCl_2$ - 1mg/kg ip plus EWH). Acetylcholine (ACh) and norepinephrine (NE) dose-response curves were performed, and the main vascular pathways involved were investigated. Biochemical assay of reactive oxygen species (ROS), lipid peroxidation, total antioxidant capacity and activity of superoxide dismutase (SOD) were measured in MRA. The results are expressed as mean and SEM, compared by ANOVA followed by the Bonferroni test with significance level of $p<0.05$.

Results: The EWH prevented: a) the increased vasoconstrictor response to NE (Rmax of the concentration response curve to NE: Untreated: 92.9±2.2; Cd: 187.2±5.1*, EWH: 93.3±2.2, EWHCd: 96.0±24.0#) b) reduction in vasodilator response to ACh c) the endothelium vasoconstrictor – modulation and nitric oxide bioavailability involvement (E-: Untreated: 50.6±11.1; Cd: -0.3±3.8*; EWH: 42.5±9.6;

EWHCd: 33.7±8.4#; L-NAME: Untreated: 43±6.7; Cd: -15.3±3*; EWH: 28.1±5.4; EWHCd: 19±3.5#, %dAUC) d) the increased ROS production from NAD(P)H oxidase (Apocynin: Untreated: 12.9±1.6; Cd: 30.4±5.3*; EWH: 15.8±4.3; EWHCd: 13.6±1.4#; ML171: Untreated: 5.1±5.6; Cd: 4.1±6.4*; EWH: 3.0±3.1; EWHCd: 21±13.1# % dAUC) and contractile prostanoids from COX-2 (NS398: Untreated: 15.9±10.3; Cd: 53.0±6.5*; EWH: 1.8± 5.3; EWHCd: 19.4±6.61#, % dAUC) e) the increased ROS production, lipid peroxidation and antioxidant capacity induced by Cd exposure.

Conclusions and Support: Therapeutic supplementation with EWH prevents vascular damage induced by exposure to high concentrations of Cd. Support: Brazilian Government (Conselho Nacional de Desenvolvimento Científico e Tecnológico – CNPq 307399/2017-6; CAPES; FAPERGS (PROBIC) and by the Spanish Goverment [MICINN AGL 89213, 2017]. (CEUA/Unipampa 012/2019)

ID: 3704

Área: FISIOLOGIA DO EXERCÍCIO

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Title: ACUTE COLD EXPOSURE IN AWAKE PHASE IMPAIRS AEROBIC PERFORMANCE AND MUSCLE STRENGTH IN MICE

Introduction: Brazilian researchers, militaries and other workers from Brazilian Antarctic Program (PROANTAR) are exposed to extreme cold exposure (CE) during labor activities (awake phase) in Antarctic field. Acute CE (ACE) decreases heat loss via cutaneous vasoconstriction and increases metabolic heat production through the oxidation of lipids and muscle glycogen during shivering thermogenesis. However, the effect of ACE on physical activity, which may impact on work capacity, are not completely understood.

Objective: to evaluate the alterations in aerobic and strength performance in a murine model of ACE during awake phase (i.e., dark light cycle), mimicking the condition experienced by Brazilian personal in Antarctica.

Methods: adult male CD-1 mice were kept in a thermoneutral environment (~29 oC; CON; n = 10) or exposed to cold environment (~4 oC; ACE; n = 9) from 7 pm to 7 am (i.e., awake phase). Seven to ten hours later, all groups performed forelimb grip strength test in grip strength meter and incremental load tests in treadmill, respectively, in order to measure peak resistance force (muscle strength) and peak oxygen consumption (VO2peak), peak running speed (Vpeak) and time to exhaustion (TTE). All experiments and protocols were approved by The Ethics Committee on Animal Use (CEUA 84/2020) from Federal University of Minas Gerais (UFMG).

Results: ACE significantly reduced TTE (14%; $P < 0.05$) and Vpeak (11%; $P < 0.05$) in incremental load test, without changing VO2peak and post-test glycaemia ($P > 0.05$). Muscle strength was also reduced by ACE (13%; $P < 0.05$). Despite increasing food intake (43%; 5,8 g in ACE vs. 4,1 g in CON; $P < 0.05$), ACE did not alter body mass ($P > 0.05$).

Conclusions and Support: ACE during awake phase impairs aerobic performance and muscle strength in mice, which may be detrimental to work capacity in Brazilian researchers, militaries and other workers in their first contact with cold environment in Antarctica. Supported by PRPq-UFMG (27764*27) e CNPq/CAPES/PROANTAR (442645/2018-0)

ID: 3455

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE DE SÃO PAULO - São Paulo - Sao Paulo - Brasil

Title: PROLONGED FAST ALTERS METABOLISM AND CARDIAC FUNCTION IN MALE WISTAR RATS

Introduction: Several studies have highlighted that food deprivation for long periods can trigger behavioral, physiological and metabolic changes.

Objective: The present study aimed to investigate the effects of a 48-hour fast on cardiac muscle metabolism and cardiac function.

Methods: Male Wistar rats aged 60 days were separated into two groups: fasted for 48 hours (FASTING) and fed (FED). After euthanasia, blood and heart were collected. The heart was excised and the left ventricular (LV) wall was separated. Analyzes of plasma biochemical parameters, dosage of metabolites, maximum activity of enzymes, as well as gene and protein expression were performed. Ventricular and hemodynamic records were also obtained.

Results: Prolonged fasting caused intense metabolic changes in LV. We observed a significant increase in the maximum activity of CPT1 (12.8% higher than FED, $p < 0.05$), a key enzyme for the oxidation of fatty acids, as well as a significant increase in ATP concentration (29.2% higher than FED, $p < 0.03$) and glycogen (32.9% higher than FED, $p < 0.03$). We also observed an increase in the maximum activity of the main enzymes of the glycolytic pathway HK (17.1% higher than FED, $p < 0.02$) and PFK1 (60.7% higher than FED, $p < 0.02$), and an increase in the phosphorylated protein AMPK (91% higher than FED, $p < 0.008$). Regarding cardiac function, we observed a reduction in contraction strength (20.5% lower than FED, $p < 0.02$) and in cardiac relaxation strength (22.9% less than FED, $p < 0.03$) after prolonged fasting. These changes were accompanied by a decrease in HR (10% lower than FED, $p < 0.03$) and an increase in diastolic filling time (20% higher than FED, $p < 0.04$). We also observed an increase in hematocrit in rats that were fasting (8% higher than FED, $p < 0.004$).

Conclusions and Support: It is possible that AMPK is involved in metabolic and physiological adaptations to prolonged fasting. Although we observed an increase in the oxidative potential and an increase in the available concentration of ATP, we believe that this long period of fasting compromises blood volume and, consequently, cardiac function. Financial Support. FAPESP (grants 2013/07607-8 and 2019/03196-0; CNPq; CAPES)

ID: 3714

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: Ê-POSTER

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Title: PROTEOMIC PROFILE OF MESENCHYMAL STEM CELL AND EXTRACELLULAR VESICLE IN A HYPOXIA CONDITION

Introduction: Mesenchymal stromal cells (MSCs) are known to be a candidate in the treatment of diverse respiratory disease mainly due to its immunomodulation, angiogenic, and tissue repair capability. However, MSC therapy presents limitations on account of the number of cells that need to be administrated and risk of thromboembolic event. On this basis, extracellular vesicles (EVs) presents as an alternative to a non-cellular treatment, since MSCs effects are mainly attributed to its paracrine secretion of EVs. Pre-conditioning of MSC in hypoxia conditions has been shown to increase the therapeutic effects of MSCs in several diseases. Here we hypothesized that EVs from MSCs conditioned to hypoxia may show a different proteomic profile compared to normoxia.

Objective: To compare the protein profile of MSC conditioned to normoxia (MSC-norm) and their EVs (EVs-norm) to MSC conditioned hypoxia (MSC-hyp) and their EVs (EVs-hyp) by proteomic analysis.

Methods: MSC cells were isolated from the bone marrow of 6 male Wistar rats. After achieving 80 to 90% of confluence, cells were then incubated in normoxia (21%$O_2$, 5%$CO_2$, 74%$N_2$) or hypoxia (1%$O_2$, 5%$CO_2$, 94%$N_2$) conditions during 48 hours. The MTT assay was performed to verify cell viability. Oxygen consummation rate (OCR) of MSC was measured using a high-resolution respirometer

(Oroboros®), in which we used the following drugs: pyruvate, malate, succinate (PMS), adenosine diphosphate (ADP), oligomycin, carbonyl cyanide 4-(trifluoromethoxy) phenylhydrazone (FCCP) and potassium cyanide. Total proteins from MSCs and EVs were isolated to mass-spectrometry analysis. Proteomic profile data were analyzed by STRING, PANTHER, and Reactome softwares.

Results: MTT assay indicated that cell viability was higher in MSC-hyp than MSC-norm ($p<0.001$). Basal respiration ($p=0.002$), ATP uncoupled respiration ($p=0.005$), maximal respiration ($p<0.001$) were lower in MSC-hyp than MSC-norm, while ATP coupled respiration ($p=0.847$), and non-mitochondrial respiration rate ($p=0.847$) did not differ. An overall of 3049 proteins were detected from MSC-norm and MSC-hyp, of which 635 proteins were identified only in MSC-norm and 250 only in MSC-hyp. Additionally, 1019 proteins were identified in EVs-norm and EVs-hyp, of which 89 were found only in EVs-norm and 316 only in EVs-hyp. Proteins found in MSC-norm and EVs-norm were mainly involved in immune system activation and angiogenesis process while proteins found in MSC-hyp and EVs-hyp were mainly involved in glycolysis and gluconeogenesis but also in immune system activation and angiogenesis process.

Conclusions and Support: Prior incubation of MSC to hypoxia conditions changed the protein profile of cells and their EVs to a more glycolytic profile, which has been shown to enhance cells' immunomodulatory and angiogenic capacity. This change in proteomic profile may provide a better therapeutic effect in respiratory diseases with an inflammatory profile and tissue damage. CEUA: 024/17 Financial Support: CNPq, CAPES, INCT-Regenera, FAPERJ

ID: 2954

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Instituto de Ciências Biomédicas - SAO PAULO - Sao Paulo - Brasil

Title: PEDUNCULOPONTINE AND LATERODORSAL TEGMENTAL NUCLEI CHARACTERIZATION IN A MOUSE MODEL OF PARKINSON'S DISEASE

Introduction: Parkinson's disease (PD) is neurodegenerative motor disorder evidenced by loss of dopaminergic neurons of Substantia nigra compacta (SNpc) which promotes a reduction of dopamine at nigrostriatal pathway. PD patients presents classic symptoms as tremor at rest, postural instability and bradykinesia. Otherwise, non-classic symptoms as neuropsychiatrics and cognitive deficiencies, sleep disturbances, sensorial dysfunction and respiratory instability could affect those patients at later stages of this disease. Important regions for sleep regulation and breathing pattern, the pedunculopontine (PPTg) laterodorsal (LDT) tegmental nuclei, are composed by cholinergic, glutamatergic and GABAergic neurons located in the pontine region

Objective: Our main hypotheses are: a) PPTg and LDT neurons have been degenerated in a PD-model; b) PPTg and LDT neurons are able to increase their activity induced by high levels of CO2, after PD-induction.

Methods: We used 30 adult mice (20-25g) that express the fluorescent green protein in cholinergic, glutamatergic or GABAergic cells specifically (Chat-cre, VGlut2-cre and VGat-cre; N=10/group). All animals were anesthetized with isoflurane (2% balanced in O2) and received intrastriatal vehicle or 6-OHDA injections bilaterally (CEUA: 6641200919). Ten days after surgery, the animals were exposed to hypercapnia (7% $CO_2$, 21% $O_2$, balanced with $N_2$, 3 hours) in order to activate chemosensitive neurons in PPTg and LTD. At the end, tyrosine hydroxylase (TH) in SNpc and fos and choline acetyltransferase in PPTg and LTD staining were performed.

Results: In order to characterize the PPTg and LDT neuronal phenotype, we have quantified ~2440 glutamatergic neurons (which 17.6% are cholinergic) and ~2284 GABAergic neurons (which 0.2% are cholinergic) in PPTg; and ~1445 glutamatergic neurons (which 15.4% are cholinergic) and ~662 GABAergic neurons (which 0.5% are cholinergic) in LDT. The number of TH neurons in SNpc from 6-OHDA injected mice shows a reduction of 77% compared to vehicle ($103 \pm 4$ vs. vehicle: $449 \pm 40$ neurons, $p<0.001$). PD-induced mice also presented 25.8% less cholinergic neurons ($440 \pm 37$ vs. vehicle: $593 \pm 30$ neurons, $p<0.05$) in LDT compared to vehicle-injected group. Evaluating fos-activated cells induced by hypercapnia in PPTg and LTD, we observed less than 1% of cholinergic cells fos-activated in both regions in control and PD-induced animals. We noticed that fos-activated glutamatergic cells in PPTg were reduced in PD-induced ($8.0 \pm 3.7$ vs. vehicle: $21.2 \pm 3.9$, $p<0.05$) compared to vehicle animals. We also recognized an expressive number of GABAergic cells hypercapnia-activated in LDT, however, no differences were observed comparing groups (PD: $140.4 \pm 30.9$ vs. vehicle: $98.2 \pm 52.3$ neurons, $p>0.05$).

Conclusions and Support: In conclusion, our data shows for the very first time a loss of cholinergic neurons located in LDT in our model of PD, which guide us for the next step of this study, correlating the present findings with breathing and sleeping deregulation in this model of PD. Financial support: FAPESP, CAPES, CNPq.

ID: 2700

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal dos Vales Jequitinhonha e Mucuri - DIAMANTINA - Minas Gerais - Brasil

Title: SWIMMING DURING PRENATAL ZIKA VIRUS EXPOSURE PREVENTS BRAIN ATROPHY, DEPRESSION, ANXIETY AND MOLECULAR CHANGES IN THE HIPPOCAMPUS OF MOUSE OFFSPRING.

Introduction: Congenital exposure to Zika Virus (ZIKV) is associated to several neurodevelopmental disorders. Besides the underlying mechanisms of ZIKV remain unknown, how physical exercise impacts over the offspring borned from ZIKV-infected pregnancy also has not been evaluated.

Objective: We tested the hypothesis if swimming performed during ZIKV-infected pregnancy could have any neuro protector effect over the offspring.

Methods: All animal care and experiments were conducted according to the Principles of Laboratory Animal Care (Brazilian Arouca Law and US National Institutes of Health) and were approved by the Ethics Committee on Animal Use of the Universidade Federal dos Vales do Jequitinhonha e Mucuri (022/2019). Twelve weeks old female and male Swiss mice were mated in our facilities in a 2:1 ratio, respectively, for 24 hours. Dams were separated from the males after this period. ZIKV (106 PFU) or an equal volume of 100uL of saline was injected intraperitoneally in the dams at embryonic day 10.5. Female mice were randomly assigned into three groups: Control group, intraperitoneally injected with saline (Control); untrained group, intraperitoneally injected with ZIKV (ZIKV); and trained group, intraperitoneally injected with ZIKV (ZIKV/swim). The exercise protocol for the dams consisted of 1 adaptation week and 4 weeks of swimming training. Swimming training sessions consisted of 60 minutes, 5 following days per week during 4 weeks and started 1 week before mating. Pup's body mass and brain weight were measured. Behavioral tests in the offspring were performed at postnatal days 30-35. Thereafter, hippocampal levels of IBA-1, GFAP and BDNF were measured by western blot analysis.

Results: Swimming during ZIKV-infected pregnancy inhibits brain atrophy, and the development of anxious and depressive behaviors. A pregnancy exposed to ZIKV leads aberrant activation of microglia (IBA-1) and astrocyte (GFAP) with a reduction in cell proliferation and survival (BDNF) in hippocampi of mice offspring, which are inhibited through physical exercise during pregnancy.

Conclusions and Support: Our findings reveal that swimming during ZIKV-infected pregnancy is a capable agent of inhibiting brain atrophy, changes in behavior and inflammation in the hippocampi in the mice offspring.Support: Coordenação de Aperfeiçoamento do Pessoal de Nível Superior (CAPES).

ID: 3212

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de São Carlos (UFSCar) - São Carlos - Sao Paulo - Brasil

Title: HORMETIC-LIKE DOSE-RESPONSE OF ALTERNAGIN-C, A PROTEIN ISOLATED FROM URUTU SNAKE VENOM, ON FISH CARDIAC CONTRACTILITY

Introduction: Alternagin-C (ALT-C) is an ECD (Glu-Cys-Asp sequence)-containing disintegrin-like/cysteine-rich domain released from metalloprotease alternagin isolated from the crude venom of the snake Rhinocerophis alternatus, popularly known as urutu. Previous studies demonstrated that ALT-C induces endothelial cell proliferation and angiogenesis both in vitro and in vivo by up regulating the expression of vascular endothelial growth factor. Therefore, ALT-C may be considered an interesting tool for experimental studies of cardiac function due to its potential application to the development of therapeutic strategies for cardiovascular diseases.

Objective: The aim of this study was to evaluate the effects of different doses of ALT-C on ex vivo cardiac contractility of the freshwater fish Hoplias malabaricus (also known as trahira), an alternative model organism to contractile function studies.

Methods: This study was performed under the approval of the Animal Ethics Committee at the Federal University of São Carlos (CEUA/UFSCar # 045/2012). Fish were treated with three different single doses of ALT-C (0.25, 0.50 or 1.00 mg kg-1, via intra-arterial, n = 10 in each group) or with sterile saline (control group, n = 10). After seven days, fish were euthanized and the hearts were carefully removed. Strips were excised from the ventricle and their ends were tied in two metal rings. One ring was attached to an isometric force transducer through a stainless steel wire, other was tied around platinum electrodes connected to a stimulator, which delivered electrical square pulses of 8 ms, and 80 V. Preparations were immersed in a bath containing oxygenated Ringer solution at 25 °C. The contraction force at different stimulation frequencies (force-frequency relationship - FFR) and cardiac pumping capacity (CPC) were evaluated under normoxic (Ringer bubbled with a gas mixture of 2% CO2 and 98% O2) and hypoxic conditions (gas mixture of 2% CO2, 3% O2; and 95% N2).

Results: Hormetic-like (biphasic) dose-response relationships were observed for cardiac force development. ALT-C treatment with 0.25, 0.50 and 1.00 mg kg-1 significantly improved FFR and CPC curves to ~325, 195, and 76% relative to controls, respectively. Low ALT-C doses also increased maximal electrical stimulation (from 2.0 to 3.0 Hz), shifting the optimum frequency curve to the right. However, the highest dose of ALT-C the maximal frequency supported by the ventricular strips (from 2.0 Hz to 1.6 Hz). A left- and downward shift in the FFR and CPC curves was detected in all experimental groups in response to hypoxia. However, ALT-C groups exhibited significantly ($P< 0.05$) higher Fc and CPC values (~264, 157, and 142%, for 0.25, 0.50 and 1.00 mg kg-1, respectively), when compared to controls in all stimulation frequencies.

Conclusions and Support: ALT-C treatment improved contractile function and provided protection of myocardium against hypoxia-induced

negative inotropism, mainly at lower doses. Future studies on the action of ALT-C on cardiac contractility in mammals are needed, given its potential application, as seen for the experimental fish heart model. FAPESP (Proc. 12/10993-4).

ID: 2701

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE FEDERAL DOS VALES DO JEQUITINHONHA E MUCURI - DIAMANTINA - Minas Gerais - Brasil

Title: EXERCISE-INDUCED CONSEQUENCES ON DEPRESSION IN OLDER ADULTS: A SYSTEMATIC REVIEW.

Introduction: Depressive disorders are common among elderly individuals. Depressive symptoms are present in 7% of older adults according to the World Health Organization, being related to higher mortality and diminished quality of life. There is a prediction that depression will be one of the highest healthcare costs in middle and higher income countries by 2030. Physical inactivity might lead to negative effects on mental health in the elderly.

Objective: The purpose of this review was to systematically explore the benefits of physical exercise (aerobic and resistance exercise) in reducing or inhibiting the development of depressive symptoms among elderly, and reporting also its biological mechanisms.

Methods: We used the following electronic databases to do our search: PubMed, LILACS and Scielo. The search was carried out through the following medical subject headings (MeSH) combination: ¨ageing¨, and ¨exercise¨, and ¨depression¨. We adopted as inclusion criteria: a) studies that evaluated humans (clinical trials or randomized clinical trials or cohort studies); b) studies that were published in the last 5 years (June-2015 until June-2020). Then, we proceeded the reading of the titles, abstracts and methodology, and we adopted as exclusion criteria all studies that did not refer to any type of physical exercise or did not mention ageing and depression as the population and condition evaluated, respectively. At the end there were 07 selected studies at PubMed and none at LILACS or Scielo.

Results: All studies (100%) revealed beneficial effects of the physical exercise intervention on the depressive symptoms. The number of sessions per week was quite different between the studies. We identified studies to use the following number of sessions: 1 (14,28%), 2 (57,14%), 3 (42,85%), or 5 (14,28%). The duration of each session was 45 (14,28%). The physical exercise protocol lasted for 12 (28,57%), 21 (14,28%), 24 (14,28%), 26 (14,28%), 38 (14,28%), and 208 (14,28%) weeks. Moderate intensity was applied in 6 studies (85,71%), while high-intensity physical exercise just in 1 (14,28%). Aerobic or resistance training, at moderate or high-intensity, enhance circulating levels of IGF-I and the expression of the proteins in PGC-1α/FNDC5/Irisin pathway, which stimulates the enhancement of the expression of IRS-1 and PI3K inhibiting inflammatory mechanisms. The activation of PGC-1α/FNDC5/Irisin pathway also inhibits GSK3β. PGC-1α/FNDC5/Irisin pathway and IGF-I also contributes to enhance the levels of BDNF and its receptor, TrkB, mainly in the hippocampus and prefrontal cortex. This process conducts to upstream of ERK that translocates from cell cytoplasm to nucleus inhibiting depressive-like behavior.

Conclusions and Support: Thus, the main findings of this systematic review together indicate that the most common used physical exercise variables to treat depression successfully in the elderly, independently of being aerobic or resistance training, were 2 sessions per week, lasting for 60 minutes each session, during 12 weeks (3 months) at moderate intensity. Aerobic and resistance training at moderate or high-intensity induce positive effects on PGC-1α, FNDC5, Irisin, IGF-I, BDNF and ERK levels. Support: Coordenação de Aperfeiçoamento do Pessoal de Nível Superior (CAPES).

ID: 2702

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: THE BEZOLD-JARISCH REFLEX ACTIVATION AND THE SYSTEMIC INFLAMMATION INDUCED BY LPS IN RATS.

Introduction: The activation of the parasympathetic branch of the autonomic nervous system is very effective in the treatment of inflammatory diseases. However, much still needs to be investigated. An unexplored approach to study this pathway is through the Bezold-Jarisch reflex, which can be activated using a 5-HT3 receptor agonist, as the phenylbiguanide (PBG), causing bradycardia and vasodilation. This method allows performing studies in unanesthetized rats, mimicking more reliably, the physiological response of the organism to systemic inflammation, without the undesired effects of anesthesia.

Objective: To evaluate the effect of the Bezold-Jarisch reflex activation in unanesthetized endotoxemic rats induced by lipopolysaccharide (LPS).

Methods: Male Wistar-Hannover rats were divided into four groups: I) Saline (n=7); II) LPS (n=9); III) PBG+Saline (n=8); IV) PBG+LPS (n=8). Under ketamine/xylazine anesthesia catheters were inserted into the left femoral artery and vein, and into the abdominal cavity. Two days later, the arterial pressure was recorded, and saline (0.2 mL/kg, i.v.) as control or PGB (5 μg/kg, i.v.) was administrated. Five minutes later, saline (5 mL/kg, i.p.) as control or LPS (5 mg/kg, i.p.) was injected to induce systemic inflammation. Ninety minutes post LPS, the spleen, heart, hypothalamus, and a blood sample were collected to quantify the levels of tumor necrosis factor (TNF), interleukin (IL)-6; IL-1β, and IL-10. All procedures were approved by the Committee of Ethics in Animal Research of the Ribeirão Preto Medical School – University of São Paulo (protocol number 161/2016).

Results: As compared to baseline, PBG reduced the mean arterial pressure (115 ± 2 vs. 88 ± 5 mmHg, $p < 0.001$) and heart rate (380 ± 7 vs. 114 ± 26 bpm; $p < 0.001$), immediately after its administration, confirming the activation of the parasympathetic and inhibition of the sympathetic system. From the immunological point of view, PBG decreased the plasma levels of TNF (LPS: 775 ± 209 vs. PBG+LPS: 302 ± 60 pg/mL; $p = 0.013$) and IL-6 levels in the spleen (LPS: 37 ± 6 vs. PBG+LPS: 24 ± 4 pg/mg of tissue; $p = 0.028$). However, PBG did not change the other cytokines in the plasma or the other tissues evaluated (all $p > 0.05$).

Conclusions and Support: These findings indicate that the Bezold-Jarisch reflex has a limited ability to control inflammation but can reduce the release of some peripheral cytokines, in line with the notion of the cholinergic anti-inflammatory pathway. Support: FAPESP (2013/20549-7; 2017/05163-6; 2018/10455-9; and 2018/20939-3), CNPq (402076/2016-8), and CAPES-PROEX (88887.505419/2020-00).

ID: 2703

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: HUMAN BODY LOVERS PODCAST AS A SUPPLEMENTAL DIDACTIC TOOL TO ENGAGE STUDENTS IN LEARNING PHYSIOLOGY.

Introduction: The increased development of mobile phone technology is paving a fortuitous condition for the acquisition of any knowledge or skill by means of using mobile technology, anywhere, anytime. This type of learning, the mobile learning (m-learning), is appreciated by millennial students and busy learners.

Objective: In this study, we present a project of a podcast developed to serve as a supplemental didactic tool for students enrolled in a human anatomy and physiology course.

Methods: The log analytics of the podcast platform and a survey of the students (N=18) were used to collect the data. The podcast, called human body lovers, was available on Spotify and Spreaker, and the episodes addressed two contents: blood and physiology of bone. Since its release on October 2019, the podcast had 529 downloads, and an average of 22 downloads per week during the period of the course.

Results: Approximately 67% of the students listened to the podcasts as a study resource. Students rated the quality of the episodes as good/excellent (92.4 %), and they considered that the episodes have highly contributed to their learning (53.8 %). The most mentioned reason (53.8 %) for using the podcast was because it allows m-learning.

Conclusions and Support: Thus, the human body lovers podcast is a didactic tool that is likely to engage student in learning physiology, as an extracurricular resource. Also, it is a easy to develop educational tool that can be used an adjuvant material in Higher Education.

ID: 3727

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: DIGESTÓRIA

Forma de Apresentação: Ê-POSTER

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Title: EXPRESSION OF PROTEINS ASSOCIATED WITH SARCOPENIA IN REFLUX ESOPHAGITIS

Introduction: Gastroesophageal Reflux Disease (GERD) is related with crural diaphragm (CD) insufficiency, which supports the idea of a skeletal muscle deficiency in reflux esophagitis. Skeletal muscle atrophy is associated with changes of AKT phosphorylation (p-AKT), MURF-1 and atrogin levels while muscle weakness is related with SERCA and phospholamban levels of intercellular calcium cycling.

Objective: Now, we aim to assess if atrophy proteins are differently expressed in CD of patients with reflux esophagitis and if there is any relation with different grades of GERD.

Methods: After approval by the local Ethical Committee, we obtained human CD biopsies from volunteers,15 females and 10 males, aged between 25-62 years, at the time of anti reflux laparoscopic surgery (esophagitis group - GERD) or gallbladder surgery (control group - CT). Esophagitis group was further divided in grades A (GERD-A, n=4), B (GERD-B, n=6) or C (GERD-C, n=3), according the Los Angeles

scale. We studied different signaling pathways (AKT, p-AKT, MURF-1 and atrogin, all normalized by GAPDH). Data are shown as mean ± SEM and compared by one-way ANOVA (*,P<0,05).

Results: Protein expressions of p-AKT and atrogin were not different between CT and GERD groups. However, MURF-1 expression of GERD-C group (1.05 ± 0.18) differs when compared to GERD-B group (0.27 ± 0.11). CT group was not different from GERD-A and GERD-B groups.

Conclusions and Support: Human CD muscles of GERD patients have detectable expression of key proteins of atrophy signaling pathways (AKT, p-AKT, MURF-1 and atrogin). Our results show that CD of GERD-C patients had increased expression of MURF-1; a protein considered as a potential marker of skeletal muscle atrophy. Therefore, reflux esophagitis seems to be able to impact on the hypertrophy/atrophy muscular pathways in CD, especially in higher grades of GERD. Further studies will be necessary to clarify their respective cellular mechanisms and find out about their relationship with contraction related proteins. CAPES, CNPq & FUNCAP

ID: 3728

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR RISK IN HOMELESS SELF- REPORTED HYPERTENSIVE IN CENTRAL REGION OF SAO PAULO

Introduction: Systemic arterial hypertension (SAH) is a multifactorial and chronic clinical condition, associated with metabolic alterations that have a close relationship with cardiovascular events, fatal or not, where there is a prevalence of high levels of systolic and diastolic blood pressure, above what is expected for the age group. The risk factors (RF) associated with SAH range from external factors, such as internal ones. With the worsening of social inequalities in Brazil, there was an increase in the number of people in situations of street vulnerability. Cardiovascular diseases (CVD) are concerns for national health policies, due to their high prevalence and low control, which, when linked to environmental, socioeconomic, physiological and RF related to this population, provide greater morbidity and mortality of these individuals.

Objective: Describe the risk factors in homeless self-reported hypertension and relate it to the most serious cardiovascular risks.

Methods: It consisted of an exploratory, transversal and quantitative study, selected 40 volunteers in situations of street chosen for convenience in the central region of São Paulo, aged between 18 and 60 years; submitted to a semi-structured questionnaire between the months of August 2018 to January 2019; characterizing the socio-demographic profile and the presence of RF for CVD associated with the measurement of blood pressure (BP) and heart rate (HR) following the recommended guidelines. Approved by the institutional Ethics Committee under Protocol 036417, CAAE: 21519413.4.0000.5511, respecting the current rules.

Results: CVDs do not have a single etiology. The onset of SAH may be associated with a set of metabolically interconnected factors, such as: unbalanced diet, abusive consumption of legal and illegal substances, genetics, socioeconomic aspects, stress, sedentary lifestyle, diabetes mellitus and dyslipidemia, presented by the street population. The marginalization of these individuals leads to an increase in habits harmful to the health of the cardiac system. The average age is 44 years, where we found the majority 53% self-declared brown and the average BP was 134x88mmHg with HR 91bpm. 73% are sedentary, 68% have a family history of coronary artery disease and 50% and 15% have already had some serious cardiovascular event, such as heart attack and cerebrovascular accident, respectively. Another 35% reported using illicit drugs, which cause hyperstimulation of the sympathetic nervous system. And 55% and 63% reported being alcoholics and smokers, respectively, whose habits trigger the changes most associated with cardiac morbidity and mortality, such as toxicity and damage to important vessels. In addition, unbalanced eating causes changes in the microvisciousness of cell membranes and blood circulation, due to the accumulation of atherosclerotic plaques, conditions directly linked to the etiology of Acute Myocardial Infarction or Stroke

Conclusions and Support: With this study, it was observed that homeless are more predisposed to develop more severe and potentially fatal CVDs. The elucidated risk factors, associated with socioeconomic inequalities, crimes and the lack of self-care, increase the appearance of CVD's and contagious infection. Interventions with the distribution of personal hygiene kits, lectures to encourage self-care, alert about the dangers of harmful habits, prevention of comorbidities and health promotion.

ID: 3217

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: GLIAL CELLS AND P2X4 RECEPTORS OF THE SPINAL CORD DORSAL HORN MODULATE THE TRANSITION FROM ACUTE TO CHRONIC MUSCLE PAIN

Introduction: Chronic musculoskeletal pain is a worldwide public health problem with an important socio-economic impact. However, little is known about the mechanisms underlying the transition from acute to chronic pain, especially the ones with inflammatory etiology. Glial cells, mainly astrocytes and microglia, and P2X4 receptors have been extensively involved in chronic pain induced by insults to the sensory nervous system.

Objective: Considering peripheral inflammation can also activate glial cells and/or P2X4 receptors, this study aimed to analyze whether microglia, astrocytes and P2X4 receptors of the spinal cord dorsal horn are involved in acute and chronic-latent muscle hyperalgesia induced by an inflammatory insult in the gastrocnemius muscle of mice.

Methods: Male Swiss mice (2 months old) were used and all procedures were approved by Animal Research Ethics Committee of the State University of Campinas (protocol 5244-1). Carrageenan (100µg) was injected into gastrocnemius muscle to induce acute muscle hyperalgesia and, 10 days later, PGE2 (1µg) was injected at the same local to reveal the state of chronic-latent muscle hyperalgesia. Mechanical muscle hyperalgesia was quantified by Randall Selitto test at different time points of the acute and chronic period. The involvement of microglia, astrocytes and P2X4 receptors were assessed by intrathecal injections (L5-L6) of minocycline (inhibitor of microglia activation, 20 µg for three consecutive days), fluorocitrate (inhibitor of glial cells metabolism, 1 ng) or 5-BDBD (a selective P2X4 receptor antagonist, 50 µg), respectively. Area Under the Curve was used to evaluate the acute and chronic period of muscle hyperalgesia and the statistical analysis was performed by ANOVA with Tukey post hoc test.

Results: Treatment with minocycline before carrageenan reduced the intensity of the acute and chronic muscle hyperalgesia ($n=3$, $p<0.05$, ANOVA, Tukey test). When minocycline was injected before PGE2, there was also a reduction of the chronic muscle hyperalgesia ($n=6$, $p<0.05$, ANOVA, Tukey test). Treatment with fluorocitrate before PGE2 reduced the chronic muscle hyperalgesia ($n=4$, $p<0.05$, ANOVA, Tukey test). Finally, treatment with 5-BDBD before carrageenan reduced the intensity of the acute and chronic muscle hyperalgesia ($n=4$, $p<0.05$, ANOVA, Tukey test). When 5-BDBD was injected before PGE2, there was also a reduction of the chronic muscle hyperalgesia ($n=6$, $p<0.05$, ANOVA, Tukey test).

Conclusions and Support: This study showed that the transition from acute to chronic muscle pain is modulated by microglia, astrocytes and/or P2X4 receptors of the spinal cord dorsal horn. We suggest glial cells and/or P2X4 receptors as targets to control chronic muscle pain conditions. Financial Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001 and The São Paulo Research Foundation, FAPESP 17/17919-8.

ID: 3729

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Nove de Julho - SP - Sao Paulo - Brasil

Title: DISABLED KNOWLEDGE AS A NURSING DIAGNOSIS FOR CARDIOVASCULAR RISK IN THE STREET SITUATION POPULATION IN SÃO PAULO, 2019-2020

Introduction: Currently, the homeless population represents 24,344 people in São Paulo and their health inspires care. Due to their fragile situation, they are more susceptible to the appearance of pathologies, such as cardiovascular diseases (CVD), which are conditions that affect the heart and blood vessels. There are several risk factors (RF) for CVD, which can be divided between modifiable and non-modifiable, and their lack of knowledge increases the chances of developing these comorbidities.

Objective: To identify nursing diagnoses that relate insufficient knowledge with the appearance of cardiovascular diseases in the vulnerable street population.

Methods: This is an exploratory, transversal and quantitative field research, carried out in the central region of São Paulo between November 2019 and March 2020. A questionnaire previously structured and approved by the institutional Ethics Committee was applied under the protocol: 036417, CAAE: 21519413.4.0000.5511, to 173 volunteers, homeless, selected for convenience, aged 18 to 60 years, where information related to cardiovascular health was collected, in addition to measuring blood pressure (BP), heart rate (HR) and anthropometric data.

Results: Of the volunteers, 52% did not even study until high school and of these, 5% claim to be illiterate, 17% just read and write, 9% studied from the first to the fourth grade and 21% from the 5th to the 8th grade of elementary school. Of the other 47%, 16% have not completed high school and 23% have completed, 6% have not completed university education and 3% have this training. With regard to knowledge of RF for CVD, 99% said they did not know dyslipidemia, 98% age, 95% obesity / overweight, 93% stress, 92% genetics, 89% drugs and tobacco and 84% alcohol, evidencing their low knowledge and lack of health education. In addition, 72% of those surveyed said they had never attended a cardiology consultation, and only 28% did. The average blood pressure found in the study was 134x87 mmHg and HR was 87 beats per minute, indicating an increase. The main nursing diagnosis raised was deficient knowledge, in addition to risk-prone health behavior and ineffective health maintenance, also found in this population.

Conclusions and Support: It was found that the schooling of those studied varies, but regardless of the level of education, there was no knowledge of RF for the development of CVD, evidencing the need for health education. In addition, it is necessary to emphasize the need to expand and revise approaches that guarantee access to all, in a comprehensive and humanized manner.

ID: 3730

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

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Instituições: universidade Nove de Julho - São Paulo - Sao Paulo - Brasil

Title: WATER REPLACEMENT BY ALCOHOL AND RELATIONSHIP WITH ARTERIAL HYPERTENSION IN THE STREET SITUATION IN SÃO PAULO

Introduction: Water is vital for the proper functioning of the organism and its substitution for alcoholic beverages can generate systemic repercussions, this exchange can be noticed in the homeless population. The 2019 census verified 24,344 homeless people and in the midst of this social inequality it is observed that this population is exposed to several risk factors for the development of cardiovascular diseases (CVD).

Objective: To describe the relationship between the exchange of water consumption for alcohol and the increase in blood pressure.

Methods: The following work used the quantitative method, being an exploratory and transversal research, approved by the Institutional Ethics Committee under Protocol 036417, CAAE: 21519413.4.0000.5511. Conducted in the Center of São Paulo, the survey included 173 volunteers on the streets, between November 2019 and March 2020, aged between 18 and 60 years old, were submitted to a previously structured questionnaire and selected for convenience, being evaluated data sociodemographic variables pointing out the risk factors (RF) for CVD, measuring blood pressure (BP), heart rate (HR), abdominal circumference (WC) and cervical circumference (WC).

Results: 173 were studied, and the mean arterial pressure found was 134 x 87 mmHg and a pulse of 87 beats per minute (bpm). Of this population, 34% stated that they consume more alcohol than water, in those who make this substitution, the average values of systolic pressure were 147 mmHg, diastolic 96 mmHg and heart rate 91 bpm, values above those recommended by the Seventh Brazilian Guideline of Arterial hypertension. They were asked about access to water and 17% said it was through donations, followed by 15% in public drinking fountains and 12% in bars. . It is evident that the influence of the exchange of water for alcoholic beverages causes a significant increase in BP and this may be related to difficulties in accessing drinking water, as its main source is donations, which makes them dependent, in addition there is influence that most volunteers claim to consume alcohol and other substances harmful to the body.

Conclusions and Support: It was observed that water is vital for the proper functioning of the organism. Inadequate or insufficient intake can cause important imbalances in the body and its substitution with alcohol has proven to influence arterial pressure values, contributing to the appearance of other comorbidities.

ID: 2708

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Medicina de Botucatu/UNESP - Botucatu - Sao Paulo - Brasil

Title: EFFECT OF AQUATIC EXERCISE ON URETHRAL STRIATED MUSCLE MYOPATHY OF LONG-TERM MILD STZ-INDUCED DIABETES PREGNANT RATS

Introduction: Gestational Diabetes Mellitus (GDM) is related to skeletal muscle dysfunction, including pelvic floor muscle dysfunction (PFMD), which contributes to high prevalence of pregnancy specific urinary incontinence (PSUI). Studies in animal models of diabetes showed that long-term mild diabetes promotes changes in urethral striated muscle of pregnant rats, which can explain the high prevalence of PSUI. Thus, physical exercise during pregnancy, specially aquatic exercise, is effective to prevent GDM. However, the effect of aquatic exercise on diabetic myopathy of urethral striated muscle is still not elucidated.

Objective: Evaluate the effect of aquatic exercise on the myopathy of urethral striated muscle myopathy of long-term mild STZ-induced diabetes pregnant rats

Methods: The study was approved by the Ethics Committe on Animal Experiments (nº007/2016). At the first day of birth Wistar newborns received Streptozotocin 100 mg/kg (diabetic group) or citrate buffer (control group) subcutaneously. At adult life, animals presenting blood glucose between 120-300 mg/dL (diabetic group) and <120 mg/dL (control group) were mated with one male rat. After mating the animals were distributed in control – sedentary and exercised and diabetic – sedentary and exercised groups, starting the aquatic exercise protocol on gestational day 0 (60 minutes/day, 6 days/week) until gestational day 20. On gestational day 17 the oral glucose tolerance test was performed to confirm mild diabetes. On gestational day 21, the animals were euthanized and urethra and vagina were extracted and

the sections were cut and analyzed by: Hematoxylin & Eosin; Masson's Thricrome staining to morphometric analysis (4 samples/group); Immunohistochemistry to identify fast and slow muscle fibers (4 samples/group); and Transmission Electron Microscopy to ultrastructural analysis (3 samples/group).

Results: Decreased blood vessels area were observed in the urethral striated muscle of both diabetic groups and control – sedentary non-diabetic group. No differences were found in total area, striated muscle area, smooth muscle area, urothelium area, total collagen area, collagen in striated muscle area and collagen in smooth muscle area. Immunohistochemical analysis showed predominance of fast fibers in urethral striated muscle of all groups, however both diabetic groups – sedentary and exercised showed thin layer of fast fibers and loss of specific localization of both fast and slow fiber type compared to control group. Ultrastructural analysis showed sarcomeres disruption areas and disorganized Z lines in diabetic sedentary group. In contrast, diabetic exercised group showed intact sarcomeres.

Conclusions and Support: The present study demonstrated that long-term mild diabetes and aquatic exercise decreased blood vessels area in the urethral striated muscle of pregnant rats. Despite the absence of other morphometric changes in the urethral striated muscle, fiber type and ultrastructural diabetes-induced changes were found, which turns possible to suggest a deleterious effect of diabetes on the structure of urethral striated muscle, without reversing diabetes-induced changes by aquatic exercise. Support: This work received financial assistance from São Paulo Research Foundation (FAPESP) number 2016/01743-5 and 2018/03361-8.

ID: 3220

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Departamento de Fisiologia Geral do Instituto de Biociências da Universidade de São Paulo - São Paulo - Sao Paulo - Brasil

Title: Evaluation of rhythmic parameters in pre-adipocytes in response to cold stimulus

Introduction: Endogenous circadian clocks are found in all tissues and cells, including adipocytes. The local biological clock participates in the adipocyte proliferation and differentiation, lipid metabolism, endocrine function, and thermogenesis. In addition, we previously demonstrated that heat-induced increase of Per1 expression in mouse melanocytes and melanoma cells requires the participation of melanopsin.

Objective: Having this in mind, we investigated the effects of thermal stimulus on the biological clock of the pre-adipocytes (3T3-L1 cell line).

Methods: 3T3-L1 cells (WT), 3T3-L1 Per1::Luc and 3T3-L1 Bmal1::Luc cells were kept under constant darkness at 37°C and subject to two medium change in a 2 hour-interval to synchronize the cell population. 24 h after the last medium change, the cells were divided into two groups: 1) Thermal effect on the expression of clock genes - 3T3-L1 WT cells were exposed to 34°C for 1 h, and RNA extraction was performed 0, 2 and 6 hours after the low temperature stimulus to evaluate Per1 and Bmal1 expression by quantitative PCR. 2) Bioluminescence measurement in response to 34°C pulses - 10-4 M Luciferin was added with the last medium change, and the 3T3-L1 Per1::Luc and Bmal1::Luc cells were transferred to a real-time bioluminescence reader (Lumicycle) and divided in a control group kept at 37oC and the cold-treated group which received a daily pulse of 34oC during 1 h for 3 consecutive days. After the third pulse, the cells remained at 37oC for 3 additional days.

Results: A 34ºC pulse for 1 h induced an acute increase of Per1 expression as compared to the 37ºC group. No effect was seen on Bmal1 expression at the chosen time points. To evaluate long term rhythmic characteristics of Per1 and Bmal1 expression, 3T3-L1 Per1::Luc and Bmal1::Luc cells subject to repeated 34oC pulses were compared to cells kept at 37oC. A marked increase of Per1 bioluminescence was seen in response to the cold pulse, corroborating the quantitative PCR data, while Bmal1::Luc showed a decay of bioluminescence immediately after each pulse. Both responses resulted in increased bioluminescence amplitude, although with opposite directions. We identified a stronger period adjustment (qui-square periodogram test) in Per1::Luc cells and Bmal1::Luc cells, and cosene curve (variance %) in Bmal1::Luc cells in response to 34°C pulses as compared to the 37°C group.

Conclusions and Support: 3T3-L1 cells responded to low temperature stimulus with increased Per1 gene expression (3T3-L1 WT cells) and increase of bioluminescence amplitude (Per1::Luc and Bmal1::Luc) immediately after the end of the stimulus, as compared to the control 37ºC group. The anti-phase relationship between Per1 and Bmal1 was observed in Per1::Luc e Bmal1::Luc cell lines, since the time of Per1:Luc maximal bioluminescence was coincident with the lowest Bmal1::Luc recording. The temperature pulses exerted effects on the astringency of the period adjustment in previously synchronized pre-adipocytes, suggesting that temperature may act as a stronger synchronizing cue as compared to medium changes. Thus, we demonstrated that temperature is a remarkable modulator of the local clock in pre-adipocytes. Financial support: Capes, CNPq and FAPESP.

ID: 3732

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE NOVE DE JULHO - SAO PAULO - Sao Paulo - Brasil

Title: SYMPTOMS AND RISK OF CARDIOVASCULAR DISEASES RELATED TO COCAINE AND ALCOHOL ABUSE FROM HOMELESS PEOPLE LIVING IN DOWNTOWN SÃO PAULO

Introduction: Historically, human biopsychosocial conditions plays a big whole in the aggravation of several diseases.[1] In São Paulo alone, the last Census counted 24,344 homeless people.[2] In this population, mitigating factors for cardiovascular risk add up to both congenital and behavioral causes: one of the most harmful is the facilitated access and use of alcohol and illicit drugs, such as cocaine.[3] However, as the user develops tolerance to the drug, he will look for ways to potentiate the desired effect, so he makes the associated use of cocaine and alcohol.4 The biotransformation of these two substances occurs in the liver and generates cocaethylene metabolite, causing liver damage and increased toxicities city heart.5 The hepatic clinical symptoms amongst population added to the referred drug use are clear and alarming. Because it has vasoconstrictive properties, cocaine abuse is associated with effects such as ischemia and acute myocardial infarction.6

Objective: To relate cardiovacular risks resulting from cocaine and alcohol abuse with their clinical symptoms in vulnerable street populations in downtown São Paulo.

Methods: Quantitative field research, exploratory and transversal. Conducted between January and March 2020, the survey included 173 volunteers in vulnerable street situations in downtown São Paulo, chosen for convenience and respecting the age group of 18 to 60 years. The volunteers were submitted to a structured questionnaire approved by the institutional ethics committee under protocol 036417, CAAE: 21519413.4.0000.5511, where data on cardiovascular health, oral mucosa and sclera integrity were collected. The BP (blood pressure) of each interviewed was measured also the HR(heart rate) respecting the 7th Brazilian Hypertension Guidelines.

Results: 92% of respondents report using or have used alcohol and 73% of cocaine. Another 49% of the total respondents reported using or having used crack (cocaine in the form of crystals). Those who reported the simultaneous use of both substances (alcohol and cocaine/ crack) add up to 34%. Of these, 48% had icteric sclera and 19%, reddish. The average arterial pressure was 135 x 87 mm Hg, with a heart rate of 87 bpm.

Conclusions and Support: It was found great popularity of drug abuse (whether legal or illegal) amongst the homeless people living in the streets downtown. It is observed that the use of ethanol is drastically superior as opposed to illicit drugs. It is noticeable manifestation of liver in individuals who signs refer to the combined use of cocaine (either powder or crystals) and the alcohol studies demonstrating the attenuated damage cocaethylene metabolite. The average blood pressure it's found above the recommended by the 7th Brazilian Hypertension Guidelines, justifying the collected data aligned to the literature on the cardiovascular risks of drug use. Therefore, it constitutes not only cardiovascular risk, but also public health.

ID: 2709

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Odontologia de Araçatuba - FOA/UNESP - Araçatuba - Sao Paulo - Brasil

Title: MATERNAL APICAL PERIODONTITIS IS ASSOCIATED WITH CHANGES IN THE FINAL STEP OF INSULIN SIGNALING AND INFLAMMATORY PATHWAY IN GASTROCNEMIUS MUSCLE OF ADULT OFFSPRING. Tsosura, T.V.S.1, Chiba, F.Y.2, Carnevali, A.C.N.1, Mattera, M.S.L.C.1, Santos, R.M.1, Ta

Introduction: Fetal programming suggests that adverse stimuli applied during fetal development can result in change in the metabolism of the offspring, increasing the risk of disease in adulthood. Previous studies have shown that maternal apical periodontitis (AP) in rats promotes in their adult offspring: insulin resistance (IR), alteration in the initial steps of insulin signaling (IS) in gastrocnemius muscle (GM) and increase in the plasma concentration of tumor necrosis factor-α (TNF-α). TNF-α can activate the nuclear transcription factor kappa B (NF-kB) that decreases the gene expression of the GLUT4 glucose transporter. In this context, more studies are needed to investigate whether changes in IS observed in adult rats, offspring of rats with AP are also present in the continuity of the insulin cascade.

Objective: To evaluate insulin sensitivity, final step of IS and inflammatory pathway in GM of offspring of rats with AP.

Methods: (Ethics Committees on Animal Use, São Paulo State University, 00383-2019). Female Wistar rats (2 months old) were distributed into 3 groups of 5 rats each: control group (CN), group with 1 AP (1AP) and group with 4 AP (4AP). To induce AP, dental pulp of the first right maxillary molar (1AP) and of the first and second right maxillary and mandibular molars (4AP) were exposed to the oral environment through the occlusal surface by using a surgical round bur 0.1 mm diameter. Thirty days later, all groups were mated with normal male rats. Male offspring were distributed into 3 groups of 16 rats each: CN offspring group (CN-o), 1AP offspring group (1AP-o) and 4AP offspring group (4AP-o). The experiments were performed when the offspring reached 75 days old. The glycemia was measured by the glucose oxidase method (n=10/group). The insulinemia was measured by enzyme-linked immunosorbent assay method (n=10/group). Insulin sensitivity was evaluated by the HOMA-IR index (homeostasis model assessment of insulin resistance) (n=10/group). The Akt serine and threonine phosphorylation status after insulin stimulus (1.5 U, intravenous), TNF-α content and NF-kB p50 and p65 phosphorylation status in GM were quantified by Western blot method. Statistical analysis was performed by analysis of variance, followed by Tukey post hoc test

($p<0.05$). Data were expressed as the mean±standard error of the mean.

Results: The results showed that maternal AP in a single tooth or in four teeth promoted a decrease in insulin sensitivity (HOMA-IR index: CN-o: 20.74 ± 2.06; 1AP-o: 40.98 ± 3.93; 4AP-o: 60.50 ± 8.15) in adult offspring. However, only maternal AP in four teeth induced a reduction in Akt serine and threonine phosphorylation status and an increase in NF-kB p50 and p65 phosphorylation status in GM of their offspring. Maternal AP does not cause changes in the glycemia and TNF-α content of the offspring.

Conclusions and Support: Maternal AP was associated with decreased insulin sensitivity in the adult offspring. This metabolic alteration may be related to the impairment in the transduction of IS and activation of inflammatory pathway in GM of this offspring. This demonstrates the importance of maintaining maternal oral health to avoid impairments in the systematic health of adult offspring. Support: grant #2019/04182-2, FAPESP.

ID: 3221

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Ciências Aplicadas - FCA/UNICAMP - Limeira - Sao Paulo - Brasil

Title: THE ESTROUS CYCLE MODULATES THE ACUTE AND CHRONIC MUSCLE HYPERALGESYA IN FEMALE MICE

Introduction: Several studies have shown that the prevalence and intolerance to painful stimuli are higher in women and that this sexual dimorphism is modulated bygonadal hormones. However, little is known about the influence of gonadal hormones in chronification of muscle pain.

Objective: This study aimed to investigate whether the estrous cycle modulates the acute and chronic muscle hyperalgesia in female mice.

Methods: Swiss male and female mice (60 days old) from CEMIB-UNICAMP were usedin this study. All experiments were approved by the Animal Research Ethics Committee of the State University of Campinas (5234-1 / 2019). Carrageenan (Cg, 100 µg) was injected into gastrocnemius muscle to induce an acute muscle hyperalgesia and, 10 days later, PGE2 (1 µg) was injected at the same site to evidence the chronic-latent muscle hyperalgesia. The mechanical muscle nociceptive thresholds were quantified by theRandall &Selittotestin different periods of the acute and chronic muscle hyperalgesia. The vaginal lavage technique before and after injections were used to assess the estrous cycle.Area Under the Curve was used to evaluate the acute and chronic period of muscle hyperalgesia and the statistical analysis was performed by ANOVA with Tukey post hoc test.

Results: To assess the sexual dimorphism in pain, we compared acute and chronic muscle hyperalgesia of male mice and female mice in the different phases of the estrous cycle. When Cg was injected in the proestrus phase, the acute muscle hyperalgesia was greater than in male mice ($p<0.05$, ANOVA, Tukey test). While, in the other phases of the estrous cycle, the females showedlower acute muscle hyperalgesia than male mice ($p<0.05$, ANOVA, Tukey test). Females which were in the estrous phase at the time of Cg injection showed similar chronic muscle hyperalgesia than male mice($p>0.05$, ANOVA, Tukey test), while those in the other phases showed lowerchronic muscle hyperalgesia than male mice ($p<0.05$, ANOVA, Tukey test). Considering our results confirmed the sexual dimorphism in pain, we next analyzed the difference among the estrous cycle phases on acute and chronic muscle pain. The femalesthat received Cg in the proestrus phase showed greater acute muscle hyperalgesia when compared to other phases($p<0.05$, Two Way ANOVA, Tukey posttest), and the females that received Cg in estrus phase showed greater chronic muscle hyperalgesia when compared to other phases($p<0.05$, Two Way ANOVA, Tukey posttest). When we analyzed the estrous phase in which the females, previously sensitized by Cg, received PGE2, there was no difference in the chronic muscle hyperalgesia ($p>0.05$, Two Way ANOVA, Tukey post test).

Conclusions and Support: Conclusion: Our results demonstratedthat the estrous cycle modulates the acute and chronic muscle hyperalgesia. It seems that the estrous cycle phase in the first inflammatory insult is more determinant to chronification than the estrous phase in the second insult. Therefore, we suggest that the estrous cycle should be considered in treatments for muscle pain. Support: CAPES—Finance Code 001.

ID: 3733

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Nove de Julho - São Paulo - SP - Sao Paulo - Brasil

Title: DEFICIENT HEALTH IN THE COMMUNITY AS A NURSING DIAGNOSIS DETECTED IN THE STREET SITUATION POPULATION IN SÃO PAULO, 2019-2020

Introduction: Cardiovascular Diseases (CVD) contemplate the main causes of death worldwide. It is recognized that the Street Situation Population (SSP) presents health problems, having a large complex of risk factors (RF) for the development of CVD. Despite current public policies, it is observed that SSP has less access to health services that are equitable to their needs.

Objective: List nursing diagnoses related to cardiovascular risks and their complications in homeless groups in central areas of São Paulo.

Methods: It constitutes an exploratory, transversal, and quantitative study, carried out between the months of November 2019 to March 2020. Approved by the Institutional Ethics Committee under Protocol 036417, CAAE: 21519413.4.0000.5511. Assigned to 173 homeless volunteers in the central region of São Paulo, aged 18 to 60 years, selected for convenience, submitted to a previously structured questionnaire characterizing the sociodemographic profile and the presence of CVD RF, associated with the measurement of blood pressure (BP) and heart rate (HR). The data were analyzed and related to the Taxonomy of International Nursing Diagnoses NANDA I 2018-2020.

Results: The pressure values in the SSP showed an average of 134x87 mmHg, a value above the recommended and HR 87 beats per minute. It is evident that 69% do not attend health services, in which difficulties and impediments are reported, being mostly waiting for care (34%), discrimination (12%) and prejudice (10%). It is noteworthy that 72% reported never having had previous assistance in a cardiology consultation and of the remaining 28%, they had diagnoses of hypertension (51%), arrhythmias (6%), coronary diseases (4%) and heart failure (4%). It is noteworthy that 91% were unable to inform the past history of CVD. Thus, the main nursing diagnoses raised were Deficient Health in the Community; Risk-prone health behavior and risk of decreased cardiac tissue perfusion.

Conclusions and Support: It is understood that health services do not meet the specificities of SSP. It is necessary to overcome challenges for equitable and efficient health care, meeting the demands of this population, to promote health promotion and prevention. It was found that public policies are intended to reduce socioeconomic barriers, requiring review, application, and expansion to ensure compliance with the law that determines health as a right for all.

ID: 3734

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

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Title: OVERWEIGHT AND OBESITY AS NURSING DIAGNOSIS FOR CARDIOVASCULAR RISK IN THE STREET POPULATION OF THE CENTRAL REGION OF SÃO PAULO.

Introduction: According to the Ministry of Health (MH), the calculation for body mass index (BMI) is one of the parameters for assessing an individual's nutritional status. BMI above the recommended values is considered a risk factor for cardiovascular diseases (CVD). In São Paulo, according to the last Census, there are 24,344 people living in Street Situation (SS). Due to socioeconomic issues, lack of access and scarcity of resources, this population has its basic human needs affected. Inadequate food and substance intake leaves them susceptible to nutritional imbalance. Obesity causes silent inflammation that can cause changes in the renin-angiotensin-aldosterone system that helps control the volume of body fluids, retaining sodium and water, consequently raising BP. In addition, a factor that is generally related to diagnoses is the increase in the concentration of lipids in the bloodstream, which favors and accelerates the process of atherosclerosis, which is predisposing to several CVDs, since it causes narrowing of the arteries.

Objective: Highlight the relationship between BMI and cardiovascular diseases in the homeless population and support nursing diagnoses.

Methods: This is an exploratory, transversal and quantitative field research, approved by the institutional Ethics Committee under Protocol 036417 CAAE: 21519413.4.0000.5511. Appointed by 173 homeless volunteers in the central region of São Paulo, aged between 18 and 60 years, they were submitted to a semi-structured questionnaire, between the months of January 2020 to March 2020; blood pressure (BP), heart rate (HR), height and weight were measured. The data were analyzed and associated with the NANDA I International Nursing Diagnostic Taxonomy 2018-2020.

Results: Of the respondents, 28% are overweight and 6% are obese. The volunteers who presented low weight and normal weight found a mean BP of 123x86 mm Hg and HR of 90 bpm, 129x84 mm Hg and HR of 87 bpm respectively. In individuals with overweight and obesity, a BP above the recommended was highlighted, of 143x93 mm Hg for overweight FC 87 bpm, 159x104 mm Hg and 90 bpm HR for grade I obesity, and 153x95 FC 82 bpm grade II obesity. The nursing diagnoses raised were overweight and obesity.

Conclusions and Support: It was noted that the population with a BMI altered to overweight and obesity has a mean BP that is relatively altered and above that recommended. It is concluded that a relevant portion of the population in SS has nursing diagnoses of obesity and overweight.

ID: 2968

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: UFSCar - São Carlos - Sao Paulo - Brasil

Title: EFFECTS OF ADRENERGIC STIMULATION ON THE REGULATION OF VASCULAR TONE AND INTRACARDIAC SHUNTING IN SQUAMATA

Introduction: The regulation of systemic and pulmonary vascular tone is important for understanding the Squamata cardiovascular physiology, since the ventricle of these animals is partially divided allowing different proportions of blood recirculation in both circuits. Some studies tried describing of autonomic mechanism influencing intracardiac shunting. However, such descriptions are usually based on data form anesthetized animals, which can lead to biased conclusions due to depression of the autonomic nervous system (ANS).

Objective: To study the role of α and β-adrenergic stimulation on the regulation of systemic and pulmonary vascular tone and intracardiac shunting in squamates.

Methods: Rattlesnakes, Crotalus durissus (n=10; CEUA/UFSCar-5036120517), were anesthetized with isoflurane and decerebrated to remove the cerebral cortex and thalamus, in order to eliminate the central processing of any nociception, and to maintain ANS functional. Snakes were instrumented with cannulas and flow probes for recording 24h after recovery of: systemic (MAPsys) and pulmonary (MAPpul) mean arterial pressures; systemic (Gsys) and pulmonary (Gpul) conductances; and shunt fraction ($\dot{Q}$ pul·$\dot{Q}$ sys-1). The role of adrenergic stimulation was assessed by injection of adrenaline (2 µg·kg-1) and phenylephrine (5 µg·kg-1) before and after α and β-adrenergic blockade with phentolamine (2 mg·kg-1) and propranolol (2 mg·kg-1), respectively. MAP was expressed in KPa and conductance in ml·KPa-1·min-1·kg-1.

Results: Adrenaline caused increase on systemic vascular tone, and this effect was associated with Gsys decrease (0.64±0.10 to 0.40±0.05). Consequently, there was increase in MAPsys (5.13±0.23 to 7.55±0.30). Gpul remained unchanged (4.25±1.80 to 3.93±1.73), while MAPpul (2.70±0.23 to 3.46±0.30) and $\dot{Q}$ pul·$\dot{Q}$ sys-1 (0.24±0.07 to 0.30±0.08) were raised, maintaining right-to-left shunt (R-L shunt). Phenylephrine also increased the systemic vascular tone causing Gsys reduction (0.65±0.07 to 0.51±0.05) and MAPsys increase (5.40±0.17 to 6.12±0.23). There were no effects on Gpul (5.32±2.41 to 5.32±2.44), MAPpul (2.75±0.40 to 2.80±0.40) and R-L shunt (0.25±0.11 to 0.30±0.15). Following phentolamine, the stimulatory effect of adrenaline (Gsys: 1.20±0.27 to 1.80±0.34) and phenylephrine (Gsys: 1.18±0.26 to 1.27±0.27) was abolished. R-L shunt was maintained stable after adrenaline (0.27±0.08 to 0.24±0.06) and phenylephrine (0.53±0.26 to 0.62±0.26). After propranolol, adrenaline caused decrease on Gsys (0.48±0.07 to 0.33±0.04) and phenylephrine not changed the Gsys (0.40±0.04 to 0.32±0.05). Adrenaline increased the $\dot{Q}$ pul·$\dot{Q}$ sys-1 (0.20±0.05 to 0.26±0.06), while phenylephrine did not change R-L shunt (0.70±0.37 to 1.40±0.72). Adrenaline and phenylephrine did not change Gpul, even after blocking α (adrenaline: 6.26±2.21 to 6.05±2.07; phenylephrine: 6.70±2.40 to 7.37±2.53) and β-adrenergic (adrenaline: 1.50±0.51 to 1.36±0.52; phenylephrine: 1.96±0.70 to 1.75±0.55) receptors.

Conclusions and Support: Adrenergic stimulation has an important role for local regulation of vascular tone in systemic circulation. Pulmonary vasculature is less reactive to adrenaline and phenylephrine, demonstrating that systemic circulation is the main target to peripheral conductance adjustments at rest. Resting vascular tone is maintained mainly by α-adrenergic stimulation. The sympathetic regulation of systemic circuit is not essential for the control of intracardiac shunting in Crotalus. Support: CAPES/FAPESP.

ID: 2713

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE DO ESTADO DO RIO GRANDE DO NORTE - MOSSORÓ - Rio Grande do Norte - Brasil

Title: IN VITRO AND IN VIVO INVESTIGATION OF REGENERATIVE EFFECT ON THE SPINAL CORD IN THE PRESENCE OF SCIATIC NERVE FRAGMENTS WITH THE ADDITION OF Hyptis suaveolens (L.) Poit AND Croton blanchetianus Baill. ESSENTIAL OILS

Introduction: The spinal cord (SC) is affected in cases of direct or indirect trauma and some studies indicate that the peripheral nerves induce an environment conducive to regeneration. In addition, several medicinal plants have secondary metabolites with activities in the central nervous system.

Objective: This study aimed to analyze the regenerative effect on SC in vitro and in vivo in the presence of sciatic nerve fragments (SNFG) with the addition of essential oils (EOS) from Hyptis suaveolens (HS) and Croton blanchetianus (CB).

Methods: The HS and CB plants were submitted to the hydrodistillation process and the analysis of the chemical composition of the EOS was perfomed by gas chromatography and mass spectrometry. For the evaluation of cellular plasticity on SC in vitro, the SC cells were collected from newborn Wistar rats, and then cultured in six groups: one control (D-10) and the others with different combinations of sciatic nerve conditioned medium (SNCM) and HS and CB EOS. Cell morphometry was evaluated after 96 hours by phase contrast microscopy, and then the immunocytochemistry was performed for GFAP, GAP-43, NeuN and plasticity was performed by scanning electron microscopy. The groups were statistically compared using the Tukey and Bonferroni tests ($p < 0.05$). Thus, it was possible to evaluate the adherence, the plastic and trophic effect in groups cultured in D-10 plus EOS, with more visible morphological changes when compared to control groups. CB EO, especially, promoted the maintenance of cell expansion, indicating its action on the plasticity of SC cells. Regarding the regenerative analysis on SC in vivo, forty Wistar rats were used; sciatic nerve was removed from four animals, and thirty-six animals were submitted to a 4 mm thick medullary transection at the lower thoracic level; the animals were later separated in 6 groups (n=6): in group 1, 10µl of saline solution (5%)(SS); in group 2, FGNS plus 10µl of SS (SS + NS); in group 3, FGNS plus HS essential oil (EO) (HS + NS); in group 4, only HS EO; in group 5, FGNS plus CB EO (CB + NS) and in group 6, only CB EO (CB + NS) were inoculated. Posterior limb performance was assessed weekly for 12 weeks, using motor behavior score (BBB) and functional deficit associated with combined score behavior (CBS). Data from the behavioral tests of the treated groups were compared statistically.

Results: The different types of treatments allowed the recovery of the hind limbs movements of the animals of the FGNI and OES groups, and they showed a better recovery when compared to the SS and SS + NS groups. However, the groups with the EO of CB showed more significant results and superiority compared to the groups with the EO of HS.

Conclusions and Support: Therefore, the combination of OES and peripheral nerves such as NI, in vitro and in vivo, provided morphological plasticity and an improvement in the functional recovery of SC.

ID: 3225

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: SPECIFIC WAVELENGTHS DIFFERENTIALLY AFFECT COLOR CHANGE IN THE SEAHORSE HIPPOCAMPUS REIDI

Introduction: Bony fish exhibit a diverse set of coloring patterns as an adaptation to environment. Light works as a trigger for the sensory and endocrine systems. The opsins constitute a large family of proteins that are capable of responding to specific wavelength and to activate different signaling pathways. Melanopsin, a non-visual opsin initially found in Xenopus laevis melanophores, responsible for the synchronization of the mammalian biological clock, has also been suggested as a skin light sensor. Hippocampus reidi has a diverse color pattern and sexual dimorphism. Being a threatened species, several studies have been conducted in the last decade focusing on how different aspects of fish physiology influence its survival and growth rates.

Objective: To characterize the color change in juvenile and adult H. reidi and the influence of specific light wavelengths on color change and survival rate.

Methods: Seahorses were kept at controlled temperature (25ºC) and salinity (27 ppm). The photoperiod regimen was 12L:12D (white LED, 1.20 mW/cm², 420-750 nm). All experimental procedures were approved by the Ethics Committee of the institution (no. 317/2018) and the Brazilian Ministry of the Environment (SISBIO no. 65473/-2). Three wavelength treatments were tested (blue 442 nm, yellow 585 nm, red 650 nm), and a control white light. Wavelength and irradiance of each lamp were measured with a spectrometer and irradiance was standardized to 1.20 mW/cm² by adjusting the distance to the object. For the juvenile seahorses, mortality rates were recorded daily, and melanin content in the eye and skin was weekly quantified. To assess color change in adults, male seahorses were single housed under the above described conditions. Adult skin pigmentation was measured in vivo with a reflectometer every 4 hours, for 48 hours. Statistical analyses were performed by two-way ANOVA with Tukey's post-test. For reflectance values acrophase was calculated and compared between treatments by one-way ANOVA.

Results: Juveniles maintained in white light showed an earlier increase (7th day) in melanin content followed by a pigment decrease. However, the skin melanin content of juveniles kept in blue, yellow, and red wavelengths showed a progressive increase up to the 14th day, with a marked increase induced by the yellow wavelength. In the eye of juveniles, the yellow wavelength also induced a substantial increase in melanin levels compared to the other treatments. In addition, blue and yellow wavelengths induced a higher juvenile mortality rate (64% and 63%) in comparison to the other treatments. Adult seahorses showed a rhythmic color change over the 24 hours, the highest reflectance values obtained in the light phase, representing a daytime skin lightening, as a result of melanophore aggregation. In addition, blue and yellow wavelengths induced a phase shift in the acrophase, with advanced peak phases to the beginning of the light cycle, which suggests an important action of blue and yellow wavelengths on melanophore aggregation.

Conclusions and Support: The yellow wavelength (585 nm) was more effective on juvenile seahorse pigmentation, while blue wavelength (442 nm) exerted stronger effect on the regulation of adult physiological color change. In addition, both stimuli led to increased mortality, thus suggesting that assessment of melanin could be a stress biomarker in juvenile H. reidi. Our next step will be to evaluate opsin expression in H. reidi. Support: CAPES, FAPESP, and CNPq.

ID: 2714

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: UERN - MOSSORÓ - Rio Grande do Norte - Brasil

Title: TROPHIC BEHAVIOR OF CARDIOMYOCYTES IN CULTURE AFTER ADDITION OF CONDITIONED MEDIUM OF THE SYMPATHETIC GANGLIA IN THE PRESENCE OF THE FIBROBLASTIC GROWTH FACTOR2

Introduction: The cardiac muscle cell, also called cardiomyocyte, has specialized functions and plays a fundamental role in the maintenance of life, since it is responsible for the electrical and contractile activity of the heart. Like other specialized cells, it does not have an effective capacity for regeneration and its death or apoptosis is always an undesirable event, with sometimes catastrophic consequences, such as in Heart Failure (HF), which is known as the "final path" of heart diseases. Nevertheless, any cardiac disease in which cardiomyocyte apoptosis is implicated will develop, at some point in time, the HF syndrome. Evidence shows the influence of several substances as strong components responsible for inducing cardioprotection after tissue damage.

Objective: In this perspective, this study aimed to analyze cardiomyocyte trophism, in the presence of conditioned medium of the sympathetic ganglia (MCGS), in addition or not, of the Fibroblast Growth Factor 2 (FGF-2).

Methods: For this, the behavior of the sympathetic ganglion in culture was analyzed, morphologically mapping the population and the ganglionar migratory profile, the growth and the morphology of the cardiomyocytes over 72 hours through the phase contrast microscopy.

Results: A statistically significant increase was observed in both the area and the cell perimeter in the group treated with MCGS and FGF-2 (Group 03).

Conclusions and Support: It is concluded, therefore, that there is an important plastic effect of FGF, potentiated by MCGS in the cardiomyocyte.

ID: 3227

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: UNESP - Araraquara - Sao Paulo - Brasil

Title: CRF2 RECEPTORS IN THE LATERAL HYPOTHALAMUS MODULATE THE BAROREFLEX FUNCTION IN UNANESTHETIZED RATS

Introduction: The lateral hypothalamus (LH) is a functionally and anatomically complex brain region that is involved in the regulation of many behavioral and physiological processes, including the control of cardiovascular function and the modulation of baroreflex responses. Expression of CRF2 receptors, as well as components of the CRF system, were identified within the LH. In addition, it has been reported that microinjection of CRF into the LH promotes changes in cardiovascular parameters. However, the specific role of CRF2 receptors present in the HL in baroreflex control has never been investigated.

Objective: We investigated the effect of bilateral microinjection into the LH of the selective CRF2 receptor antagonist antisalvagine-30 in the control of cardiac responses of baroreflex in conscious rats.

Methods: Male Wistar rats (250g) had cannula-guide bilaterally implanted within the LH. A catheter was implanted into the femoral artery and vein to blood pressure (BP) and heart rate (HR) recording and infusion of vasoactive drugs, respectively. Independent sets of animals received antisalvagine-30 (0.01 nmol/100nL) or vehicle (saline, 100nL) into the LH. Cardiovascular parameters were recorded for 15 minutes after LH treatment for baroreflex activity assessed using the sequence analysis technique. Then, phenylephrine and sodium nitroprusside were intravenously administrated for assessment of baroreflex function using the pharmacological approach. All experiments were carried out under the approval of the Committee on Ethics and Use of Animals (CEUA) n ° 08/2019.

Results: The analysis of baroreflex activity using the sequence analysis method indicated that bilateral microinjection of antisalvagine-30 into the LH increased the "down" sequence ($F=23.65$, $P<0.05$) and the mean of all the sequences (i.e., mean of the "up" and "down" sequences) ($F=8.50$, $P<0.05$). The analysis did not indicate the effect of LH pharmacological treatment on the "up" sequences ($F= 6.773$, $P>0.05$) and the baroreflex effectiveness index (IEB) ($F = 1.904$ $P>0.05$). Analysis of baroreflex function using the pharmacological approach did not indicate effect of LH treatment with the CRF2 receptor antagonis ($P>0.05$).

Conclusions and Support: : These findings indicate that CRF neurotransmission within the LH control baroreflex function during narrow range of physiological arterial pressure variations. Results obtained indicate that LH CRF2 receptors has an inhibitory influence in tachycardiac response during spontaneous decreases of blood pressure. Support: FAPESP, CNPq, CAPES.

ID: 3739

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Estadual de Londrina - LONDRINA - Parana - Brasil

Title: EFFECTS OF PROLONGED TREATMENT WITH GLUCOCORTICOID ON ENERGY HOMEOSTASIS AND ADRENAL GLANDS IN NEONATAL OVERFED MALE RATS

Introduction: One of the neonatal programming models that has been widely used is the manipulation of the litter size in the first days of

life, which results in higher body weight gain and adiposity of small litter animals, accompanied by higher concentration of circulating glucocorticoids. It is known that obese rodents are more sensitive to the anabolic effects of glucocorticoids and less responsive do glucocorticoids feedback on hypothalamic-pituitary-adrenal (HPA) axis than lean animals.

Objective: Thus, the objective of the present work was to evaluate the effects of glucocorticoids on litter size reduction-induced responses on energy homeostasis and adrenal glands.

Methods: For this purpose, male Wistar rats (n=65) were obtained by mating of females and males from Central Facility of the State University of Londrina (UEL). On postnatal day 3 (DPN), 3 pups (small litter - SL) or 10 pups (normal litter - NL) were kept with each female. From PND 60 to 88, animals received Water or Corticosterone (CORT-15mg/L) as the only liquid. Body weight and food intake were evaluated during these 28 days of treatment. On 27th day of treatment, animals were subjected to glucose tolerance test, and on the following day, animals were euthanized by decapitation for trunk blood collection and visceral adipose tissues and adrenal glands removal. The experimental procedures were approved by the Ethics Committee on the Use of Animals undergoing experimentation for approval (CEUA: 3457.2109.11).

Results: After 28 days of treatment with corticosterone in NL animals, there was increase in body weight gain, food intake, LEE index, glucose intolerance, total and LDL cholesterol, and adrenal medulla, in addition to decrease in plasma concentration of corticosterone, weight and cortex of adrenal glands. For SL animals, corticosterone induced increase in body weight gain, food intake and LEE index, in addition to reduction in weight and medulla of adrenal glands. In Water-treated animals, litter size reduction caused glucose intolerance, increased weight of epididymal adipose tissue, plasma concentrations of total and LDL cholesterol, triglycerides, free fatty acids and corticosterone, as well as in adrenal medulla. For animals treated with corticosterone, reduction of litter size promoted greater weight of epididymal adipose tissue and plasma concentrations of triglycerides, free fatty acids and corticosterone.

Conclusions and Support: In summary, treatment with glucocorticoid promoted anabolic responses and litter size reduction induced obesity-related metabolic changes; however, the anabolic effects of glucocorticoids were not potentiated in neonatal overfed animals. On the other hand, glucocorticoid treatment reduced corticosterone plasma levels and adrenal cortex only in NL group, without effects on SL animals. Thus, different from other experimental models of obesity, neonatal overfeeding does not change the responsiveness to the anabolic effects of glucocorticoids, but it seems to reduce the feedback responses of glucocorticoids on HPA axis. Financial Support: PROAP CAPES, CNPq.

ID: 3740

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de São Paulo - São Paulo - Sao Paulo - Brasil

Title: RENAL AND CARDIOVASCULAR COMPLICATIONS IN MICE WITH SEVERE LIPODYSTROPHY

Introduction: Lipodystrophy is a group of diseases characterized by body fat loss and predisposition to insulin resistance, dyslipidemia, fatty liver, renal disease and cardiomyopathies. Deletion of nuclear receptor peroxisome proliferator-activated receptor gamma (PPARγ) exclusively in adipocytes lead to adipocyte apoptosis, loss of body fat and severe lipodystrophy in mice.

Objective: To investigate renal and cardiovascular function in mice with severe lipodystrophy and explore underlying mechanisms.

Methods: This study was approved by CEUA of USP - nº 115/2016. Two experimental groups were investigated: wild type-control mice (AT-PPARγ WT) and mice with PPARγ deletion in adipocytes (AT-PPARγ KO). Male mice of 24 weeks of age were kept in metabolic cages for evaluation of water intake, urinary volume, and food intake. Glycosuria was measured with a glucometer (OneTouch®). Gene expression was evaluated uin the kidney by qPCR. GAPDH was used as housekeeping gene. Kidney GLUT1 and GLUT2 protein content was evaluated by Western blotting and inflammatory cytokines (TNF-α, IL-1β and IL-10) by ELISA. Arterial pressure was monitored in conscious freely moving mice with an arterial catheter, and data were acquired via digital system (PowerLab, ADInstruments).

Results: AT-PPARγ KO had significantly increased water intake (KO: 19.56±1.85*, n=8 vs. WT 6.80±0.44ml, n=8, $p<0.05$), food intake (KO: 12.45±0.61*, n=6 vs. WT 6.11±0.38g, n=8, $p<0.05$), urinary volume (KO: 9.51±1.61*, n=7 vs. WT 1.47±0.29 ml, n=8, $p<0.05$) and glycosuria (KO: 605±0.00*, n=4 vs. WT 98.25±8.76mg/dL, n=4, $p<0.05$) compared AT-PPARγ WT. SGLT2 (KO: 1.42±0.08*, n=6 vs. WT: 1.00±0.05 mRNA, n=8, $p<0.05$), GLUT2 (KO: 1.54±0.07*, n=5 vs. WT: 0.99±0.06 mRNA, n=8, $p<0.05$), TGF-β1 (KO: 1.20±0.05*, n=6 vs. WT: 1.00±0.05, n=8;) and collagen type I (Col1a1) (KO: 2.50±0.19*, n=6 vs. WT: 1.00±0.08, n=8, $p<0.05$) mRNA levels were significantly increased in AT-PPARγ KO compared to AT-PPARγ WT. Furthermore, mRNA levels of CD86 (KO: 1.31±0.09*, n=5 vs. WT: 1.00±0.06 mRNA n=8, $p<0.05$) and CD206 (KO: 1.80±0.15, n=6 vs. WT: 1.00±0.10 mRNA, n=8, $p<0.05$) were significantly elevated in AT-PPARγ KO compared to AT-PPARγ WT. Kidney GLUT1 (KO: 1.00±0.15, n=7 vs. WT: 1.00±0.13, n=7) and GLUT2 (KO: 1.15±0.38, n=7 vs. WT: 1.00±0.35, n=7) was not different between groups observed statistical difference between the studied groups. There were no changes in serum concentrations of IL-6 (KO: 21.81±3.80, n=6 vs. WT: 22.45±5.36pg/mg, n=7), IL1β (KO: 48.56±8.43, n=5 vs. WT: 60.95±9.02pg/mg, n=7) and TNF-α (KO: 56.61±12.66, n=6 vs. WT: 68.37±19.46pg/mg, n=6) between groups. Finally mean arterial pressure was higher in KO mice (126±4.2*, n=5, $p<0.05$), when compared to WT mice (110±5.9, n=6), but the heart rate did not differ between the groups.

Conclusions and Support: Severe lipodystrophy is associated with, hyperphagia, polyuria, glycosuria, renal macrophage infiltration and fibrosis and hypertension in mice. FAPESP, CNPq and CAPES.

ID: 2720

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF NICOTINE EXPOSURE DURING POSTNATAL PERIOD OF MICE AND THE INFLUENCE ON BEHAVIORAL SENSITIZATION AND ANXIETY Amorim, G.E.S1; Júnior, A.A.P1; Almeida, C. A. F1 ;Silva, A.O1; Ribeiro, J.M1; De Paula, M1; Ângelo, M.L1;; Ceron, C. S1; Dias, M.V.S

Introduction: Worldwide, about 25% of pregnant women are active smokers. The use of harm reduction strategies, such as nicotine replacement therapies, e-cigarettes, has been adopted to decrease the exposure to smoking. However, little is known about the effects of nicotine during a critical period of the brain development.

Objective: The aim of this study is to evaluate the effects of the exposure to nicotine during the early postnatal period on behavioral sensitization to nicotine and anxiety during adulthood.

Methods: Swiss mice were exposed to nicotine during breastfeeding, by osmotic mini-pumps implanted in the mothers (8 mg/kg/day) (Ethics Com. 54/2018). In the adulthood, mice were treated intraperitoneally with nicotine (1 mg/kg) or a saline solution every other day for 13 days (D1, D3, D5, D9, D11, D13) and their locomotor activity was evaluated. After, mice had four days of nicotine withdrawal. An elevated plus maze test (EPM) was performed on the third day of withdrawal. After withdrawal period, mice were challenged with a single dose of saline solution or nicotine to measure their locomotor activity [groups (n=14): SAL postnatal/SAL/SAL, SAL postnatal /NIC/NIC, NIC postnatal /SAL/SAL, NIC postnatal /NIC/NIC].

Results: In the acquisition phase of sensitization (D1-D13) there was an increase on the locomotor activity in the groups SAL postnatal / NIC/NIC ($p < 0,05$) and NIC postnatal NIC/NIC ($p < 0,01$). Comparisons of D13 with challenge day (expression of sensitization) revealed an increase in the locomotor activity only for the NIC-NIC group ($p < 0.01$). In addition, mice from the NIC postnatal NIC/NIC showed an increase on the time spent in open arms when compared to SAL postnatal/SAL/SAL ($p < 0,05$).

Conclusions and Support: These data suggest that only the animals exposed to nicotine during the early postnatal period and during adulthood show acquisition and expression of a behavioural sensitization to nicotine. Moreover, mice exposure to nicotine during the early postnatal period and during adulthood show an anxiolytic-like behaviour. Financial support/Acknowledgments: CAPES, CNPq and FAPEMIG

ID: 3232

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE FEDERAL DOS VALES DO JEQUITINHONHA E MUCURI - Diamantina - Minas Gerais - Brasil

Title: SWIMMING DURING ZIKA VIRUS-INFECTED GESTATION PREVENTS CHANGES IN BEHAVIOR IN MICE OFFSPRING

Introduction: Zika virus (ZIKV) is an arbovirus member of the Flavivirus genus in the Flaviviridae family, which was first described after blood analyses of sentinel Rhesus monkeys in 1947 in Uganda. Congenital exposure to ZIKV is associated to a number of neurodevelopmental disorders. How swimming during gestation would impact over the offspring cognitive function and social interaction remain unknown. Thus, we tested the hypothesis if swimming performed during ZIKV-infected gestation would have these effects over the offspring brain and behavior

Objective: the aim of this study was to investigate the neurological consequences of exercise during prenatal ZIKV exposure to the mice pups.

Methods: Twelve weeks old female and male Swiss mice were obtained from Federal University of Minas Gerais (UFMG) and mated in our facilities in a 2:1 ratio respectively for 24 hours. Dams were separated from the males after this period. ZIKV (106 PFU) or an equal volume of 100uL of saline (Mock) was injected via intraperitoneal (i.p) in the dams at embryonic day 10.5. The exercise protocol for the dams consisted of 1 adaptation week and 4 weeks of swimming training. Swimming training sessions consisted of 60 minutes, 5 following days per week during 4 weeks and started 1 week before mating

Results: Results indicate that ZIKV-infected gestation leads to impairment of the social interaction in mice, which is inhibited through

swimming during gestation. Cognitive function was not changed in offspring mice borned from ZIKV-infected gestation. Western blot analysis of syntaxin 1 for the hippocampi did not reveal statistical difference between the groups suggesting no alterations in synaptic function

Conclusions and Support: These results together indicate that 4 weeks of swimming during ZIKV-infected gestation is capable to inhibit the impairment of social behavior in mice offspring. Acknowledgments We thank Coordination for the Improvement of Higher Education Personnel (CAPES)- Brazil. Authors also acknowledge the Integrated Center for Graduate Studies and Health Research (CIPq) from the Federal University of the Jequitinhonha and Mucuri Valleys for providing equipment and technical support for the experiments.

ID: 2721

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Alfenas - Alfenas - Minas Gerais - Brasil

Title: EFFECTS OF QUETIAPINE HEMIFUMARATE TREATMENT ON CARDIOVASCULAR AND METABOLIC PARAMETERS IN WISTAR RATS Amorim, G.E.S1 , Perissinato, N.G2, Da Silva, C.L2, Santos, W.S 2, Ruginsk, S.G2 1Department of Food and Drugs, School of Pharmaceutical Sciences, Fede

Introduction: Schizophrenia is a psychiatric disorder characterized by hallucinations and delusions, among other symptoms. The treatment consists of administration of antipsychotics such as quetiapine hemifumarate. The pathology has been related to increased risks for cardiovascular risk disease and metabolic syndrome, which are further enhanced by quetiapine treatment.

Objective: Therefore, the aim of the present study was to evaluate the effects of quetiapine treatment on indicators of metabolic and cardiovascular health. The experiments were carried out on 28 male adult Wistar rats, obtained from the Central Animal Facility of the Federal University of Alfenas. All the experimental procedures underwent previous ethical approval (protocol number 09/2017)

Methods: The animals received a diary intragastric injection of either quetiapine hemifumarate (12.5 mg/kg/day, treated group) or vehicle (NaCl 0,9%, control group) for 7 or 14 days. At the end of treatment, the animals were euthanized for blood and other tissue samples collection. Treated and control animals equally increased their body weight over the time.

Results: This response was accompanied by an increase in white adipose tissue perigonadal depots, which was only statistically significant in the treated group, when compared 7 and 14 days of treatment ($0.78 \pm 0.04$ versus $1.06 \pm 0.05$ g/100 g b.w., $p<0.05$). The same pattern of response was observed for the brown adipose tissue in the treated group ($83.86 \pm 13.50$ mg/100 g b.w. versus $142.03 \pm 6.82$ mg/100 g b.w., $p<0.001$). Casual glycemia also increased in the group treated with quetiapine during 14 days, if compared with the group treated during 7 days ($138.14 \pm 8.96$ versus $169.00 \pm 7.26$ mg/dL, $p<0.01$). We also observed a mild decrease in plasma nitrate concentrations (indicative of endothelial nitric oxide production) in animals treated with quetiapine for 14 days, in comparison with those treated for 7 days ($8.21 \pm 0.91$ versus $4.44 \pm 0.75$ µM, $p<0.05$). No significant changes related to treatment or time were found in renal or cardiac index, as well on cholesterol the triglycerides plasma concentrations.

Conclusions and Support: In conclusion, the present results support the evidence that quetiapine hemifumarate administration has a time-dependent potential for altering important parameters associated with metabolic and cardiovascular health, what ultimately may result in increased risk for the development of cardiovascular disease and metabolic syndrome. Financial Support: CNPq and Fapemig

ID: 3233

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de São Paulo - SÃO PAULO - Sao Paulo - Brasil

Title: GLAUCOMATOUS MICE AS A MODEL OF CHRONODISRUPTION

Introduction: Glaucoma is a leading cause of blindness worldwide, characterized by retinal ganglion cell degeneration and damage to the optic nerve. It has the elevated intraocular pressure (IOP) as one of the most important risk factors. Healthy eyes provide the connection between environmental light and the suprachiasmatic nucleus (SCN), the central biological clock, leading to circadian biological clock synchronization. Chronodisruption, that might happen as a consequence of the loss and/or misalignment of this connection, has attracted great attention due to its consequence in the body homeostasis. Thus, this study proposes to characterize chronodisruption in mice that spontaneously develop glaucoma, since they lost environmental information to the SCN.

Objective: To investigate the correlation between IOP and the SCN-driven rhythms of spontaneous locomotor activity (SLA) and core body temperature (Tc) in DBA/2J mice which spontaneously develop glaucoma.

Methods: Three-month old mice were housed in 12:12 light-dark cycle (LD, light on at 7 AM and off at 7 PM, intensity from 300 to 400 lux per cage) at 25 °C ± 1, with water and food ad libitum. To monitor SLA and Tc, telemetric transmitters were surgically i.p. implanted in anesthetized DBA/2J. After five days, mice were monitored up to 9-month old. IOP was measured on 3, 6, and 9-month-old freely behaving mice. All procedures were performed according to the Ethics Committee on Use of Animals of the Institute of Biomedical Sciences protocol N° 8143290819. To determine the significance of differences between ages, IOP measurement and circadian parameters were compared by One-way Anova followed by Tukey test.

Results: A gradual increase in the IOP was found throughout glaucoma development (12.5 ± 0.28, 13.88 ± 0,36 and 17.70 ± 0.14 mmHg respectively 3, 6, and 9 month). Eight- and 9-month old mice displayed a delay in the offset of SLA and Tc rhythms compared to 5-month old mice. No alteration in the onset or acrophase of SLA and Tc rhythms were found among different ages. SLA of 7, 8, and 9-month old mice was lower than 5-month at night phase. The robustness of a circadian rhythm measured by qui-square periodogram (Qp) can serve as an index of the strength of the rhythm. It was found a gradual reduction in the robustness of SLA or Tc rhythms during glaucoma development, without any effects on the period. This result indicates that the progression of glaucoma is associated with lower strength of SLA and Tc rhythms.

Conclusions and Support: Altogether these results indicate that increased intraocular pressure, a feature of glaucoma development, induced a significant alteration in the rhythmic parameters of SLA and Tc. Although the consequences of these alterations on the whole circadian time system needs to be better investigated, DBA/2J mice seems to be a suitable model to study chronodisruption. Financial Support: FAPESP and CNPq.

ID: 3235

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: VITAMIN D EFECTS ON CISPLATIN-INDUCED ACUTE TUBULAR LESION

Introduction: Cisplatin (CP) is one of the most widely used antineoplastic drug in the treatment of various solid tumors. However, 25-30% of the patients treated with CP can develop changes in renal function and structure after a single dose, characterized by intense inflammation and necrosis of the renal tubular cells with loss of the renal function. The lesion is reversible, however, even after the recovery of renal function, residual areas of fibrosis persist in the renal tissue. Several studies have shown the effect of Vitamin D on the inflammatory process and endothelial injury, important events that contribute to changes in renal function and structure caused by CP.

Objective: This study evaluated the effect of calcitriol administration on CP-induced acute kidney injury and inflammatory process.

Methods: Wistar Hannover male rats treated with calcitriol (6 ng / day) or vehicle (0.9% NaCl) for 15 days using mini osmotic pumps were injected with CP (5 mg/kg) or vehicle (SAL) 10 days after the start of calcitriol or vehicle administration. They were divided into 4 groups: (1) SAL, (2) SAL + Calcitriol, (3) CP and (4) CP + Calcitriol. On the fifth day after the injection, urine and plasma samples were collected for analysis of renal function: plasma creatinine levels (mg %) and glomerular filtration rate (ml/ $min^1$ 100 $g^1$). Renal tissue was also collected for analysis of tubular damage and inflammatory process by immunohistochemistry assay for vimentin (Score for vimentin) and ED1 (positive cells /0.100 $mm^2$), respectively. The results were expressed as mean ± SEM and considered significant when $p < 0.05$.

Results: The animals injected with CP showed an increase in plasma creatinine levels (6.18 ± 0.7) and a decrease in the glomerular filtration rate (0.03 ± 0.0). They also presented tubular damage, characterized by the presence of vimentin staining in the renal tubules (score 1.70 ± 0.1) and intense inflammation evidenced by the higher number of ED1 positive cells (66.2 ± 4.4 ), in the renal outter medulla of the animals. The changes observed in renal function (Creat.: 1.89 ± 0.4; GFR: 0.52 ± 0.1) and in the the inflammation (18.7 ± 5.2 ) were attenuated in animals treated with calcitriol. The tubular damage was also less intense in these animals (1.39 ± 0.2).

Conclusions and Support: Vitamin D treatment attenuated the alterations in renal function induced by CP. This effect was associated with decreased inflammatory process in the renal tissue of these animals. CAPES e CNPq (Grants: 302516/2017-4).

ID: 3237

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: Department of Physiology, Institute of Biosciences, University of São Paulo - São Paulo - Sao Paulo - Brasil

Title: TRANSCRIPTOME REANNOTATION AND VALIDATION OF THE BLUE CRAB, Callinectes sapidus, mRNAs

Introduction: Callinectes sapidus is an estuarine decapod with economical and gastronomical value. Its molt cycle, a growth-related process, is regulated by endogenous and environmental circadian and seasonal factors, such as photoperiod, temperature, and tidal cycle. C. sapidus perception system for these stimuli is poorly known and, as for most non-model organisms, there is few genomic information.

Objective: To reanalyze C. sapidus de novo transcriptome in an attempt to characterize clock genes, opsin, and TRP channel genes, through the design and validation of oligonucleotides.

Methods: Our first step was to perform an automatic Blast reannotation of C. sapidus transcriptome deposited in http://neigellab.agelus.net/index.php/resources/. The analysis of the obtained sequences (from March to July 2018) was conducted in collaboration with Tau GC Bioinformatics. To obtain the sequences of the interest genes, BlastN of C. sapidus transcripts were aligned against the GenBank (NCBI) transcripts of the model species: Drosophila melanogaster, Daphnia pulex, and Danio rerio. Primers were designed using the Primer-BLAST (NCBI), based on the conserved sequences. We then performed a quantitative PCR, and for the products with acceptable amplification, PCR reactions were made, and Sanger sequenced (ACTGene). The obtained sequences (forward and reverse) were aligned and analyzed with Bioedit software to obtain the consensus sequences.

Results: Initially, from the transcriptome, fifteen pairs of primers were designed. Of these, eleven proved to show acceptable amplification cycle and specificity to the target sequence by displaying a single peak melting curve. After sequencing, seven pairs of primers were validated: four sequences of clock genes, comprising two period sequences (without isoform specificity), period 1, and timeless; two sequences of opsins, opn3, and opn1lw; and one sequence of TRP channels, trpa1 Altogether, the transcriptome assembly had insufficient reads coverage to fully characterize C. sapidus transcriptome. However, some interest sequences were found.

Conclusions and Support: Our study was able to validate primers related to the molecular machinery of the clock and possible photo- and thermoreception system of C. sapidus. The transcriptome analysis is a relevant tool for the knowledge of non-model organisms; however, it is necessary the data to be robust and with a higher reads coverage to obtain better characterized gene sequence. With our results, experimental designs of physiological protocols became possible at the molecular level, thus unraveling a new field of investigation in Callinectes sapidus. Financial Support: FAPESP, CAPES, and CNPq.

ID: 2726

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: FMRP - USP - Ribeirão Preto - Sao Paulo - Brasil

Title: EVALUATION OF HEART RATE FRAGMENTATION IN YOUNG AND ADULT HEALTHY RATS

Introduction: Rapid heart rate (HR) variations at respiratory frequency range are well accepted as a marker of cardiac vagal modulation. Nevertheless, a new pattern of ultra-rapid HR variation has been recently described and named heart rate fragmentation (HRF). Clinical studies have shown that aging and cardiovascular diseases increase the HRF.

Objective: To evaluate the effect of aging on HRF in a rat model.

Methods: Conscious freely moving Wistar Kyoto rats at 2 distinct ages, 4 to 6 weeks, (n=10) or 12 to 15 weeks (n=7) had their electrocardiogram (ECG) recorded for 40 minutes. RR interval series were calculated and transformed into a sequence of symbols "-1", "0" or "1" when the difference between successive values was positive, zero, or negative, respectively. In addition, the transitions between symbols "-1" and "1" were classified as "hard" (H) while those between "-1" (or "1") and "0" were classified as "soft" (S). Next, sequences of 4 consecutive symbols were classified according to the number and type of transition, i.e. S, M or H, where M represents mixed transitions (H and S). The total percentage of inflection points (PIP) was also quantified. Results were expressed as means±SEM and examined using Student's t test ($P<0.05$).

Results: There were no differences in the PIP between young and adult rats (88.3 ± 0.8 and 87.2 ± 1.0%). A similar percentage of sequences without (W0, 0.12 ± 0.06 and 0.26 ± 0.06%), with one (W1, 3.3 ± 0.7 and 4.5 ± 0.5%), two (W2, 27.7 ± 1.6 and 28.1 ± 2.3%) or three (W3, 68.7 ± 1.8 and 67.1 ± 2.6%) inflections points was found between groups. Similarly with the number, the analysis of the transition type, also did not find any difference in the percentage of sequences with transitions type H (WH, 72.0 ± 1.9 and 73.2 ± 2.3%), S (WS, 3.8 ± 0.7 and 4.5 ± 0.6%) and M (HM, 24.1 ± 4.7 and 21.7 ± 1.6%) between young and adult rats.

Conclusions and Support: HRF has been previously demonstrated to be a promising biomarker in aging and cardiovascular studies. It is known that the HRF is increased in elderly patients. In the present study, the HRF calculated did not reveal any difference using the animal model. This study was conducted with adult and young rats; thus, future studies must be conducted to evaluate whether there is an increase of HRF in elderly rats. SUPPORT: CNPq, FAPESP (Grant: 2013/20549-7).

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Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: INTERACTION BETWEEN LACTATE AND ASTROCYTES TO MODULATE WATER AND SODIUM INTAKE IN DEHYDRATED RATS

Introduction: The increase in osmolality by Na + in the Central Nervous System promotes the release of lactate by astrocytes, which is transported to neurons participating in the inhibitory pathway of modulating sodium intake through the activation of GABAergic interneurons (SHIMIZU et al., 2007; SONG; ROUTH, 2005).

Objective: To evaluate the participation of astrocytic lactate in the behavioral modulation of water and sodium intake in animals subjected to water deprivation (WD).

Methods: Wistar rats underwent stereotaxy surgery for intracerebroventricular (icv) cannula implantation. We performed the icv microinjection of sterile 0.9% saline in normohydrated animals submitted to WD for 24h and 48h and α-CHCA (3 µg / 0.5 µl-MCT4 astrocytic lactate transporter inhibitor) in WD 48h. After, water and sodium intake was measured for 2 hours. At the end of the protocols, urine was collected to assess volume and osmolality. Lactate was measured in the Subfornicial Organ (SFO), ex vivo model, in normal osmotic medium (145mM Na+) and hyperosmotic (170mM Na+). Results were expressed as mean ± EPM and analyzed by One-way or Two-way (ANOVA) (Tukey post hoc, Prisma GrafPad, v.6, $p < 0.05$). Ceua / UFPB n. 3013270618.

Results: WD 48h increased the water (9.41 ± 0.50 vs. 4.27 ± 0.51 ml / 100g, n = 10) and sodium (3.28 ± 0.31 vs. 1.21 ± 0.17 ml / 100g, n = 7) intake in relation to WD 24h. However, WD 48h promoted aversion to sodium in the first 5 minutes after microinjection (0.09 ± 0.07 vs. 0.85 ± 0.21 ml / 100g, n = 10), which was not observed in animals WD 24h. α-CHCA increased water (10.04 ± 0.74 vs. 8.48 ± 0.29 ml / 100g, n = 6) and sodium (3.89 ± 0.31 vs. 2.78 ± 0.20 ml / 100g, n = 8) intake. There was no change in volume (0.23 ± 0.07 vs. 0.05 ± 0.05 ml / 100g, n = 5) and osmolality (1.12 ± 0.13 vs. 1.17 ± 0.03 osmol / Kg, n = 5) urinary in the WD 24h in relation to normohydrate. Urine volume increased in animals WD 48h in the saline (0.46 ± 0.09 vs. 0.05 ± 0.05 ml / 100g, n = 6) and α-CHCA (0.46 ± 0.08 vs. 0 , 05 ± 0.05 ml / 100g, n = 7) groups, whereas osmolality was lower in the saline (0.42 ± 0.04 vs. 1.17 ± 0.03 osmol / kg, n = 6) and α -CHCA (0.52 ± 0.03 vs. 1.17 ± 0.03 osmol / Kg, n = 6) compared to normohydrate group. There was a higher concentration of lactate in the SFO in hyperosmotic medium (1.17 ± 0.15 vs. 0.64 ± 0.18 mmol / l, n = 7).

Conclusions and Support: Astrocytic lactate participates in the behavioral modulation of water and sodium intake in conditions of hypertonicity in the extracellular environment. Support: Capes / Cnpq.

ID: 3242

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Pampa - UNIPAMPA - Uruguaiana - Rio Grande do Sul - Brasil

Title: EFFECTS OF ACUTE EXERCISE AND NOVELTY EXPOSITION ON MEMORY DEFICITS CAUSED BY EARLY-LIFE STRESS IN RATS

Introduction: During the neonatal period, stressful events influence brain development and impact adult life, promoting learning and memory deficits. In contrast, the acute exercise and exposure to a novelty could modulate memory consolidation and prevent memory deficits.

Objective: To verify the modulatory effects of acute exercise and exposure to a novelty in the learning of rats submitted to maternal deprivation (MD).

Methods: Eighty male wistar rats initially divided into MD and non-maternal deprived (NMD) were used. Subsequently, the groups were subdivided into: NMD (n=10); NMD+Exercise (n=10); NMD+Habituation to the exercise apparatus (n=10); MD (n=10); NMD+Novelty (n=10); MD+Exercise (n=10); MD+ Habituation to the exercise apparatus (n=10); and, MD+Novelty (n=10). All animals were submitted to the Object Recognition (OR) memory test. The animals of the exercise groups were submitted to a running session on a treadmill (30 min, 60-75% VO2max) immediately after OR training. The animals of the exercise groups were previously habituated to the treadmill. We included groups submitted to treadmill habituation only, to control any effect of novelty due to the treadmill exposure. Animals from the novelty groups were exposed to a new environment (A rectangular metallic box with the glass front wall with dimensions in mm: height 350 x width 280 x length 500) for 5 minutes, 30 minutes prior to the OR training session. Memory consolidation and persistence OR tests were performed 24h and 7 days after training. The exploration time of the objects in OR was converted to a percentage of the total exploration time and the one sample Wilcoxon test was used to compare the percentage with a theoretical mean of 50%. The results are expressed as mean ± SD; significance was set at $P < 0.05$.

Results: During OR training, the rats from all groups explored the two objects by a similar percentage of total exploration time, ~50% of the total exploration time each one (P = 0.704, t (8) = 0.393). In the 24 h test, the control group (NMD) explored significantly more than 50% of the new object (P = 0.039, t (8) = 2:513). In persistence tests (7 day test), this difference was not observed (P = 0.250, t(8) = 1.718), NMD+Exercise animals presented memory consolidation (P = 0.015, t(8) = 2.513/24h test) and persistence (P = 0.015, t(9) = 4264/7d test). The same was observed in the NMD+Novelty animals (P=0.003, t (9) = 5.496; 24h test; P=0.002, t (9) = 7.312/7d test). The animals from MD group were not able to consolidate memory (P = 0.570, t(9) = 0.8847/24h test). The MD+Exercise animals presented memory consolidation (P = 0.002, t(9) = 0.8847/24h test) and persistence (P = 0.007, t(9) = 2,366/7d test). The same was observed in the MD+Novelty animals (P=0.002, t(9) = 11.16/24h test; P=0.003, t(9) = 4.721/7d test).

Conclusions and Support: Conclusions. Our results show that a single session of aerobic exercise, as well as the exposure to a novelty, both performed after OR learning, are strategies able to modulate positively the learning of MD rats; both strategies promote memory consolidation and persistence. Support. Procad/CAPES; FAPERGS/CAPES; L'Oreal/Unesco.

ID: 2731

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: HNF4α IS ESSENTIAL TO THE HFD-INDUCED B-CELL MASS EXPANSION. Ramos, F.C.1, França, L.C.1, Barth, R.1, Santos, G.J.1. 1Laboratory of Investigation in Chronic Diseases, Department of Physiological Sciences, Federal University. Florianópolis, SC, Brazil.

Introduction: Diabetes Mellitus (DM) is a metabolic dysfunction characterized by chronic hyperglycemia with a disturbance on carbohydrate, lipid, and protein metabolism. It is due to the destruction of the pancreatic β-cell mass (DM1) or due to an insulin resistance state (DM2). Any type of DM presents a reduction in the insulin-secretory cell mass, therefore it is important to investigate pathways that increase this cell type mass. Targets to the treatment/cure of DM involve processes that promote the functional β-cell mass restoration, such as differentiation, transdifferentiation, and/or cellular replication. HNF4α is an important transcription factor (TF) for the pancreatic β cells, because, in addition, to participate in the insulin gene expression, it regulates the expression of genes related to glucose metabolism. Furthermore, it is known that HNF4α is crucial in the pregnancy-induced β-cell mass increase. However, the role of HNF4α in the β cell expansion in response to increased metabolic demand, such as insulin resistance state, is still unknown.

Objective: In this context and based on the fact that it may be a potential therapeutic target for DM, we aimed to unveil the role of HNF4α in the mechanisms involved in the high-fat diet (HFD)-induced pancreatic β cell proliferation.

Methods: For this purpose, we used WildType (WT) (HNF4αloxp/loxp) and a β-cell-specific and time-conditional HNF4α Knockout (KO) mice (HNF4αloxp/loxp;InsCre), fed with or without HFD. After 20 weeks of HFD, we evaluated the glucose tolerance (ipGTT) and insulin sensitivity (ipITT), pancreatic morphometry and the expression of genes involved in proliferation/transdifferentiation of pancreatic islet cells.

Results: As expected, WT animals fed with HFD presented glucose intolerance without alteration in the fasting glycemia. On the other hand, we observed that KO animals are more susceptible to HFD action, presenting augmented 10-hours fasting glycemia and profound glucose intolerance. The phenotype observed in the KO animals fed with HFD was similar to a diabetic profile. Additionally, insulin sensitivity was reduced in all animals exposed to HFD, although the KO animals presented a higher reduction in insulin action when compared with WT animals. Our initial hypothesis was that the HNF4α-KO animals would present an inability to increase its β-cell mass faced to an HFD challenge. In accordance, our preliminary data, from IHQ and IF, demonstrated that, when compared to the WT-FD, KO-HFD animals presented impairment in the ability to increase the insulin-secreting cell mass.

Conclusions and Support: Taking together the fact that (1) KO mice are more susceptible to the HFD to the point to become diabetes and (2) KO-HFD have no ability to increase β-cell mas in an augmented demand scenario, we conclude that HNF4α is essential to the adaptations of the pancreatic islet induced by HFD. Support: CAPES, CNPq and FAPESC.

ID: 3243

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: OVERFEEDING PROTOCOL WITH COMMERCIAL FEED IN ADULT ZEBRAFISH MODULATES BODY PARAMETERS WITHOUT CHANGING FASTING BLOOD GLUCOSE

Introduction: The growing epidemic of obesity and type 2 diabetes represents one of the most urgent and expensive medical challenges of contemporary society. Animal models with abnormal lipid and glucose metabolism are undoubtedly useful and Zebrafish has been widely used as a model for studying various metabolic diseases.

Objective: This study aimed to evaluate weekly evolution of body and metabolic changes produced by overfeeding with commercial TetraMinTM feed in adult Zebrafish, in order to use this model to investigate obesity and possible therapeutic factors.

Methods: Adult male and female Zebrafish, with 3 or 6 months, were subjected to standard nutritional management (Control) or to the overfeeding protocol (received six times the daily weight of commercial feed) for 6 or 8 weeks. Body weight, body length, condition factor, and body mass index (BMI) were evaluated weekly. Fasting blood glucose was assessed by commercial glucometer. All procedures were approved by the Ethics Committee of State University of Londrina (protocol 298.2018.17, of.06/2018). Data were expressed as mean ± standard error and a significance level of 5% ($p<0.05$). The significance was tested by Student's T-test and correction of multiple comparisons by Holm-Šídák method, in addition to two-way ANOVA with Tukey post-test.

Results: The body weight of Overfed 3-months-old fish (including males and females) showed an increase after the third week and this difference was progressively increased until the eighth week (Control: 0.290±0.022 g; Overfed: 0.443±0.023 g). The same was observed for 6-months-old animals (a group composed only of male fish) during the eight weeks (Control: 0.407±0.017 g and Overfed: 0.447±0.016 g). The body length of 3-months-old animals after the first week showed a gradual increase in both experimental groups until the eighth week (Control: 2.627±0.064 cm; Overfed: 2.850±0.040 cm), with the Overfed group showing an increased body length. However, the body length of 6-months-old animals was similar between the experimental groups over the weeks, demonstrating that there was no interference of growth in the body weight gain at this age. After the second week treatment of the 3-months-old fish, it was observed a progressive increase in BMI in the Overfed until the eighth week (Control: 0.041 ± 0.002 g/cm2; Overfed: 0.054 ± 0.002 g/cm2). Similar results were observed in the 6-month-old animals, with the Overfed showing the highest BMI from the first to the eighth week (Control: 0.045±0.001 g/cm2; Overfed: 0.050±0.001 g/cm2), emphasizing obesity induction. The condition factor, a parameter widely used in fish to assess tissue energy reserves, showed the maximal difference value in the eighth week when comparing Overfed animals to Control, which was also observed in 6-months-old Overfed adults. Fasting blood glucose showed no difference between the experimental groups after the sixth and eighth weeks, with normoglycemia being maintained.

Conclusions and Support: The overfeeding protocol in Zebrafish with commercial feed was effective in inducing obesity, producing an increase in body weight, BMI, and condition factor even without supplementation with lipids rich foods. However, it did not change fasting blood glucose, which is indicative of insulin sensitivity maintenance. Support: Fundação Araucária.

ID: 3244

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EVIDENCE THAT THE β2 – ADRENOCEPTOR IS INVOLVED IN MYOBLAST DIFFERENTION BY MODULATING NF-Kb ACTIVATION

Introduction: Skeletal muscle regeneration is a highly controlled process, which initiates after injury. Afterwards there is the installation of an inflammatory process, followed by satellite cells activation and proliferation, myoblast differentiation and myofiber maturation in order to repair the damaged muscle tissue. β2-adrenoceptor (Adrβ2) has been described as an important player of skeletal muscle regeneration. However, the role of this receptor in myoblast differentiation during muscle regeneration is not well understood.

Objective: The aim of this study was to investigate the influence of Adrb2 on myoblast differentiation during muscle regeneration.

Methods: β2 adrenoceptor knockout (β2ko) and FVB mice (2 months of age) had the tibialis anterior (TA) muscles cryolesioned and analyzed at 10 days post injury (d.p.i.). Muscle cross-sections were stained with hematoxylin and eosin. After 10 d.p.i., western blotting was used to determine the expression of phosphorylated IKK (Ser32) (IkappaB kinase) and NFkB (nuclear factor kappa B). Immunofluorescence was performed to quantify the number of NFkB-p65 positive nuclei at 10 d.p.i. and in isolated myoblasts incubated in differentiation medium for 48 hours. T-test was used for statistical analysis and $p\leq0.05$ was considered significant. This project was approved by the Ethics Committee of Animal Research of the Institute of Biomedical Sciences at the University of Sao Paulo (ICB/USP) registered under Protocol CEUA nº106/2017.

Results: Regenerating muscles from the β2ko group showed a persistent inflammatory process at 10 d.p.i. and a reduced percentage of centrally nucleated myofibers in comparison with FVB group, which suggests a delay in the resolution of inflammation and muscle regenerative process. In line with that, b2ko mice presented an increase in the number of NFkB-p65 positive nuclei in muscles at 10 d.p.i (70.2%, $p<0,05$). In addition, the decrease of fusion index (43.10%, $p<0.05$) demonstrated a delay in the differentiation of myoblasts from β2ko group accompanied by increased of 82% nuclear expression of NFkB-p65. No difference was observed in the expression of phosphorylated IKK (Ser32) and NFkB among the muscle groups.

Conclusions and Support: The results of the present study suggest that the Adrβ2 is important to the installation of inflammatory process and myoblast differentiation in regenerating muscles by modulating NFkB activation. CAPES, FAPESP (14/23391-8; 17/09069-4; 18/24946-4), CNPq (312142/2018-8), PIBIC/CNPq.

ID: 2733

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: HOW PEER INSTRUCTION METHODOLOGY ASSOCIATED WITH PLICKERS APP PROMOTES THE ENGAGEMENT AND INCREASES STUDENTS` PERFORMANCE IN IMMUNOLOGY CLASSES IN A PUBLIC SCHOOL. Sá, V. A 1,2, Vieira, A. 2, Dias, G. P 1, Lellis-Santos, C. 1 1Department of Biological Sc

Introduction: Active methodologies are essential in promoting more participative and challenging learning, as well as help to overcoming the unsatisfactory performance of underrepresented minority students. However, this practice has not been yet consolidated in public school classrooms in Brazil.

Objective: We aimed to investigate the effectiveness of the peer instruction methodology (PI) using plickers app on the performance and acceptance of low-income students in immunology classes.

Methods: A mixed-method of educational research was used to collect data from middle school students and its teacher. The school EMEF Padre Aldo da Tofori is located in an area of social vulnerability on the outskirts of the city of São Paulo. Students were submitted to a lecture followed by the PI activity using plickers app and quick response code cards to gather students' performance in each question. Lecture and video-based methodologies were used to compare the effectiveness of PI. Surveys were applied to collect data on the opinion of students and the teacher. The content covered during PI methodology was immunology, which is recommended for the physiology curriculum for grade 8 in Brazil.

Results: Less than 20% of the students did not have a personal smartphone and only 60% of them had their parents` permission to bring the device to school. Students significantly improved their performance on questions after participating in PI method with plickers (pre $48.8 \pm 23.2$ vs post $81.2 \pm 22.6$; $p = 0.0009$; $N = 12$). When PI methodology was compared to lecture- or video-based teaching methods, the students' performance on final exams was significantly higher. Students considered that the PI methodology engages them in learning, helps to learn with peers, and positively evaluated the didactic strategy. The teacher rated the interaction among students, discipline, and engagement of the students as excellent, regular, and good, respectively.

Conclusions and Support: The use of PI methodology promoted positive responses in the learning and engagement of the students, as well as in the perception of the teacher. The application of PI methodology using plickers app is effective and suitable for teaching students from low-income schools.

ID: 3245

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF HIGH-INTENSITY INTERVAL TRAINING AND CONTINUOUS LOW INTENSITY TRAINING ON RENAL FUNCTION AND ELECTROLYTE BALANCE IN RATS WITH ACUTE KIDNEY INJURY INDUCED BY CISPLATIN

Introduction: The chemotherapeutic cisplatin (CP) is often associated with several adverse effects, including Acute Kidney Injury (AKI), which is characterized by decreased glomerular filtration rate (GFR), increased serum creatinine, tubulointerstitial injury, and increased urinary excretion fraction (EF) of electrolytes. Recently, aerobic exercise has been reported to be renoprotective, however it is not yet known which intensity is the most effective in providing renoprotection.

Objective: Therefore, the aim of this study is to compare the effects of high-intensity interval training (HIIT) with continuous low intensity training (LIT) on changes in renal function and electrolytic spoliation in female rats with CP-induced AKI.

Methods: The animals were submitted to a maximum running test and were randomly divided into 4 experimental groups (n=6): C+S, saline control sedentary; CP+S, animals treated with CP and sedentary; CP+LIT, animals treated with CP and submitted to LIT (45 to 55% of the maximum capacity); CP+HIIT, animals treated with CP and submitted to HIIT (85% of the maximum capacity). The training protocols consisted in running on a motorized treadmill, 5 days/week, for a period of 8 weeks. In the end of the training protocols, blood samples

were collected to analyze renal function parameters. The CP+S, CP+LIT and CP+HIIT groups received a single dose of cisplatin (5mg/kg,i.p.) 48h after the end of the training protocols, and on the sixth day they were introduced into metabolic cages to collect 24h urine. On the seventh day, the rats were euthanized by decapitation and blood was collected for biochemical analysis. The analysis of creatinine and proteinuria were performed by colorimetry, and the GFR was determined by the creatinine clearance. The Na+ and K+ levels were measured by potentiometry, and excretion fractions (EF) of each of these ions were calculated. This study was approved by the Ethics Committee in Animal Experimentation of the UFBA/IMS (protocol 056.2018).

Results: Data are presented as mean±SEM or median and percentile 20% and 75%. Statistical differences were defined when $p<0.05$. The CP+S group [0.94(0.75;6.13)] showed an increase in serum creatinine (mg/dL) compared to C+S [0.26(0.21;0.30)] ($p<0,001$), while only the HIIT reduced this parameter in CP+HIIT [0.43(0.37;0.54)] compared to the CP+S group. The LIT was not able to reduce the serum creatinine levels [CP+TL: 0.64(0.57;1.57)]. The CP+S [0.05(0.02;0.21)] group suffered a fall in the GFR (mL/min/100g) compared to C+S [0.74(0.39;0.98)] ($p<0,01$), while only CP+HIIT [0.47(0.29;1.21)] presented GFR greater than the CP+S ($p<0.05$). The CP+S group (96.5 ± 31.6) showed an increase in FEK+ compared to C+S (22.5 ± 6.4) ($p<0.05$), while the CP+HIIT(30.61±8.0) showed a decrease in FEK+ when compared to the CP+S group ($p<0,05$). The CP+S group [1.5(0.9;3.5)] showed an increase in the FENa compared to C+S [0.54(0.39;0.74)], while HIIT reduced this parameter in CP+HIIT [0.50(0.19;0.78)] compared to CP+S ($p<0,05$). There were no differences in urinary flow and proteinuria between groups.

Conclusions and Support: In conclusion, HIIT was more effective than LIT at attenuating renal dysfunction and electrolyte excretion in rats with CP-induced AKI. This study was supported by CNPq and PIBIC-UFBA.

ID: 3250

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Instituições: UFBA-IMS/CAT - Vitória da Conquista - Bahia - Brasil

Title: EFFECTS OF HIGH-INTENSITY INTERVAL EXERCISE AND CONTINUOUS LOW INTENSITY EXERCISE ON THE EXPRESSION OF TGF- β AND FIBRONECTIN IN THE KIDNEY OF RATS WITH ACUTE RENAL INJURY INDUCED BY CISPLATIN

Introduction: The acute kidney injury (AKI) induced by chemotherapeutic cisplatin (CP) is associated with increased expression of proteins of extracellular matrix (ECM), such as fibronectin, via pro-sclerotic and fibrogenic cytokine TGF-β. Recent studies have reported that aerobic exercise exerts renoprotective actions, however it is not yet known which intensity is most effective to optimize their effects.

Objective: Thus, the aim of this study is to compare the effects of high-intensity interval training (HIIT) with continuous low intensity training (LIT) on the renal expression of TGF-β and fibronectin in rats with CP-induced AKI.

Methods: Therefore, 28 rats were randomly divided into 4 experimental groups (n=7): C+S, sedentary control; CP+S, sedentary animals treated with cisplatin; CP+LIT, animals treated with cisplatin and submitted to a LIT (45 to 55% of the maximum capacity); CP+HIIT, animals treated with cisplatin and submitted to a HIIT (85% of the maximum capacity). The training protocols consisted of running on a motorized treadmill, 5 days/week, for a period of 8 weeks. In the end of the training protocols, the rats of the CP+S, CP+LIT and CP+HIIT groups received a single dose of cisplatin (5 mg/kg, i.p.), and 07 days later they were euthanized by decapitation. The kidney was weighed, fixed, paraffinized, cut in 4 μm sections and submitted to hematoxylin eosin staining and immunohistochemical reactions with anti-TGF-β and anti-fibronectin antibodies. The histopathological analysis was performed by light microscopy using a semi-quantitative score in 30 fields of the renal outer medulla. The quantification of the immunoreactions by means of the Image-J software in 20 fields (original magnification x200) of the renal outer medulla, and expressed as percentage. This study was approved by the Ethics Committee in Animal Experimentation of the UFBA/IMS (protocol 056.2018). Data are presented as mean ± SEM. Statistical differences were defined when $p<0.05$.

Results: The CP-treated groups showed increased expression of TGF- β when compared to the C+S group (7.4±1.1), however only the HIIT protocol was able to reduce this parameter in CP+HIIT (13.7±1.7) ($p<0.05$) compared to the CP+S group (20.5±1.6) ($p<0.001$). The CP+S (20.3±1.4) and CP+LIT (20.3± 2.7) groups showed an increase in fibronectin expression in relation to C+S (11.4±2.4) ($p<0.05$), meanwhile the CP+HIIT group (13.5±0.9) didn't show statistically significant difference in relation to C+S group. The CP+S (2.8±0.3) and CP+LIT (2.7±0.2) groups presented increased tubulointerstitial lesions compared to the C+S group (0.1±0.1) ($p< 0.001$), however only the HIIT was able to reduce these lesions in the CP+HIIT group (0.8±0.3) ($p<0.001$) in relation to the other CP-treated groups. Furthermore, the CP+S (0.4±0.03) and CP+LIT (0.4±0.03) groups presented an increase in kidney weight in relation to C+S (0.3±0.01) ($p<0.01$) group, meanwhile the CP+HIIT(0.3±0.01) group didn't show a statistically significant difference in relation to the C+S group.

Conclusions and Support: In conclusion, HIIT was more effective than LIT in providing renoprotection, decreasing tubulo-interstitial lesions, as well as TGF-β and fibronectin expressions in the renal outer medulla of CP-induced AKI rats.

ID: 2739

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: STRENGTH TRAINING IMPROVES SERUM METABOLIC PROFILE AND MITOCHONDRIAL PROTEIN LEVELS IN OBESE RATS FED HIGH-FAT DIET

Introduction: Obesity has become a serious public health problem worldwide. Although there are several approaches, physical exercise is one of the most known,cheap and promising tool to control the weight. Exercise stimulates mitochondrial biogenesis, increasing the number of these organelle The role of mitochondria in the skeletal muscle is based on the ATP production through oxidative phosphorylation (OXPHOS), involving protein complexes (I-V) of the respiratory chain. To reach a satisfactory regulation of mitochondrial function, the transcriptional coactivator PGC-1ahpha regulates the expression of genes, integrating several physiological signals favoring mitochondrial biogenesis. Physical training increases the content and/or activity of the PGC-1alpha and OXPHOS protein complexes; however, it unclear whether strenght training can promote similar effects on the expression of that proteins even under intake of high-fat diet.

Objective: To determine if the strength training can improve the mitochondrial proteins levels (OXPHOS complexes and PGC1alpha) in the gastrocnemius skeletal muscle of rats fed a high-fat diet.

Methods: The study was approved by local Ethics Committee on the Use of Animals (CEUAs) #01/2017. After 7 days of adaptation, twenty four male Wistar rats were randomly separated into 4 groups (n=8/group): Sedentary non-obese (S), Exercised non-obese (E), Sedentary Obese (SO) and Exercised Obese (EO). A high-fat diet was offered to the obese groups for 12 weeks, and the ingestion was controlled along the study. Strength training consisted of climbing on a ladder with load progression along 12 weeks (from 50% - 100% ML), based on the Maximum Load (ML) test for each animal. For euthanasia, anethesia was injected and blood was collected for fasting glycemia and triglyceridemia determination by comercial kits. Gastrocnemius skeletal muscle tissue was removed for OXPHOS complexes (I-V) and PGC-1alpha proteins qunatification by Western Blotting. The image of the blots was analyzed using free ImageJ software. Two-way ANOVA tests with Tukey's post-hoc tests were used for comparison of the results.

Results: SO showed higher feed efficiency coefficient compared with the others groups ($P<0.05$), which can be associated with heavier body weight ($P<0.05$ vs S and E). EO also showed heavier body weight compared with E ($P<0.05$). SO and EO showed increased absolute fat mass (2.5x and 2.0x, respectively, $P<0.05$) compared with S and E, while EO showed reduced relative weight of the fat mass compared to SO ($P<0.05$). Glycemia and triglyceridemia were increased in the SO rats ($P<0.01$ vs S, E and EO), while E showed the lowest glycemia level compared with S and SO ($P<0.01$). E rats showed higher protein levels of complex CII and CV compared with SO ($P<0.05$), and EO showed increased protein levels of complex V compared with SO ($P<0.05$). No change was detected on the protein expression of OXPHOS complexes I, III and IV. PGC-1alpha protein level was increased in E rats ($P<0.05$) compared with S rats.

Conclusions and Support: We can conclude that the high-fat diet promoted weight gain due to higher development of the fat mass and consumption of calories, and impaired metabolic profile. On the other hand, strength training reduced fat mass gain in rats fed high-fat diet, contributing to improvement of serum metabolic profile. Strength training can improve the expression of mitochondrial proteins in the skeletal muscle of rats fed standard or high-fat diet.

ID: 3508

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Minas Gerais - Belo Horizonte - Minas Gerais - Brasil

Title: AEROBIC TRAINING IN THE HEAT REQUIRES LOWER ABSOLUTE EXERCISE INTENSITY TO PROMOTE SIMILAR EFFECTS OF TEMPERATE ON PERFORMANCE

Introduction: Short- and medium-term heat acclimations (HA; < 3 weeks) lead to several physiological adaptations that improve physical performance, but the effects of longer periods of HA (≥ 8 weeks) are unknown.

Objective: Characterize the long-term adaptations of metabolic and thermoregulatory systems and aerobic exercise capacity in a novel murine model of running training in the heat.

Methods: 2-month-old male swiss mice were divided in 4 groups: 1) sedentary (SED) mice kept in the temperate (T) environment (22 °C; SED/T), 2) SED kept in the heat (H) (32 oC; SED/H), 3) mice trained (TRA) in treadmill (1 h/day, 5 days/week for 8 weeks, 60% of maximal speed (Vpeak), 60 min and inclination angle of 5o) in T (TRA/T), and 4) TRA in H (TRA/H). All groups performed incremental load tests in treadmill and peak oxygen consumption (VO2peak), maximum abdominal body temperature (ABTmax), Vmax and time to exhaustion (TTE) were evaluated in both T and H before (pre-training) and after 4 and 8 weeks of training. Relative exercise intensity (60% Vpeak) in T and H groups was prescribed according to its respective Vpeak obtained in T or H test. All experiments and protocols were approved by The Ethics Committee on Animal Use (CEUA: 220/2019) from Federal University of Minas Gerais.

Results: Comparing tests in different environmental temperature in pre-training period, Vpeak (~27%) and TTE (~38%) in TRA/H during H test was lower than in TRA/T during T test. On the other hand, ABTmax in TRA/H during H test (~41,7 oC) was higher than in TRA/T during T test (~40,0 oC) and VO2peak did not change amongst groups. Despite the aforementioned alterations, pre-training tests revealed no difference amongst the 4 groups in either T or H environment. In T test, after 4 weeks, although TRA/H exercised at a lower (~26%) absolute intensity than TRA/T, VO2peak (~11%), Vpeak (~20%) and TTE (~26%) was similarly increased in both TRA groups compared with SED/T. Additionally, it was noted a tendency toward increasing (~10%, P=0,065) Vpeak in TRA/H compared with SED/H, without any change in VO2peak and TTE. In T test, after 8 weeks, Vpeak (~23%) and TTE (~33%) were higher in both TRA groups compared with SED/T. Vpeak was also increased (~15%) in TRA/H compared with SED/H. VO2peak was increased (~11%) in TRA/T compared with SED/T, but no difference was detected between TRA/H and SED/H anymore. In H tests after 4 and 8 weeks, however, VO2peak, Vpeak and TTE were similar amongst 4 groups. ABTmax did not differ amongst all groups during the tests in either T (~39,7 oC) or H (41,3 oC) at different time points.

Conclusions and Support: Aerobic training in hot environment seems to be an alternative to training in temperate environment because it is performed in lower absolute exercise intensity and promotes similar effects on performance. These findings may help to develop new strategies to induce physiological benefits of physical training avoiding excessive mechanical stress, which may be important for training obeses and treating injured patients. Supported by PRPq-UFMG (27764*27) e CNPq/CAPES/PROANTAR (442645/2018-0) Keywords: Aerobic training; Heat stress; Peak oxygen consumption;

ID: 2742

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de Lisboa - - - Portugal

Title: INFLUENCE OF NOVELTY EXPLORATION TRAINING ON MODULATION OF HIPPOCAMPAL SYNAPTIC PLASTICITY BY ENDOGENOUS VIP ACTING ON VPAC1 RECEPTORS. Caulino-Rocha, A.1, Aidil-Carvalho, F.3, A. Ribeiro, J.3, Cunha-Reis, D.1,2,3. 1Departamento de Química e Bioquímica,

Introduction: VIP, expressed in hippocampal interneurons targeted by septal GABAergic and median raphe serotonergic afferents, is a modulator of hippocampal synaptic plasticity (LTP, LTD and depotentiation) essentially through VPAC1 receptor activation and modulation of disinhibition1,2. Mismatch novelty exploration training enhances both LTP and depotentiation in the hippocampal CA1 area3.

Objective: We now evaluated how VIP modulation of LTP and depotentiation is changed in animals exposed to mismatch novelty exploration training.

Methods: Male Wistar Han rats (3 weeks-old) were trained for two weeks by exploring the location of three objects always presented in a new spatial configuration. Electrophysiological recordings were performed in hippocampal slices as described3. LTP was induced by theta-burst stimulation (TBS, five 100Hz bursts, 4 stimuli, separated by 200 ms). Depotentiation was induced by low frequency stimulation (LFS, 1Hz, 15min), preceded in 1h by TBS-induced potentiation. Changes were assessed 50-60 min after stimulation. VIP, VPAC1 receptors and serotonin transporters were evaluated by western blot.

Results: fEPSPs slope was enhanced by 28.9±1.2% (n=5) 1h after TBS and the selective VPAC1 antagonist PG 97-269 100nM enhanced this LTP to 51.3±3.8 (n=7). A depotentiation of fEPSP slope (14.2±4.8%, n=3) was observed 1h after LFS and was enhanced to 26.7±1.2 (n=3) by PG 97-269 100nM. Mismatch novelty training enhanced mildly LTP induced by TBS (25.5±1.2% vs 35.8±1.5, n=7) and caused an enhancement of depotentiation caused by LFS (-12.1±1.4% vs 23.1±1.7, n=6). The effect of PG 97-269 on LTP expression was markedly reduced in mismatch novelty trained animals and the effect of PG 97-269 on depotentiation was strongly enhanced.

Conclusions and Support: Thus, there is a restraining effect of endogenous VIP on TBS LTP and on LFS-induced depotentiation through activation of VPAC1 receptors in young rats. Novelty training decreased the influence of endogenous VIP on LTP expression but reinforced the influence of VIP on depotentiation expression thus shifting the paradigm of VIP modulation of hippocampal synaptic plasticity. This might reflect an altered control of disinhibition mechanisms by hippocampal serotonergic inputs. 1.Cunha-Reis et al., 2010, J Mol Neurosci 42:278 2. Cunha-Reis et al., 2014, Hippocampus 24:1353 3. Cunha-Reis et al., 2017, Neurobiol Learn Mem, 145:240
This work was supported national and international funding managed by the Fundação para a Ciência e a Tecnologia (FCT, IP), Portugal. Grants: UIDB/04046/2020 and UIDP/04046/2020 centre grants (to BioISI) and research grant FCT/POCTI (PTDC/SAUPUB/28311/2017) EPIRaft grant (to DC-R). Researcher contract: Norma Transitória – DL57/2016/CP1479/CT0044 to DC-R.

ID: 3510

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Estadual de Maringá-UEM - Maringá - Parana - Brasil

Title: HIGH-FAT DIET DURING ADOLESCENCE INDUCES LONG-TERM HYPERTENSION IN ADUL TRATS

Introduction: Introduction: Exposure to high fat diet during gestation and lactation programs high blood pressure in adulthood and evidences suggest that adolescence is another programming window but still little is explored.

Objective: The present study aims to evaluate whether high fat diet exposure during adolescence induces cardiovascular dysfunctions in adulthood.

Methods: Methods: The research ethics committee approved the study under CEUA nº 1527130815. Thirty day-old Wistar rats were exposed to a high fat (HF, 35% lard w/w n:24) diet until 60 days of age then fed a normal fat diet (NF, 4.5% w/w of fat n:24) for a further sixty days. Control animals received the NF diet throughout life. Body weight and food consumption were evaluated throughout the protocol. At 120 days of age biometric, histological analysis and cardiovascular parameters were evaluated. Statistical comparisons were performed by Student´s T test.

Results: Results: The animals HF showed lower food intake (2526±40,40 vs 2225±18,44 p<0,0001) and higher caloric intake (1446±23,01 vs 1598 ±29,83; p<0,0038) during HF exposure compared with control group. At 120 days of life, the HF diet induced an increase in body weight (+ 14%; p <0.002). Systolic (SBP), diastolic (DBP) and mean (MBP) blood pressure increased in HF (+ 10%, + 4% and + 17%, respectively; p <0.009, p <0.004 and p <0.01), but the heart rate remained unchanged. After intravenous injections of atenolol (4 mg/kg) and methylatropine (3 mg/kg) the bradycardia and, tachycardia response and intrinsic heart rate, respectively, were similar between groups. The baroreflex sensitivity (ΔHR / ΔMAP) in response to phenylephrine (8 μg / kg, iv) and sodium nitroprusside (50 μg / kg, iv) was similar between groups. The depressor response to hexamethonium (30 mg/kg, iv), a ganglionic blocker, was greater in the HF group (+26%; p <0,01). The histological analysis in the heart showed increased perivascular and interstitial fibrosis (+42%; +%62 respectively; p<0,02 and p<0,0001) and left ventricular hypertrophy in HF animals (+29%; p<0,0001).

Conclusions and Support: Conclusions: Exposure to HF in adolescence programs to cardiovascular dysfunctions in adulthood, characterized by hypertension, hyperactivity of the vascular sympathetic nervous system and cardiac structural changes. Our study points to the susceptibility of adolescence as a critical window of development, capable of programming for diseases later in life. Key-words: high fat diet; high blood pressure; rats. Funding: CNPQ and Capes.

ID: 2743

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: FACULDADE DE MEDICINA DE RIBEIRÃO PRETO - RIBEIRÃO PRETO - Sao Paulo - Brasil

Title: EFFECT OF PERIODONTITIS IN AUTONOMIC FUNCTION, MYOCARDIAL INFLAMMATION AND PLASMA OXIDE NITRIC LEVELS IN SPONTANEOUSLY HYPERTENSIVE RATS

Introduction: The association between periodontitis and hypertension is widely addressed. Recently, experimental studies have shown that hypertension aggravates periodontal disease (PD). However, the role of periodontitis in the development or worsening of cardiocirculatory diseases deserves thorough studies.

Objective: To evaluate the effect of PD on hemodynamics, the variability of heart rate (HRV) and arterial pressure (APV), plasma nitric oxide (NO) levels and myocardial IL-1β concentrations in spontaneously hypertensive rats (SHR) and their normotensive counterparts Wistar-Kyoto (WKY) rats.

Methods: Three weeks after bilateral ligation of the first mandibular molar, or Sham-operation (control groups), SHR and WKY (N= 6 to 10 in each group) received catheters into the femoral artery and had their arterial pressure (AP) directly recorded at the following day. Subsequently, plasma, heart and jaw were collected. Series of successive values of pulse interval (PI) and systolic AP were generated, and variability of AP and PI were evaluated in time and frequency domain (FFT spectral analysis), as well as by symbolic analysis. All procedures were approved by the Ethics Committee of Ribeirão Preto Medical School, University of São Paulo, São Paulo, Brazil (protocol number 218/2019).

Results: The linear alveolar bone loss in jaws of SHR with PD was higher than in all other groups. AP and heart rate were higher in SHR than in their WKY counterparts. SHR with PD showed a lower AP (153 ± 2 mmHg) as compared to control SHR (171 ± 3 mmHg). The variability the indices of HR and AP were, as expected, different between SHR and WKY rats; however, no difference was found between the animals with PD and their control counterparts. Baroreflex function, evaluated by the sequence method, was impaired in SHR; but, similarly, with the variability indices, no difference was found between the subjects with or without PD. Plasma NO levels were higher in SHR with PD as compared to control WKY (63 ± 239 vs. 20 ± 2 μM). The myocardial concentrations of IL-1β were higher in SHR with PD as compared to control WKY rats (23 ± 6 vs. 9 ± 2). A significant correlation was found between linear alveolar bone loss and both plasma NO levels (r =0.7) and myocardial IL-1β concentrations (r= 0.4) in the animals.

Conclusions and Support: Our results suggest that PD elicits a hypotensive effect in SHR, probably due to a pro-inflammatory mechanism involving the systemic release of NO. Even though PD did not affect either HRV or APV, it did induce myocardial inflammation, which can determine cardiovascular dysfunction in the future. Further studies should be conducted to evaluate cardiovascular function in experimental PD in hypertension. Support: FAPESP (Grants: 2013/20549-7; 2018/20939-3; and 2018/10455-9).

ID: 2747

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Santa Catarina (UFSC) - Florianópolis - Santa Catarina - Brasil

Title: DOES PDE3 INHIBITION PLAY A ROLE IN THE MANAGEMENT OF SEPSIS? Oliveira, J.G.1, Sordi, R.1, Anton, E.L.1, Oliveira, M.R.P.2, Fernandes, D.1 1Department of Pharmacology, Universidade Federal de Santa Catarina, SC, Brazil. 2Department of Structural Biology

Introduction: Sepsis is a life-threatening organ dysfunction caused by a dysregulated immune response to infection leading to cardiovascular collapse and multiple organ dysfunction. The cyclic nucleotides (cAMP and cGMP) exhibit a crucial role in signal transduction regulating many critical physiological processes that are impaired during sepsis, such as cardiac function, inflammation, platelet aggregation and endothelial stabilization. The cyclic nucleotides levels are controlled by phosphodiesterases (PDEs) that hydrolyzes and inactive these nucleotides. Thus, inhibition of PDE can enhance or prolong the effects of physiological processes mediated by cAMP e cGMP. PDEs are a conserved superfamily of enzymes, among them, PDE3 exhibit dual specificity, controlling cAMP and cGMP hydrolysis, and it is mainly expressed in the cardiovascular tissues. Cilostazol (CLZ) is a PDE3 inhibitor approved for the treatment of chronic peripheral vascular diseases, and that by increasing cAMP and cGMP bioavailability improves tissue blood flow.

Objective: Investigate whether PDE3 inhibition by cilostazol might attenuate the multiorgan dysfunction of sepsis in an experimental rat model.

Methods: Sepsis was performed by cecal ligation and puncture (CLP) procedure in male Wistar rats. CLZ (15 mg/kg, vo) or vehicle was administered six h after the surgery. Twenty-four h after treatment after CLP blood pressure, heart rate, renal blood flow, vascular reactivity in isolated aorta. After that, blood samples were collected for measurement of nitrite/nitrate (NOx) serum, aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate and hematological analyzes. Lastly, tissues were collected to myeloperoxidase activity (MPO), Evans blue (EB) leakage, histopathology and Western blotting analysis. In the second experimental set, after the CLP surgery, the blood pressure was measured at different times over the 24 h. Finally, the percent survival after the CLP procedure was analyzed until five days. The procedures were approved by the University Institutional Ethics Committee (Protocol number 1667100417).

Results: CLP procedure resulted in hypotension, hyporesponsiveness to vasoconstrictors, renal blood flow reduction, systemic inflammation, multiorgan dysfunction development and mortality over time (CLP 15% of survival in five days; control 100%). CLZ improved renal blood flow (CLP 251.9 ± 42; CLP CLZ 394.2 ± 25.9, $p<0.05$), responsiveness to vasoconstrictors in vivo, and in the isolated aorta rings. Furthermore, the CLZ reduced lactate level (CLP 50.9 ± 7.9; CLP CLZ 27.1 ± 4.7, $p<0.05$), lung MPO (CLP 4.2 ± 1.6; CLP CLZ 0.5 ± 0.1, $p<0.05$). CLZ also reduced in 90 and 45% lung histopathologic score and lung EB leakage, respectively, but the difference was not statistically different ($p=0.21$ and $p=0.08$, respectively). CLP and CLZ did not change PDE3A expression in the heart and thoracic aorta.

Conclusions and Support: CLZ, a PD3 inhibitor, improved tissue blood perfusion and reducing organ injury in sepsis. Thus, CLZ administered at the proper time can represent a useful supplementary tool in sepsis management. CAPES Foundation (Ministry of Education of Brazil) and the National Council for Scientific and Technological Development (CNPq, Brazil).

ID: 3003

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Zootecnia e Engenharia de Alimentos da Universidade de São Paulo (FZEA-USP) - Pirassununga - Sao Paulo - Brasil

Title: PROTEINURIA AND DETECTION OF NEPHRIN mRNA IN URINE OF DOGS WITH CHRONIC KIDNEY DISEASE.

Introduction: Persistent proteinuria with an inactive urine sediment is an indicative of chronic kidney disease (CKD) in dogs. The loss of selectivity of the glomerular filtration barrier (GFB) is one of the mechanisms responsible for proteinuria. In the GFB, the foot processes of podocytes are connected by the slit diaphragm, which prevents the passage of plasma proteins, mainly due to its central component, the nephrin. Detection of podocyte mRNA in the urinary sediment, such as NPHS1 encoding the nephrin, could be useful in evaluating dogs with CKD.

Objective: The objective of this study was to evaluate proteinuria and the presence of NPHS1 in the urinary sediment of dogs at different stages of CKD.

Methods: Clinically normal dogs (n=10) and dogs diagnosed with CKD (n=18) were recruited from the veterinary hospital routine. Dogs with CKD were divided into two groups, according to disease stage (early stage, n=7; late stage, n=11). Urine was collected by free catch or catheterization. Urinary protein and creatine concentrations were measured by pyrogallol red protein dye-binding assay and Jaffe method,

respectively, and then the protein/creatinine ratio (UPC) was calculated. Total RNA was extracted from the urinary sediment using 1 mL Trizol reagent plus 20 mg/mL glycogen, 1 mL isopropanol and 3M sodium acetate. cDNA was synthesized using commercial kit. NPHS1 was quantified by real-time PCR using specific primers. The NPHS1 relative expression was normalized by 18s (endogenous control) and urinary creatine concentration. Comparisons between mean UPC values and NPHS1 expression were made by the Student's T-test and the frequency of NPHS1 detection was compared by the Chi-square test ($p<0,05$). (CEUA protocol: 5180200917).

Results: All the dogs with CKD had UPC above 0.2 and no inflammation or infection in the urinary tract, which indicates proteinuria of renal origin. In the CKD group, the mean UPC value was higher compared to control group (1.75±0.41 (n=18) vs. 0.15±0.014 (n=10), respectively) ($p<0.0001$). Mean UPC values did not differ between the early and late stages of CKD (1.95±0.67 (n=7) vs. 1.62±0.65 (n=11), respectively) ($p=0.328$). NPHS1 detection in the urinary sediment was higher in the early stage (3/5) and lower in the late stage (1/9) of CKD compared to control group (4/10) ($p<0.001$). The relative expression of NPHS1 in the urinary sediment did not differ between the groups and CKD stages ($p=0.511$). But, numerically, it was higher in the early stage of CKD (1.13±1.51 vs. -0.49±0.68 in control group and -1.17±1.07 in late stage of CKD).

Conclusions and Support: Proteinuria was elevated in both stages of CKD. However, the detection of NPHS1 in the urinary sediment was variable, that is, high in the early stage and low in the late stage. In dogs with CKD, this difference could be related to an active glomerular lesion and progressive podocyte depletion, respectively. Support: CAPES and FAPESP grants 2014/02493-7 and 2019/03651-9.

ID: 3008

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Medicina do ABC- Centro Universitário Saúde ABC - SANTO ANDRÉ - Sao Paulo - Brasil

Title: BLOCKADE OF VASOPRESSIN RECEPTORS REDUCES THE THRESHOLD OF MICTURITION REFLEX IN FEMALE WISTAR RATS.

Introduction: The impairment of urinary bladder functions affects men and women, as well as children worldwide, with the majority of cases of urinary incontinence occurring in women. The neuro-humoral control of micturition and urine storage involve a complex mechanism not yet well known.

Objective: To evaluate whether the blockade of vasopressin receptors would affect the micturition reflex in anesthetized rats.

Methods: All the procedures were approved by the Animals Ethic Committee (CEUA-FMABC/CUSABC-protocol # ). Female Wistar rats were anesthetized with 2% isoflurane in 100% O2 and submitted to the cannulation of femoral artery and vein for mean arterial pressure (MAP) and heart rate (HR) recordings in a data acquisition system (PowerLab 16 SP, ADInstruments) and infusion of drugs, respectively. The urinary bladder was cannulated for cistometry and the following parameters were analysed: baseline intravesical pressure (IP), threshold of micturition reflex, IP emptying, intermicturition pressure, interval between contractions, latency for peak of IP, spontaneous bladder activity, capacity of bladder, bladder compliance, and volume of saline injection for cystometry. Cystometry was evaluated after i.v. saline or V1a or V2 receptor antagonista (10 µg/kg). Data are shown as mean±SEM and were submitted to unpaired Student t-test ($p<0.05$).

Results: Blockade of V1a receptors significantly reduced the threshold of micturition reflex (18.95±4.52 mmHg) compared to saline (29.12±2.42 mmHg). After intravenous V2 receptor antagonist, the threshold of micturition reflex was also diminished (19.88±4.32 mmHg) compared to saline (29.12±2.42 mmHg). No difference was observed in the threshold of micturition reflex comparing V1a and V2 receptor blockade. All the other parameters evaluated in the cystometry were similar after V1a or V2 receptor antagonist compared to saline. No diferences were observed in baseline MAP and HR and after the V1a or V2 receptor blockade compared to saline.

Conclusions and Support: Vasopressin is importante for the maintainence of the normal threshold of micturition reflex. Support: CAPES scholarship, FAPESP, and NEPAS.

ID: 3266

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Espirito Santo - VILA VELHA - Espirito Santo - Brasil

Title: PROBIOTIC KEFIR ADMINISTRATION IMPROVES CARDIAC FUNCTION AND REDUCES PUMONARY CONGESTION EVEN IN CONDITIONS OF HIGH BLOOD PRESSURE IN RATS

Introduction: A healthy heart is a sine qua non condition to keep an adequate supply of blood flow and oxygen to all body tissues. When a cardiac dysfunction occurs, the blood pumping to organs and tissues is compromised. If this situation is not corrected, it can disturb the body homeostasis and become a serious health issue. Lately, functional foods have become an exciting research field due to their therapeutic actions besides nutritional properties. Kefir is a probiotic food that has been extensively used as support treatment of several cardiovascular diseases including arterial hypertension (AH) and cardiac hypertrophy (CH). Although studies have shown positive effects of kefir intake on lowering blood pressure and reverts CH, it´s not clear if CH improvement was due to the kefir anti-hypertensive effects or to a direct effect of this probiotic on the heart.

Objective: To investigate the kefir effect on cardiac function, CH, and pulmonary congestion (PC) in an experimental model of AH

Methods: The project was approved by the institutional Ethical Committee for Animal Research, number 09/2019. Five months old, male Wistar and Spontaneously Hypertensive Rats (SHR) were divided into 3 groups and treated with whole milk or Kefir by gavage for 30 days: Wistar whole milk (W-WM, 0.3 mL/100 g, n=7), SHR whole milk (SHR-WM, 0.3 mL/100 g, n=7) and SHR Kefir (SHR-K, 0.3 mL/100 g, n=7). Blood pressure (BP) was measured before and after probiotic intake. Rats were anesthetized and a catheter inserted through left carotid artery for left ventricular measurements of cycle duration (CD), heart rate (HR), left ventricular systolic pressure (LVPS), dP/dtmax, dP/dtmin and left ventricular relaxation time constant (Tau) parameters. After, they were euthanized for CH and PC inspection. Data were expressed as mean ± SEM

Results: As expected, no significant differences were observed in BP among groups. The same as above, we did not find any statistical differences when CD, HR, dP/dtmin and Tau parameters were analysed. On the other hand, PC was increased in SHR-WM compared to W-WM group (53±3 mg/mm vs. 45±2 mg/mm, respectively, $p<0.05$) and Kefir intake prevented this increase in the hypertensive animals (SHR-K: 41±2 mg/mm, $p<0.05$ vs. SHR-WM). Similar result was observed in LVPS and cardiac contractility index, dP/dtmax, respectively: SHR-WM (148±7 mmHg; 3364±190 mmHg/s) vs. W-WM group (106±3 mmHg; 2500±54 mmHg/s, $p<0.05$) and SHR-K animals (130±2 mmHg; 2860±30 mmHg/s, $p<0.05$ vs. SHR-WM). In parallel study, we have observed a significant decrease in plasma lipid peroxidation (0.07564±0.007 µMol/mg vs. 0.06135±0.003 µMol/mg, $p<0.05$) and plasma myeloperoxidase activity (0.03367 ±0.004 a.u vs. 0.02459 ±0.003 a.u, $p<0.05$) in SHR-K vs. SHR-WM treated for 7 days, respectively

Conclusions and Support: These results support our hypothesis that probiotic Kefir administration, can improve cardiac function and decrease pulmonary congestion, through a pressure-independent mechanism. This mechanism could be partially due to kefir strong local and systemic anti-oxidative and inflammatory effects. Support: CAPES and CNPq

ID: 2755

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Odontologia de Araçatuba - FOA/UNESP - Araçatuba - Sao Paulo - Brasil

Title: ANALYSIS OF ENZYMATIC AND NON-ENZYMATIC ANTIOXIDANT DEFENSE IN THE PAROTID GLANDS OF WISTAR RATS AFTER ORCHIECTOMY AND HORMONE THERAPY

Introduction: There are many factors that influence the oral health of men, such as variations of serum testosterone concentration. In men, the hypogonadism is associated with several clinical signs. For example, loss of density mineral bone, decreases muscle strength, signs contributing to more prevalence periodontal disease and gum inflammation, and decreasing quality of life. The hormone replacement therapy (HRT) appears as a therapeutic option, with the objective to achieve physiological testosterone levels with little fluctuations. However, studies have shown that the influence of testosterone on oral health are limited to contextualizing its effect on periodontist. It neglects the importance of salivary glands and saliva in oral homeostasis.

Objective: The objective of the study was to assay the effects of orchiectomy (ORX) and HRT on enzymatic and non-enzymatic antioxidant defense in the parotid glands in Wistar rats.

Methods: Forty male Wistar rats (three-month-old) underwent surgical orchiectomy or sham surgery and were randomly assigned to four in experimental groups: SHAM, ORX, ORX+ testosterone cypionate (ORX+TC, 10 mg/kg WB, via IM, weekly) and ORX+ testosterone undecanoate (ORX+TU, 100 mg/kg WB, via IM, monthly). Water and food were available ad libitum throughout the experiment. The protocol was approved by the Ethics Committee on the Use of Animals of School of Dentistry, São Paulo State University-UNESP, Araçatuba (Protocol FOA nº 00956-2018). At the end of treatment, the rats were euthanized, blood samples were collected and plasma testosterone was measured and the parotid glands were removed, weighed, and stored at -80 °C. Parotid gland homogenate supernatants were used for spectrophotometric assays: total protein concentration (TP), alpha-amylase activity (AMY), oxidative damage to lipids was analyzed TBARS method (reactive substances to thiobarbituric acid), protein oxidative damage was determined by the Carbonyl Protein method (CP). Non-enzymatic antioxidant capacity was evaluated by the antioxidant power of total ferric reduction (FRAP), total glutathione (tGSH), and uric acid (UA). Enzymatic antioxidant capacity was determined by the activity of the enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Data were analyzed by one-way ANOVA followed by Tukey's post hoc tests, considering

a significance level of 5% ($P < 0.05$).

Results: The ORX group, presented serum concentrations of testosterone below the sensitivity of the test ($P < 0.0001$), while in both groups HRT the concentrations were supraphysiological compared to the SHAM group (ORX+TU, $P < 0.05$; ORX+TC, $P < 0.0001$). ORX group decreased AMY activity about SHAM ($P < 0.05$), while the groups ORX+TC and ORX+TU showed an increase in AMY activity about that, reversing the situation (ORX vs. ORX+TC $P < 0.01$; ORX vs. ORX+TU $P < 0.05$). In addition, the ORX group increased lipid oxidative ($P < 0.05$) and protein ($P < 0.001$) oxidative damage, as well as increased non-enzymatic antioxidant defense, FRAP levels ($P < 0.05$), UA ($P < 0.05$) and tGSH ($P < 0.05$) compared to SHAM. In turn, antioxidant enzymes (SOD, CAT, and GPx) have not been modulated as a function of testosterone.

Conclusions and Support: These findings suggest that the non-enzymatic antioxidant defense exhibits a compensatory role concerning the enzymatic antioxidant defense against oxidative stress caused by ORX. PIBIC/Reitoria/ UNESP 2018/2019 - EDITAL 04/2018 - PROPe (Pedido 51744).

ID: 3267

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto - Universidade de São Paulo - Ribeirão Preto - Sao Paulo - Brasil

Title: THE INFLUENCE OF THE POST-PULMONARY SEPTUM ON VENTILATORY MECHANICS OF TRACHEMYS SCRIPTA THUNBERG IN SCHOEPFF, 1792 (CRYPTODIRA: EMYDIDAE).

Introduction: Compared to mammals, reptiles possess large and compliant lung, where the greatest mechanical resistance resides within the body wall. Turtles have a rigid shell and also possess a post-pulmonary septum (PPS) that partially isolates the lung from the other viscera. The influence of the PPS on the mechanics of the turtle respiratory system has never been studied. Through an analysis of static and dynamic compliance, and by calculating mechanical work of breathing in intact animals, in turtles with their respiratory system exposed with and without the PPS, it was possible to quantify the influence of the PPS on breathing mechanics of turtles.

Objective: The objective of the present study was to evaluate and quantify the influence of the post-pulmonary septum on the static and dynamic compliance, and in the total work of breathing of the respiratory system of Trachemys scripta turtles.

Methods: Standard experimental procedures to analyze ventilatory mechanics (see Reichert et al. 2019 doi:10.1242/jeb.193037) were applied to ten animals ($MB = 0.23 \pm 0.08$ kg) in three treatments: 1) intact in a supine position, 2) with an open body cavity and lungs exposed but with intact PPS, and 3) open body cavity with lungs exposed lungs but with PPS attachments removed. All data were analyzed through a generalized estimating equation (GEE), and the experimental protocol was approved by the Comissão de Ética na Utilização de Animais (CEUA – FFCLRP), protocol number: 2020.1.267.59.9. SISBIO number: 35221-10.

Results: Static compliance showed no significant differences between groups with and without PPS, but dynamic compliance was significantly reduced by PPS removal. In contrast, removal of the PPS significantly increased work of breathing, and the estimated energetic costs of mechanical ventilation (percentage of $O_2$ consumed needed to generate ventilatory movements) showed exponential growth, varying from 0,02% under normoxic to 16% under hypercarbic conditions.

Conclusions and Support: The PPS showed to be functionally important within the turtle's breathing mechanics, possessing a positive influence regarding dynamic compliance, working against the lungs tendency to collapse and thereby facilitating its inflation. Although a greater energetic cost seems necessary to operate the respiratory system with this structure, the increase in dynamic compliance seems to be more advantageous in this ventilatory trade-off. We acknowledge the financial support of Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP process nº 2020/01289-8) and the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) (process n° 308249/2019-4).

ID: 3269

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE FEDERAL DO ESPIRITO SANTO - UFES - VITÓRIA - Espirito Santo - Brasil

Title: LOW CONCENTRATION OF EUPHORBIA TIRUCALLI (AVELOZ) MODIFIES VASCULAR FUNCTION: IN VITRO CARACTERIZATION OF AVELOZ LATEX EFFECTS ON AORTA VASCULAR REACTIVITY

Introduction: Euphorbia tirucalli (Aveloz) is a plant originated in Africa, which has been distributed in regions of tropical climate. Its

branches, when broken, release a latex containing bioactive compounds that have been used for numerous diseases. In Brazil, its used mainly as support for cancer treatment even though there isn´t any clinical studies that prove its efficacy. Although in vitro studies have appointed a low cytotoxicity of Aveloz in health cells, there are still a lack of research focusing on its effects in organ function.

Objective: To investigate the effects of Aveloz in the isolated thoracic aorta of rats.

Methods: Sixteen male Wistar rats from 3 months old were euthanized and thoracic aorta was carefully dissected, cleaned from connective tissue, cutted in small rings, placed in an organ bath with 5 mL of Krebs-Henseleit at 37°C and bubbled with carbogen. Aortic rings were used to evaluate vascular responses to crescent doses of phenylephrine (Phe, 3x10-10 to 3x10-5 mol/L) and acetylcholine (Ach, 3x10-10 to 3x10-5 mol/L) before (control, CT) and after Aveloz incubation (AV 50ng/mL). To access the role of nitric oxide, aortic rings were also incubated with L-NAME (100 μM). In some aortic rings the endothelium was withdrawn to evaluate its role on Aveloz effects. Differences in the maximum response (Emax), sensitivity (pD2 -log one-half of Emax) and area under the curve (dAUC) were evaluated. Results were expressed as mean ± SEM and were considered significant when $p<0.05$. This study was approved by the institutional Ethical Committee for Animal Research, CEUA-UFES number 09/2019.

Results: Aortic ring vasoconstriction to Phe response was not different after incubation with AV when compared to CT aortic rings (Emax: 74±17% vs. 95±15%; pD2: 7±0.5 vs. 7±0.4; dAUC: 188±57 a.u. vs. 274±47 a.u., respectively, $p>0.05$). The endothelium-dependent vasodilator response to Ach showed a significant decrease after aortic ring incubation with AV when compared to CT rings (Emax: 53±6% vs. 82±2%; dAUC: 166±51 a.u. vs. 286±23 a.u., respectively, $p<0.05$). When the nitric oxide synthase blocker L-NAME was applied to the aortic ring, vasodilator response to Ach was totally abolished. The removal of aorta endothelial cells decreases significantly Phe vasoconstrictor response in Aveloz incubated aortic rings compared with control aortic rings (Emax: 24±2% vs. 87±5 %; dAUC: 115±8 a.u. vs. 247±15 a.u., respectively, $p<0.05$).

Conclusions and Support: Our results shown that Aveloz can acutely interfere with vessel function by decreasing the endothelium vasodilator response to Ach. This decrease is greatly exacerbated when eNOs inhibitor L-NAME was incubated with Aveloz, suggesting a synergic effect of these two drugs. In addition, an observation of weak vasoconstrictor response to Phe in Aveloz incubate vessel after endothelium removal, suggests that Aveloz effects is mediate through some receptor present in the endothelial cell. CAPES and CNPq

ID: 2762

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Anhembi Morumbi - São José dos Campos - Sao Paulo - Brasil

Title: URINARY BIOMARKERS IN GESTATIONAL DIABETES AND HYPERTENSION. Valias G.R. 1, Gomes P.R.L.2, Amaral F.G.3, de Oliveira C.R.4, Gianneschi S. 5, Monteiro D. 6, Zangaro R. 7, Cipolla-Neto J. 8, Baltatu O.C. 9, Campos, L.A.10. Jacareí, SP, Brasil.

Introduction: A large research portfolio indicates that an activated renal renin-angiotensin system or a deficit on melatonin is associated with several cardiovascular pathologies. In this observational clinical study, we assessed the hypothesis that gestational hypertension or diabetes are associated with alteration in renal angiotensinogen or melatonin.

Objective: The objective of our study is to evaluate urinary melatonin and angiotensinogen as new biomarkers, predictive of the disease, that are present and measurable in the urine of pregnant women.

Methods: This was a prospective cross-sectional observational study. Urinary angiotensinogen and 6-sulfatoximelatonin were measured by sensitive and specific ELISAs in first morning void urine samples. To avoid patient selection bias, the patient selection was consecutively, and the diagnosis was blinded at the level of urine collection. After the completion of 100 urine samples collections, 22 pregnant women without diagnosed pathologies were recruited as healthy volunteers.

Results: Urinary levels of angiotensinogen were significantly higher in the gestational diabetes [angiotensinogen-to-creatinine ratio median (25th, 75th): 0.11(0.06, 0.17)] and gestational hypertension [0.08(0.05, 0.18)] groups than in those with healthy pregnancy [0.05(0.04, 0.06]; 6-sulfatoxymelatonin levels were significantly lower in the gestational diabetes [ug/h: median (25th, 75th): 0.12(0.08, 0.17)] and gestational hypertension [0.13(0.10, 0.17)] groups than in those with healthy pregnancy [0.20(0.14, 0.38]. Neither protein/creatinine ratio nor 24-hour urine protein estimate were significantly different between the study groups.

Conclusions and Support: These results suggest that urinary angiotensinogen levels may indicate an intrarenal RAS activation while melatonin production appears to be defective in gestational diabetes or hypertension. An angiotensinogen-melatonin-creatinine ratio is suggested for identification of gestational diabetes or hypertension.

ID: 3018

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Comissão de Ética da Universidade Lusófona - - - Portugal

Title: THE PASSIVE MOBILIZATION OF THE LEG TISSUES INCREASES LOCAL PERFUSION IN BOTH LIMBS

Introduction: Many studies have been developed over the years to try to better understand the microcirculatory adaptations during movement (gait or exercise) or in static or quasi-static conditions. This is also important from the pathophysiological perspective (vascular impairment) to better prevent disease as for a more effective rehabilitation. Therapeutic massage has been empirically referred to imply a variety of beneficial results. However, only a few studies have been able to objectively identify and describe the physiological impacts involved in this type of manipulative technique.

Objective: Our goal was to identify the impact one of the most popular massage techniques, the effleurage, in the lower limb microcirculation.

Methods: Two short-term massage techniques were applied - one in the upward direction and the other in the downward direction with each participant in a supine position in a climatized room. Young healthy volunteers (n=32, 19.8 ± 1.6 year old) both sexes, were selected in accordance with the Helsinki Declaration principles (Ethics Commission approval nº 3/2013). Massage was applied in a single randomly chosen limb, after informed written consent. Each protocol included a 10-min baseline (Phase I), a 5-min massage (Phase II), and a 10-min recovery (Phase III) register and were performed in a random order with a 30-min washout period separating both protocols. Perfusion was assessed with both laser Doppler flowmetry (LDF) and reflection photoplethysmography (PPG), sensors applied distally in both second and first toes, respectively, in both feet plantar aspect. Blood pressure and pulse rate were also recorded. LDF signals were further analyzed in their oscillatory components by the Morlet wavelet transform. Nonparametric statistics were used for phase comparisons ($p<0.001$).

Results: Both effleurage protocols consistently evoked a significant perfusion increase ($p < 0.001$) in the massaged limb and a similar effect, although non-significant in the contralateral limb. This adaptive response, observed with both LDF and PPG, was equivalent in both sexes, although known sex perfusion differences between sexes were detected as expected. The component analysis of LDF signals revealed for both massage techniques, that effleurage evokes substantial increases in cardiac, respiratory, and myogenic components, as well as a reduction of sympathetic and endothelial components specially in the massaged limb. Similar changes although with minor magnitude were detected in the contralateral no massaged limb.

Conclusions and Support: A passive short duration / intensity mobilization of tissues as this effleurage, clearly increases skin microcirculatory flowmotion specially in the tested limb, also affecting the contralateral limb, and all systemic hemodynamics. The component analysis of the LDF signal suggests that these procedures, although brief and superficial, affects multiple components of cardiovascular integration, with cardiac, respiratory, and myogenic components appearing to play a major role in reestablishing distal microcirculatory homeostasis.
Support: Fundação de Ciência e Tecnologia (FCT) UIDB/04567/2020 and UIDP/04567/2020

ID: 2763

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Instituições: Anhambi Morumbi - São José dos Campos - Sao Paulo - Brasil

Title: FUNCTIONAL OUTCOMES OF HYDROTHERAPY DURING CHILDBIRTH FOR STRESS RELIEF Dias, R.A. 1,3,5, Cardoso, C.F. 1,3,5, Baltatu, O.C. 1,3,4, Campos, L.A. 1,2,3 1 Center of Innovation, Technology and Education (CITE) at Sao Jose dos Campos Technology Park, Brazil

Introduction: Hydrotherapy, as immersion in a warm shower, has been used with benefits of stimulation of physiological childbirth patterns. Hydrotherapy has been associated with neuroendocrine stress changes promoting adaptation to stress during childbirth. Therefore, further studies with quantitative outcomes are needed to provide additional support for the adoption and implementation of such non-pharmacological support procedures during childbirth.

Objective: This study aimed to investigate the effect of warm shower hydrotherapy on the heart rate variability stress parameters during childbirth.

Methods: This study was interventional, randomized, single blind. The cardiac autonomic function was determined through measures of heart rate variability during a deep breathing test in 42 pregnant women in the first stage of labor.

Results: Eighty-five percent of women reported reduced anxiety after a 30 minutes of warm shower hydrotherapy. The deep breathing test demonstrated an increase in parasympathetic tone (83.4 +/- 2.0 vs 87.3 +/- 1.9 before vs after the hydrotherapy, respectively), with its associated %ranking of 24.3 +/- 3.9 vs 15.6 +/- 2.8, before vs after hydrotherapy, respectively).

Conclusions and Support: This study demonstrates that warm shower hydrotherapy is effective in improving parasympathetic modulation during childbirth and consequently decreasing anxiety and stress during the first stage of labor. The reliability of hydrotherapy as a non-pharmacological strategy is related to the fulfilment of more clinical studies showing evidence to support indications relating to stress and birth progress.

ID: 3019

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Lusófona - - - Portugal

Title: COMPARING THE FOOT FLOWMOTION PATTERNS FROM LASER DOPPLER FLOWMETRY AND PHOTOPLETISMOGRAPHY AFTER A LOWER LIMB MASSAGE IN DIFFERENT AGE GROUP

Introduction: The skin microcirculatory flowmotion is accessible through specific analytical tools such as the wavelet transform (WT). Originally applied to laser Doppler flowmetry (LDF) signals it allows to identify each of those different oscillatory components operating at different frequencies.

Objective: In the present study we compared microcirculatory flowmotion assessed by LDF and photoplethysmography (PPG) in young and older healthy individuals after the application of an effleurage massage in the lower limb.

Methods: Forty-eight participants were selected after informed written consent in accordance with the Helsinki Declaration principles (Ethics Commission approval nº 3/2013). Group I, 32 young healthy subjects (mean 19.8 ± 1.6 yo), both sexes (16 female, 16 male), body mass index (BMI) < 22.21 kg/m2, ankle-brachial index (ABI) of 1.06 and Group II, 16 older healthy subjects (53.8 ± 6.2 yo), both sexes (8 female, 8 male), body mass index (BMI) < 24.80 kg/m2, ankle-brachial index (ABI) of 1.14 All participants were non-smokers having no cardiovascular and/or metabolic disease. These were left to acclimatize in the lab room (21 ± 1°C – 40-60% RH) lying supine for 20 minutes. One massage technique known as effleurage was applied continuously and with constant pressure, with a centripetal direction (UpM), in a single randomly chosen limb. The protocol consisted in a 10-min baseline (Phase I), a 5-min massage (Phase II), and a 10-min recovery (Phase III) register. Blood perfusion was measured, by LDF and PPG, with sensors on both feet in the second and first toes, respectively. Pulse rate, calculated from PPG signal and blood pressure were also obtained. WT analysis was applied to decompose LDF and PPG signals into their main activity components (cardiac, respiratory, myogenic, sympathetic, endothelial NO-dependent (NOd) and endothelial NO-independent (NOi)). Nonparametric statistics were used for phase comparisons ($p<0.05$).

Results: The massage protocol evoked a significant perfusion increase in the test foot and also an increase in the control foot with both technologies. The observed flow increases and components response seems to be less pronounced in the older individuals (group II). A significant decrease in pulse rate and blood pressure was also noted in both groups, but only significant in group I. WT signal decomposition analysis evidenced a similar components response in both groups, both for LDF and PPG during massage, mainly consisting in an increase in the cardiac, respiratory and myogenic activities, and a decrease in the sympathetic and endothelial activities. This increase in the myogenic component and the decrease in sympathetic component, observed in both feet, and for both groups, might explain the observed blood flow increase associated to the massage.

Conclusions and Support: Flowmotion patterns from LDF and PPG can be assessed through WT and seem to be similar under these conditions. This massage technique (effleurage) was able to increase perfusion in both limbs during massage, although a more pronounced contralateral response is detected in group I. This flowmotion pattern shows that massage evokes a very sensitive microcirculatory regulation that seems to be age-dependent. Support: Fundação de Ciência e Tecnologia (FCT) UIDB/04567/2020 and UIDP/04567/2020

ID: 2764

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Anhembi Morumbi - São José dos Campos - Sao Paulo - Brasil

Title: QUANTITATIVE EVALUATION OF CARDIAC DYSAUTONOMIA AFTER PREGNANCY LOSS

Introduction: Although acute stress disorder and post-traumatic stress disorder (PTSD) are conditions that may cause significant distress on health outcomes, they often go undiagnosed. The working hypothesis of this study was that quantifying cardiac dysautonomia may help in evaluating the severity of PTSD in women after pregnancy loss.

Objective: To assess dysautonomy in women after pregnancy loss.

Methods: The DSM-5 (Diagnostic and Statistical Manual of Mental Disorders) PTSD scale and a short-version-Posttraumatic Diagnostic Scale (sv-PDS) scale were used to the severity of PTSD in women after pregnancy loss. The cardiac autonomic function was determined through heart rate variability (HRV) measures at a deep breathing test.

Results: Sympathetic and parasympathetic modulation reflected through SDNN (standard deviation of all RR intervals) was significantly higher in patients with aggravated (mild to severe) symptoms in comparison with those with slight symptoms. The sv-PDS scale score

had a statistically significant association with HRV indices (SDNN; RMSSD, root-mean square of differences between adjacent normal RR intervals; pNN50, NN50 represents the number of pairs of successive RRs that differ by more than 50 ms). With an AUC = 0.83 +/- 0.06 (95%CI 0.94, $p < 0.0001$) of the ROC model, the deep breathing test HRV's SDNN is good at distinguishing between patients with aggravated (mild, moderate and severe) and those with slight disease diagnosed with DSM-5 score.

Conclusions and Support: This study suggests that quantifying cardiac dysautonomia may complement the evaluation of acute stress disorder and PTSD in women after pregnancy loss.

ID: 2765

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de São Paulo - São Paulo - Sao Paulo - Brasil

Title: MODULATION OF EXTRA-PINEAL MELATONIN SECRETION IN RESPONSE TO AN IMMUNE CHALLENGE WITH LPS IN TOADS (Rhinella icterica). Cyrino, J.C.1 Figueiredo, A.C.1 Gomes, F.R.1 Titon, S.C.M.1 / 1. Departamento de Fisiologia, Instituto de Biociências/Universidade de

Introduction: Melatonin is a hormone well-known for its circadian production by the pineal gland. However, the melatonin production in extra-pineal sites shows other regulatory functions, such as immune regulation. Pineal and extra-pineal production of melatonin is modulated through pathogens associated molecular patterns. While central production of melatonin is lowered, its production in other tissues, specially by immune cells enhances in response to an immune challenge in mammals. The occurrence of the extra-pineal melatonin production in different tissues and periods, and its modulation by an immune stimulus, would represent an important contribution to understanding the melatonin role in anuran's physiology.

Objective: The goal of this project is to investigate melatonin production in different organs of (pineal vs. extra-pineal) of cururu toads (Rhinella icterica). We predicted that plasma melatonin would be higher at night when compared with the day; and that an immune challenge with lipopolysaccharide (LPS) would decrease the central production of melatonin (showed through the plasma concentration) and increase the production in extra-pineal sites (lungs, liver, bone marrow and intestine).

Methods: The animals were held in a 12:12 L/D cycle and received an LPS (2mg/kg) or saline injection at 10 a.m. and 10 p.m. and were sampled 2 hours after the injection (noon and midnight). Blood samples were collected by cardiac puncture for plasma melatonin quantification followed by decapitation. Then, the following tissues were collected: bone marrow, lungs, liver, and intestine. The tissues were weighed (60mg), homogenized in TRIS-HCl (400ul), and then assayed for melatonin quantification. Plasma and tissue homogenates melatonin were determined by ELISA kits (IBL).

Results: Melatonin concentration in bone marrow and liver were affected by the body mass, in which larger animals displayed lower and higher melatonin concentration in bone marrow and liver, respectively. Melatonin concentration in the bone marrow was affected by the interaction treatment*period, being higher in the LPS group when compared with the saline group, during the day. Also, the melatonin in the bone marrow in the LPS group is higher during the day, when compared with LPS in the night. Otherwise, in the liver, melatonin showed a tendency for higher concentration in the LPS than in the saline-injected toads, during the night. The melatonin concentration in the intestine was affected only by the period, with the higher melatonin during the night. Plasma melatonin levels and lung melatonin concentration were not affected either by the treatment or the period.

Conclusions and Support: Our results showed that melatonin is present in extra-pineal tissues in R. icterica toads, and its concentration is modulated in different tissues by an immune challenge. Moreover, the melatonin in extra-pineal sites seems to be locally produced, since melatonin concentration in the organs is much higher values than those levels measured in plasma. Interestingly, the period of increased response of melatonin production in response to LPS differ between tissues, evidencing the complexity of individual defense against pathogens.

ID: 2767

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: A SINGLE SESSION OF PHYSICAL EXERCISE IMPROVES MEMORY PERSISTENCE BY A MECHANISM DEPENDENT ON HIPPOCAMPAL D1-DOPAMINERGIC RECEPTORS

Introduction: A single session of physical exercise is able to improve recognition memory, promoting its persistence through a process dependent on dopaminergic receptors of the D1 family (D1 and D5 receptors). However, it is not clear whether the effects of physical

exercise on memory depend on a specific dopaminergic pathway.

Objective: To investigate the involvement of the D1 and D5 dopaminergic receptors in the modulatory effect of a single session of physical exercise on object recognition memory.

Methods: The experiments were approved by the Animal Care and Use Ethics Committee (033/2019) of local institution. Adult male Wistar rats were trained in the object recognition (OR) task and, immediately after, received intra-hippocampal infusion of vehicle for Control group (i) or SKF 3839 (agonist D1/D5) for Control + SKF 3839 group (ii). The physical exercise groups were submitted to a single exercise session on a treadmill (60-70% of VO2 maximum) and, received an intra-hippocampal infusion of vehicle or drug(s) according to their experimental group, which were: (iii) Physical exercise + Vehicle; (iv) Physical exercise + SCH 23390 (blocker D1/D5); (v) Physical exercise + Rp-cAMPS (PKA inhibitor; PKA is the second messenger from D1 receptors); (vi) Physical exercise + Go 6976 (PKC inhibitor; PKC is the second messenger from D5 receptors); (vii) Physical exercise + SCH 23390 + Sp-cAMP (PKA stimulator); (viii) Physical exercise + SCH23390 + PMA (PKC stimulator). All animals were tested in the OR task 24 hours and, 7, 14 and 21 days after training. One-sample t test was used to compare the percentage of the total exploration time of each object with a theoretical mean (50%) (n = 8-10/group). Results were considered significant when $P < 0.05$.

Results: All animals consolidated their memory 24h after OR training (learning session). However, the control group did not present memory persistence (P = 0.6/7th-day test), indicating a physiological forgetfulness. D1/D5 agonist hippocampal infusion promoted recognition memory persistence until 21 days (P = 0.0156). The physical exercise promoted memory persistence until 14 days (P = 0.0004). When D1/D5 receptors were blocked after exercise, memory persistence was not observed (P = 0.2304/7th-day test). We observed the involvement of a specific dopamine receptor when we inhibit the second messenger of D1 receptors after exercise – this block avoided memory persistence (P = 0.5296/7th-day test). On the other hand, the inhibition of D5 receptors' second messenger did not alter the effects of exercise on memory persistence (P = 0.002/14th-day test). Similarly, the blocked of D1/D5 receptors followed by D1 second messenger stimulation allowed the memory persistent (P = <0.0001/14th-day test) – the same was not observed when we made the second messenger D5 stimulation (P = 0.0780/7th-day test).

Conclusions and Support: A single session of physical exercise after learning is able to promoted memory persistence and this effect involves hippocampal mechanisms dependent on dopamine D1 receptors activation. Support: CAPES/DS.

ID: 3023

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CHEMOREFLEX ACTIVATION IN INFLAMMATORY RESPONSE INDUCED BY LPS IN UNANESTHETIZED RATS.

Introduction: Over the past twenty years, many studies have shown the effect of the autonomic nervous system on the modulation of the immune response. More recently, reports suggested that the chemoreflex has a protective role in the inflammatory response. However, these findings were obtained through the denervation of the chemoreceptors. Thus, it is considered important to evaluate the role of the chemoreflex in the inflammatory response through its activation, and not by its removal.

Objective: To examine the role of pharmacological activation of the chemoreflex, using potassium cyanide (KCN), on the modulation of the systemic inflammatory response to lipopolysaccharide (LPS) administration.

Methods: Surgical procedures were performed in male Wistar Hannover rats for catheterization of the femoral artery and vein, for arterial pressure recording and drug administration, respectively. Moreover, a catheter was inserted into the abdominal cavity for the administration of LPS. After 48h of surgical recovery, arterial pressure and heart rate from unanesthetized rats were recorded. The baseline recording of cardiovascular parameters was performed for 15 minutes, followed by the administration of KCN (40 μg, i.v.), to activate the chemoreflex, or saline in the control groups. Five minutes after KCN injection, LPS (5 mg/kg, i.p.) was administered to induce the inflammatory process. Ninety minutes after LPS administration, plasma, heart, spleen and hypothalamus were collected for analyzing cytokines levels. All procedures were approved by the Ethics Committee of Ribeirão Preto Medical School, University of São Paulo, São Paulo, Brazil (protocol number 161/2016).

Results: KCN quickly (within the first 5 s) increased the mean arterial pressure (106 ± 2 vs. 137 ± 5 mmHg) and decreased the heart rate (368 ± 4 vs. 157 ± 18 bpm) compared to baseline. Moreover, all endotoxemic animals exhibited an increased heart rate at the 10th and 90th minutes after LPS administration. However, no difference was observed in arterial pressure, over time, post LPS or saline. Concerning the plasma cytokine levels, LPS administration increased the plasma levels of pro-inflammatory cytokine [tumor necrosis factor (TNFα)] and the anti-inflammatory cytokine [interleukin 10 (IL-10)], but, KCN injection did not prevent these responses. LPS plus saline increased the levels of TNFα in the heart, spleen and hypothalamus and also IL-10 in the spleen; again, no difference was observed in these parameters with KCN treatment. Nevertheless, KCN plus LPS increased IL-10 concentration in the heart as compared to the saline plus saline group (1 ± 0.2 vs. 4 ± 1 pg/mg tissue).

Conclusions and Support: Our results suggest that KCN administration did not affect the cytokine release induced by LPS in plasma,

spleen or hypothalamus; however, increased the IL-10 in the heart compared to rats that received Saline plus Saline. Therefore, further cytokines analysis should be conducted to evaluate the KCN effect in systemic inflammation. FAPESP (#2013/20549-7, #2018/10455-9 and #2017/05163–6) and Programa Unificado de Bolsa da Universidade de São Paulo (PUB-USP).

ID: 2769

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Odontologia de Araçatuba - FOA/UNESP - Araçatuba - Sao Paulo - Brasil

Title: ANALYSIS OF ENZYMATIC AND NON-ENZYMATIC ANTIOXIDANT DEFENSE IN THE SUBMANDIBULAR GLANDS OF WISTAR RATS AFTER ORCHIECTOMY AND HORMONE THERAPY.

Introduction: Many factors influence men's oral health, as well as variations in serum testosterone concentration. In men, hypogonadism is associated with several clinical signs such as loss of bone mineral density, decreased muscle strength, as well as contributions to a higher prevalence of periodontal disease and inflammation of the gums, decreasing the quality of life of those affected. Hormone replacement therapy (HRT) is one of the therapeutic options, with the aim of reaching physiological levels of testosterone. However, studies that study the influence of testosterone on oral health are limited to contextualizing its effect on the periodontist, neglecting the importance of salivary glands and saliva in oral homeostasis.

Objective: The objective of the study was to assay the effects of orchiectomy (ORX) and HRT on enzymatic and non-enzymatic antioxidant defense in the submandibular glands (SM) in Wistar rats.

Methods: Forty male Wistar rats (three-month-old) underwent surgical orchiectomy or sham surgery and were randomly assigned to four in experimental groups: SHAM, ORX, ORX+ testosterone cypionate (ORX+TC, 10 mg/kg WB, via IM, weekly) and ORX+ testosterone undecanoate (ORX+TU, 100 mg/kg WB, via IM, monthly). Water and food were available ad libitum throughout the experiment. The protocol was approved by the Ethics Committee on the Use of Animals of School of Dentistry, São Paulo State University-UNESP, Araçatuba (Protocol FOA nº 00956-2018). At the end of treatment, the rats were euthanized, blood samples were collected and plasma testosterone was measured and the SM were removed, weighed, and stored at -80 °C. SM homogenate supernatants were used for spectrophotometric assays: total protein concentration (TP), alpha-amylase activity (AMY), oxidative damage to lipids was analyzed TBARS method (reactive substances to thiobarbituric acid), protein oxidative damage was determined by the Carbonyl Protein method (CP). Non-enzymatic antioxidant capacity was evaluated by the antioxidant power of total ferric reduction (FRAP), total glutathione (tGSH), and uric acid (UA). Enzymatic antioxidant capacity was determined by the activity of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Data were analyzed by one-way ANOVA followed by Tukey's post hoc tests, considering a significance level of 5% ($P < 0.05$).

Results: The ORX group, presented serum concentrations of testosterone below the sensitivity of the test ($P < 0.0001$), while in both groups HRT the concentrations were supraphysiological compared to the SHAM group (ORX+TC vs. SHAM $P < 0.0001$; ORX+TU vs. SHAM $P < 0.05$). The ORX group showed a reduction in TP ($P < 0.01$ vs. SHAM; $P < 0.0001$ vs. ORX+TC; $P < 0.001$ vs. ORX+TU), and for AMY activity there was no difference. The ORX group increased oxidative lipid ($P < 0.01$) and protein ($P < 0.001$) damage compared to SHAM. There was also an increase in non-enzymatic antioxidant defenses in ORX (FRAP: $P < 0.0001$; GSH: $P < 0.05$; UA $P < 0.01$), and also in antioxidant enzymes (SOD: $P < 0.001$; CAT: $P < 0.05$; GPx: $P < 0.05$). HRT did not reduce oxidative damage markers and decreased antioxidant defenses compared to ORX.

Conclusions and Support: The testosterone concentration modulates the functional parameters and oxidative stress. Castration was responsible for decreasing functional activity and increasing oxidative damage, while HRT, in turn, restored functional activity, but did not reduce oxidative stress. PIBIC/Reitoria/ UNESP 2018/2019 - EDITAL 04/2018 - PROPe (Pedido 51793).

ID: 3025

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Escola de Ciências e Tecnologias da Saúde - Universidade Lusófona, Portugal

Title: ABOUT THE QUANTIFICATION OF MICROCIRCULATION IN VIVO – A FOCUS ON ANALYTICAL STRATEGIES

Introduction: Microcirculation perfusion signals are attributed to the contribution of multiple tissues and organs, which make up for a complex oscillatory and multiscaled pattern termed flowmotion, making analysis and interpretation both a delicate and cumbersome process.

Objective: Here we describe the application of analytical strategies to assess the most important features of the microcirculation perfusion signals in vivo, using data from healthy human subjects of different ages (young – 18-35 y.o.; older – 40-65 y.o.) while performing challenge tests such as suprasystolic limb occlusion, normobaric hyperoxia and postural changes.

Methods: Commonly used quantification technologies include laser Doppler flowmetry (LDF), photoplethysmography (PPG) and non-contact polarization spectroscopy (NCPS), each using different biophysical principles, from which different information is extracted. LDF and PPG are preferable for continuous measurements, with PPG displaying lower temporal variability, while also being restricted to highly perfused sites. The intrinsic variability of LDF and PPG can be considerably decreased with the wavelet transform (WT), a tool that decomposes the signals into their spectral components – cardiac, respiratory, myogenic, sympathetic and endothelial – excellent for elaborating the physiological mechanism behind a given vascular response.

Results: LDF and PPG generate different frequency spectra, with the former being mainly of low frequency origin, while the latter receiving especially high frequency contributions. NCPS has the great advantage of allowing continuous measurements of large skin areas and being insensitive to movement artefacts. NCPS perfusion images can be converted into continuous signals which only seem to show the myogenic and cardiac (under high perfusion) components. Another important feature of perfusion signals is entropy, which reflects the adaptability of the cardiovascular system. Although entropy is typically calculated with 'classic' tools such as the multiscale entropy analysis, our group has demonstrated an equivalent and more straightforward approach, based on the texture analysis based of the signals' WT scalograms.

Conclusions and Support: Our data highlights that (1) given their different biophysical backgrounds, these techniques should, whenever feasible, be used in association rather than separately; (2) analytical tools show promise in decreasing the intrinsic variability of these techniques, making their transition from bench to bedside more feasible. This work was supported by funds from FCT—Fundação para a Ciência e Tecnologia, I.P (Portugal) within the project UID/DTP/04567/2019

ID: 3026

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Escola de Ciências e Tecnologias da Saúde - Universidade Lusófona - - - Portugal

Title: MAPPING THE UPPER LIMB MICROVASCULAR REACTIVITY WITH TISSUE VIABILITY IMAGING (TIVI®) – A PILOT STUDY

Introduction: Microvascular function assessment with optical techniques, such as laser Doppler flowmetry and photoplethysmography, is largely hindered by the small areas assessed, therefore preventing us from getting a "broader" view of perfusion distribution. Recently, the Tissue Viability Imaging (TiVi®) device, based on non-contact polarization spectroscopy, was introduced offering to tackle this limitation by obtaining good quality images over large skin areas in real time. Despite its analytical potential, only a few applications have been tested so far.

Objective: Our aim was to use this device to map the cutaneous reactive hyperemia (RH) response in the upper limb during a classic suprasystolic occlusion test.

Methods: Six healthy subjects (22.0 ± 3.0 y.o.) were included in this study, giving informed consent. After a three minute resting period, a three minute suprasystolic occlusion of the brachial artery was performed, after which a final three minute recovery period was given. Regions of interest (ROI) were marked in both forearms fingertip, wrist, and middle forearm. For each ROI the concentration of moving red blood cells was calculated and followed throughout the protocol. Additionally, we propose a novel quantification parameter for RH analysis, the 212reperfusion velocity, calculated by the distance between ROIs divided by the time interval between RH peaks.

Results: Significant differences were observed for the amplitude, time of onset and duration of RH, as well as for the reperfusion velocity between sites.

Conclusions and Support: TiVi® is a novel technique with a full potential to tackle many of the common difficulties observed with the current gold standard techniques, as suggested with the present data, and should be further explored in the future. This work was supported by funds from FCT—Fundação para a Ciência e Tecnologia, I.P (Portugal) within the project UID/DTP/04567/2019

ID: 3282

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: DIFFERENT DOSES OF RESVERATROL PREVENTS CARDIAC DIASTOLIC DYSFUNCTION INDUCED BY ISOPROTERENOL IN RATS

Introduction: Introduction: Resveratrol (RESV), one of the main polyphenols found in grape skin and red wine, has shown several cardiovascular benefits in experimental models. For instance, RESV increased the survival rate of heart failure animals, acting as a potent inhibitor of cardiac hypertrophy and preventing contractile dysfunction.

Objective: Objective: To evaluate the effect of different doses of RESV on cardiovascular function in rats with isoproterenol(ISO)-induced cardiac dysfunction.

Methods: Methodology: Wistar rats were treated with two doses of RESV (2.5 or 10 mg/kg, p.o.) or vehicle (0.05% tween 80) for 14 days, starting 1 week before ISO or vehicle (saline) administration. Cardiac dysfunction was induced by ISO treatment (5mg/kg/day, i.p.) for 7 days. Thus, animals were divided into 6 groups: Control (C); C+RESV2.5; C+RESV10; ISO; ISO+RESV2.5; ISO+RESV10. The rats were weighed weekly and, at the end of the treatment, they were anesthetized and a polyethylene catheter was inserted into the right carotid and advanced until left ventricle (LV) to record intraventricular pressure. Then, the animals were euthanized for heart withdrawal and calculation of heart weight/body weight ratio. CEUA-UNAERP Approval No02/2016.

Results: Results: ISO and RESV 2.5 mg/kg administration, associated or not, reduced weight gain in animals (C: 56±5; C+RESV2.5: 31±4; ISO: 33±3; ISO+RESV2.5: 19±3), while 10 mg/kg of RESV did not change this parameter (C+RESV10: 48±3; ISO+RESV10: 42±2). The heart weight/body weight ratio was higher in ISO groups than control (C: 3.45±0.07; ISO: 3.81±0.12). RESV at dose of 10 mg/kg decreased the heart weight/body weight ratio in C+RESV10 (2.94±0.03) compared to control, whereas the dose of 2.5 mg/kg increased this parameter in ISO+RESV2.5 (4.22±0.09) compared to ISO group. Both doses of RESV elevated LV systolic pressure, heart rate and dP/dTmax in control groups. However, only the dose of 10 mg/kg had this effect in ISO rats. In control groups, only 10 mg/kg of RESV improved dP/dTmin (C: -9198±664; C+ RESV10: -11428 ± 403). On the other hand, both doses of RESV prevented the decrease in dP/dTmin in ISO rats (ISO: -6165±648; ISO+RESV2.5: -8510±642; ISO+RESV10: -9088±507).

Conclusions and Support: Conclusion: RESV at 2.5 or 10 mg/Kg doses had different effects on weight gain, heart weight/body weight ratio, heart rate and cardiac systolic function in control and ISO rats. However, both doses of RESV were able to prevent cardiac diastolic dysfunction induced by ISO in rats. Support: CNPq and UNAERP.

ID: 2774

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: "THE PRIOR KNOWLEDGE OF SCIENCE AND MATH TEACHER TRAINING STUDENTS ABOUT THE HUMAN BODY CONTENTS PRESENTED IN THE NATIONAL COMMON CURRICULAR BASE." Paiva-Dias, G.1, Sá, V. A 1, Lellis-Santos, C. 1 1Department of Biological Sciences, Institute of Enviro

Introduction: In 2020 it is mandatory to implement the Common National Curricular Base (BNCC) for science education in the Brazilian schools. However, the science teachers might not be proficient and confident in teaching all the competencies and skills required in the official regulation. It is not known the scientific literacy of science teachers about human body concepts, neither if they were trained to teach these concepts.

Objective: This study focused on identifying the scientific literacy of Science and Math freshman students about anatomy and physiology of the human body as it is required in the Common National Curricular Base.

Methods: First year Science and Math students (N=93) answered a questionnaire applied in the first week of the course Human Body: Structure and Function of the Federal University of São Paulo. The survey addressed their knowledge in the itens of BNCC related to the human body, considering their proficiency, prior learning, and confidence in teaching. Mixed methods of educational research was used to analyze data.

Results: The overall proficiency of the participants was low; however, the skills in which students showed significant proficiency were about health education. The items EF08CI11 (sexuality) and EF01CI03 (body care) were pointed as the highest values for prior learning and confidence in teaching, respectively. The items related to the nervous system were rated as the less proficient. Correlational study revealed that the item concerning the human vision was negatively significant correlated to the proficiency of biology-interested students and to the competency of private school students in teaching the content of the item in the future. Counterwise, the human vision item was positively correlated to the confidence in teaching of female students.

Conclusions and Support: Freshman students enrolled in science and math teacher training program presented low skills of proficiency and confidence in teaching about the items related to the human body as required in the BNCC. This study reinforces the importance of physiology education for elementary education and higher education students. Financial Support: self-funding

ID: 3030

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: universitys' School of Health Sciences Ethical Commission - - - Portugal

Title: ABOUT THE PERFUSION ASYMMETRY OF THE HUMAN (LEFT AND RIGHT) LOWER LIMBS

Introduction: Slight perfusion asymmetries between the individual paired feet have been systematically noticed in many of our studies. These differences are known for quite some time, although not fully understood. A recent study suggested that those could be related with morphometric asymmetries of femoral arteries in paired legs affecting several haemodynamic indicators.

Objective: Our purpose was to look further into these asymmetries in participants with different ages.

Methods: This study included twelve healthy volunteers, divided into two groups according to age, Group I including six young adults (21 ± 1.1 years old) and Group II including six older individuals (55.8 ± 3.0 years old). All participants had normal vascular function evaluated by the ankle-arm index. After adaptation to the temperature-controlled room, perfusion was measured in the anterior-medial region of both feet using three different techniques - Laser Doppler Flowmetry (LDF), Photoplethysmography (PPG) and Polarized Spectrometry (TiVi). Measurements took place in a static standing position (Phase 1) and after a 5 min gait exercise (Phase 2).

Results: During Phase 1 we found that all systems detected differences for all flow related variables between both feet although not significant. Nevertheless, we are aware that these systems, although based on similar optical principles, do not measure at the same tissue depth providing, therefore, different information. Apparently, women seem to have higher resting values when compared to men during this static measurements. Exceptions were found, for the younger group, regarding the blood volume pulse (PPG) and, for the older group, the concentration of red blood cells detected by the TiVi system. It is also apparent that all these flow related variables seem to have higher values in the younger participants group. Still in this static phase, the right-left comparisons shows that there seems to exist a predominance of the right foot values over the left foot values detected with the three different measurement systems. As referred before, these differences have been recently related with morphometric variations of the femoral artery capable of affecting the lower limb hemodynamics. However, we believe that posture and the individual gait biomechanics might also have a contribution. Finally, it is important to underline that, after gait, these differences have different destinies in both groups. Measurements obtained immediately after gait in the older group show that these right-left foot differences practically disappeared, while in the younger group those differences still exist with a similar expression to the one registered before gait.

Conclusions and Support: Our study shows that the perfusion related asymmetries between the right and left feet during rest, remain present in the post-gait period at least in the younger group of participants. Reasons beyond these differences seems to attenuate with (healthy) ageing probably resulting from the contribution of other not only morphometric, determinants that need to be further identified.

ID: 3286

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: TEMPERATURE EFFECT ON THE ENDOCRINE AND CIRCADIAN SYSTEMS OF Danio Rerio. AN IN VIVO APPROACH

Introduction: Temperature is an abiotic factor with important influence on the behavior and physiological processes in teleosts. Thermal changes also participate as stressors with increase of cortisol and affect the rhythm of other hormones such as melatonin and growth hormone, in both endo- and ectothermic organisms.

Objective: Our aim was to investigate how low chronic temperature (23°C for 6 days) modulates the expression of melanopsins (opn4), growth hormone, cortisol and melatonin pathway genes, as well as their relationship with clock genes in Danio rerio.

Methods: D. rerio adult males (AB strain) were kept in 7 L-tanks for 5 days at 28°C, 14:10 (LD), after which the animals were submitted to 23°C for 6 days. The animals were euthanized 2 hours (ZT2) and 16 hours (ZT16) after the lights turned on. Brain, eyes, liver, and muscle were removed and then homogenized for RNA extraction and purification. For the qPCR opn4m1/m2, per1/2, cry1/2, aanat1/2, mtnr1aa/bb, gh1, ghra/b, igf1ra/b, and gr genes were analyzed. We performed a Pearson correlation analysis to determine the level of association between the expression of clock genes and all others in the different tissues Whole-body was extracted for the cortisol determination and processed according to the kit instructions (Salivary Cortisol ELISA kit, Salimetrics, CA, USA). All procedures were performed according to the Ethics Committee on Use of Animals (CEUA) of the Institute of Biosciences, protocol N° 331/2018.

Results: The opn4m1 had a higher expression at ZT16 compared to ZT2 at both temperatures. We found a decrease in the expression of opn4m2 at 23°C at ZT2 compared to the control group at the same ZT. To determine which of the organs had a higher expression of opn4m1 and opn4m2, we compared the total daily mRNA levels (ZT2+ZT16). This analysis demonstrated higher expression of both opsins in the eye, at both temperatures, when compared to the brain. At 28°C, per1/2 had the highest expression at ZT2 compared to ZT16 in all tissues analyzed, evidencing the diurnal rhythmic behavior of the gene peaking in the light phase. In the brain, eye and muscle there was

a remarkable decrease in per expression at 23°C at ZT2. In all the tissues evaluated (except the brain), the expression of cry1/2 at ZT2 was significantly higher than at ZT16 at 28°C and decreased at 23°C at ZT2. There was an increase of aanat2 mRNA in the brain and of aanat1 in the eye of animals at 23°C at ZT16. The mtnr1aa was more expressed in the eye than in the brain. Interestingly, the eye showed a reduction of mtnr1aa and mtnr1bb total transcripts at 23°C. The growth hormone axis was also affected: chronic low temperature reduced the expression of the gh1 gene at ZT16. Both ghra/b and igf1ra/b transcripts exhibited a significant decrease at 23oC when compared with control group. Finally, we observed an increase in cortisol in animals at 23°C at ZT2 as compared to the control group at the same ZT, with a decrease of its receptor (gr) transcripts in the liver. In all tissues analyzed, we observed positive and negative correlations between clock genes, melanopsin and genes related to hormonal pathways.

Conclusions and Support: We showed that low temperature modulates the expression of melanopsins, hormone related, and clock genes. The results indicated a direct correlation of the clock molecular mechanism with the analyzed endocrine systems, especially the growth hormone and melatonin axes, and with melanopsin in various tissues of D. rerio. Support. CAPES, FAPESP, and CNPq

ID: 2775

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF THE ASSOCIATION AMONG HIGH FAT DIET, MELATONIN AND APICAL PERIODONTITIS ON INSULIN SENSITIVITY AND TNF-α PLASMA CONCENTRATION IN RATS Santos, R.M.1, Tsosura.1, T.V.S.1, Mattera, M.S.L.C.1, Belardi, B.E.1,Chiba, F.Y.2, Tavares, Dourado, N. G.1,

Introduction: Models that simulate diet-related obesity are widely used in animal studies to understand changes in this disease in humans. Obesity is currently recognized as a chronic low-grade inflammatory disease that is linked to metabolic disorders, including type 2 diabetes mellitus and insulin resistance (IR). Therefore, it is essential to verify the relationship between excess weight induced by diets associated with associated endodontic infections such as apical periodontitis (AP), as both share systemic effects such as IR and an increase in inflammatory mediators such as TNF-α. Currently, melatonin (ME) has been used in clinical settings for several chronic diseases (diabetes, dyslipidemia, cardiovascular diseases) in addition to oral pathologies; all thanks to its antioxidant and anti-inflammatory properties. Therefore, it is essential to verify the relationship between excess weight induced by diets as well as its association with periodontitis. In addition to checking the beneficial effects of ME in this association of pathologies.

Objective: To evaluate the water intake, food and energy, body weight, total weight of periepididymal white adipose tissue (WAT) and gastrocnemius muscle (GM), glycemia, insulinemia, insulin sensitivity and levels of TNF-α in plasma in rats fed with high fat diet (HFD) with AP and treated with ME.

Methods: Ethics Committees on Animal Use, São Paulo State University, 00574-2019). Eighty rats (Wistar, male, 60 days old) were used, divided into 8 groups (n=10): 1) control (CN); 2) AP; 3) HFD; 4) HFD + AP (HFDAP); 5) CN + ME (CNME); 6) AP + ME (APME); 7) HFD + ME (HFDME); 8) HFD + AP + ME (HFDAPME). Initially, groups with HFD were fed for 107 days on a diet consisting of 45.5% of standard diet +22.7% of animal lard +22.7% of vegetable fat +9% of sugar; the other groups received a standard diet. On the 7th day, the groups with AP were submitted to AP induction and, after 70 days, they were treated with ME (5mg / kg, diluted in drinking water, for 30 days). Glycemia was assessed using the glucose oxidase method; insulinemia and TNF-α were assessed using the ELISA method; insulin sensitivity was assessed using the HOMA-IR index (model for assessing insulin resistance homeostasis).Statistical analysis was performed by analysis of variance ANOVA 3-way, followed by Tukey post hoc test ($p<0.05$). Data were expressed as the mean ± standard error of the mean.

Results: There was a decrease in body mass evolution, food and water intake in groups fed with HFD. Groups fed with HFD energy intake was significantly higher compared to the standard diet. The HFD and HFDAP groups showed an increase in the weight of WAT and a decrease in GM. The HFD and HFDAP groups showed an increase in glycemia; HFDAP increase in insulinemia; AP and HFD and HFDAP decrease insulin sensitivity; AP, HFD and HFDAP increase in plasma concentrations of TNF-α. The treatment with ME resulted in the improvement of the altered parameters analyzed, except in the evolution of body mass, food, energy and water intake as well as weight of GM.

Conclusions and Support: HFD, in association or not with AP, promotes changes in insulin sensitivity in addition to promoting an increase in WAT, ME was shown to have a protective role in the altered parameters analyzed. Therefore, we emphasize the importance of maintaining oral health and healthy eating habits, thus avoiding losses in systematic health. Support: grant #2019/08520-0, FAPESP.

ID: 2776

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

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Title: THE CAROTID SINUS NERVE STIMULATION ATTENUATES PRO-INFLAMMATORY CYTOKINES RELEASE INDUCED BY PERIODONTITIS IN RATS

Introduction: Periodontitis is caused by a chronic inflammatory response to a periodontal biofilm that can disseminate to extraoral tissues. Our laboratory showed that stimulation of the baroreflex and chemoreflex modulates the inflammatory response in different experimental models. However, the effect of these reflexes on periodontitis has not hitherto been investigated.

Objective: The present study aimed to examine the role of the electrical stimulation of the carotid sinus nerve (CSN) in rats with periodontal disease (PD), to investigate whether the baroreflex and chemoreflex activation attenuate the pro-inflammatory cytokines in plasma, gingival tissue and gut (ileal and colonic mucosa).

Methods: Electrodes were implanted around the CSN combined with bilateral ligation of the first mandibular for PD induction, or SHAM (fictitious surgery for ligation around the right and left first molars). The rats were divided into four groups: SHAM + CSN non-stimulated; SHAM + CSN stimulated; PD + CSN non-stimulated; and PD + CSN stimulated. Next, the CSN was stimulated daily for 10 minutes during nine days in unanesthetized animals. On the eighth day, a catheter was inserted into the left femoral artery, and in the next day, the effectiveness of the CNS electrical stimulation was confirmed. After the arterial pressure recording, the blood sample, gingival specimens, and gut were collected for analyzing cytokines (TNFα, IL-6, IL-1β, and IL-10) levels. All procedures were approved by the Ethics Committee of Ribeirão Preto Medical School, University of São Paulo, São Paulo, Brazil (protocol number 252/2017).

Results: As expected, the CSN electrical stimulation was effective to decrease the arterial pressure in SHAM and PD rats. Nevertheless, this hypotensive response was similar among groups. Moreover, CSN electrical stimulation did not change the heart rate in SHAM or PD rats. Concerning the plasma cytokine levels, CSN electrical stimulation reduced the IL-6 levels in PD rats, as compared to rats with PD but not submitted to CSN stimulation [183.2 ± 69.3 (n = 6) vs. 9.2 ± 6.8 pg/mL (n = 8)]. Nevertheless, no differences were observed in the plasma levels of TNFα, IL-1β or IL-10 in all groups. PD increased mRNA expression of TNFα and IL-1β in the gingival tissue compared to the SHAM groups. However, the expression of TNFα in the gingival tissue decreased in PD rats submitted to electrical CSN, when compared to PD rats with CSN non-stimulated [343.8 ± 37.4 (n = 4) vs. 17.12 ± 17.1 2 2ΔΔCt (n = 3)]. On the other hand, the same was not observed in IL-1β expression in gingival tissue. No changes were found in the expression of IL-6 and IL-10 in the gingival tissue in all evaluated groups. In ileal and colonic mucosa, PD or CSN electrical stimulation did not change any cytokines concentrations.

Conclusions and Support: Thus, the CSN electrical activation attenuates systemic (plasma) and local (gingival) pro-inflammatory cytokines induced by PD in rats. The current findings provide new evidence concerning the anti-inflammatory effects of the baroreflex and chemoreflex electrical activation in PD. SUPPORT: FAPESP (#2013/20549-7, #2018/10455-9 and #2017/05163–6).

ID: 3288

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: University of São Paulo - SÃO PAULO - Sao Paulo - Brasil

Title: THE ROLE OF TRPA1 CHANNEL IN THE CIRCADIAN EXPRESSION OF CLOCK AND THERMOGENESIS-RELATED GENES IN BROWN ADIPOSE TISSUE

Introduction: The Transient Receptor Potential Ankyrin 1 (TRPA1) channel is a cold-activated non-selective cation channel. Temperature changes affect the circadian periodicity of physiological processes, especially of peripheral tissues, leading to adaptative metabolism gene reprogramming and thermogenic activation in the brown adipose tissue (BAT) in mammals. In this line, natriuretic peptides (NPs) released by the heart, under environmental cold stimulus and through sympathetic activation, interact with their receptors NPR-A, -B, and -C, and consequently modulate thermogenic activity of BAT.

Objective: We aimed to investigate the role of TRPA1 channel and time-dependent temperature effects on gene expression of circadian rhythms and thermogenesis related genes in BAT of mice kept at 30°C (thermoneutral temperature) and 22°C (cold exposure).

Methods: C57BL/6J wild type (WT) and Trpa1 KO (C57BL/6J background) male mice were bred and raised in the Department of Physiology (IB-USP) (Animal License (CEUA) number , 350/2019) and were acclimated for 2 weeks at 29°C +1 under 12:12 light/dark cycle (800 to 1000 lx inside the cages). Then the animals were segregated into four groups: WT or Trpa1 KO mice at 22°C +1 or at the thermoneutrality condition, 29°C +1, for 2 or 4 weeks. The transcript levels of the core clock genes (Per1 and Bmal1), NP receptors (Npra, Nprb, and Nprc), and Ucp1 were measured atZT2 (2 h after lights on) and ZT14 (2 h after the lights off). The data were analyzed according to the 2−ΔΔCt method and by Two-way ANOVA followed by Bonferroni.

Results: The classical antiphase between Bmal1 and Per1 mRNA levels was found in both genotypes under 29 or 22°C for 2 and 4 weeks; there is, Bmal1 peaked in the light phase and Per1 in the dark phase. Interestingly, the cold temperature led to increased Bmal1 transcript levels in both genotypes after 4 weeks, but it did not affect Per1 gene expression. Since Bmal1 transcript level increased in Trpa1 KO mice, the lack of TRPA1 channel does seem to affect clock gene oscillatory pattern under light/dark cycle. For Npra, Nprb, and Nprc genes, we observed decreased transcript levels of Npra and Nprc in cold-stimulated WT after 2 and 4 weeks, whereas in Trpa1 KO animals there was a decrease only after 4 weeks. As to Nprb receptor, there was a marked decrease of the transcripts in both WT and Trpa KO animals after 2 and 4 weeks at 22oC. For Ucp1 gene, the cold-mediated response led to increased gene expression after 2 and 4 weeks in the WT mice; however, the significantly increased Ucp1 transcript was evidenced in Trpa1 KO mice only after 4 weeks. Conclusion: TRPA1 channel does not seem to alter the oscillatory patterns of clock genes in BAT, but it may influence NPRs gene expression in animals kept in or below thermoneutrality. We also evidenced the effect of cold-induced increase on Ucp1 gene expression in both genotypes, but the lack of TRPA1 channel may have induced a delay of the thermogenic response (Ucp1 increase after 4 weeks), which is a matter for future investigation.

Conclusions and Support: TRPA1 channel does not seem to alter the oscillatory patterns of clock genes in BAT, but it may influence NPRs gene expression in animals kept in or below thermoneutrality. We also evidenced the effect of cold-induced increase on Ucp1 gene expression in both genotypes, but the lack of TRPA1 channel may have induced a delay of the thermogenic response (Ucp1 increase after 4 weeks), which is a matter for future investigation. Supported by FAPESP, CNPq, and CAPES.

ID: 3033

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Rio de Janeiro - Macaé - Piaui - Brasil

Title: EFFECTS OF COMBINED ORAL CONTRACEPTIVE ASSOCIATED WITH HYPERLIPIDIC DIET IN FEMALE REPRODUCTIVE TISSUES AND MAMMARY GLAND OF MICE

Introduction: The combined oral contraceptive (COC) is an effective method of contraception used by 140 million women in reproductive age worldwide. Many women choose continuous use of contraceptives to avoid menstruation and symptoms of premenstrual tension. However, information about the effects of continuous use associated with obesity on reproductive is poor.

Objective: This study evaluated the effects of continuous use of a COC compound by drospirenone (DRSP) and ethinyl estradiol (EE) associated with the high-fat diet (HFD) in female reproductive tissues and mammary gland of mice.

Methods: Swiss mice of 80 days old received daily for 65 days, via gavage, 0.2mL of distilled water (vehicle), or COC composed of 0.6 μg of EE and 60 μg of DRSP, associated with the normolipidic diet (groups CTL and COC, respectively) or HFD (CH65 and COH65 groups). After 35 days of treatment, the CTL and COC groups were redistributed, and half of the animals started receiving HFD (CH30 and COH30). Vaginal cytology was recorded throughout the treatment, and after 65 days the animals were euthanized and the uterus and ovaries were weighed. Mammary gland was collected and submitted to histologic procedures and whole mount assay. Data were evaluated by Shapiro-Wilk and compared by parametric tests (ANOVA followed by Newman-Keuls) or non-parametric tests (Kruskal-Wallis followed by Dunns), $P < 0.05$ (CEUA approval UFRJ-Macaé nº.: MAC039).

Results: During the treatment, the COC, COH30 and COH65 groups stopped cycling normally and vaginal cytology had characteristics of metestrus and proestrus phases, this effect is known as "COC hormonal stimulation". There was an increase in the uterus weight of animals treated with contraceptive and high-fat diet for 65 days compared with animals that did not receive contraceptive but were fed with high-fat diet throughout the treatment (OH65: 6.313 ± 0.59 and CH65: 3.489 ± 0.51). There was no significant difference in ovary weight between animals (COH65: 0.5240 ± 0.06957 and CH65: 0.47 ± 0.079). The number of mammary branches (COC:19.60 ± 2.28 and CTL: 29.93 ± 4.8; COH30: 17.63 ± 2.9 and CH30: 17.62 ± 3.3; COH65 20.93 ± 2.9 and CH65: 14.95 ± 3.9) and alveolus (COC: 46.3 ± 11.3 and CTL: 59.86 ± 9,2; COH30: 48.73 ± 12.73 and CH30: 46.41 ± 11.37; COH65: 50.67 ± 9.98 and CH65: 46,41 ± 11.37) were similar between the groups. In addition, there was no difference in the mammary gland adipocytes diameter (COC: 52.7 ± 1.7 and CTL: 51.10 ± 5.4; COH30: 92.43 ± 10.7 and CH30: 88.23 ± 4.9; COH65: 67.57 ± 6.19 and CH65: 93.9 ± 9.8).

Conclusions and Support: Continuous treatment with drospirenone and ethinyl estradiol increased the weight of the uterus in animals that were fed with a high-fat diet and was effective in altering the regular pattern of vaginal cytology. Finnancial Supports: CNPq, FAPERJ, CAPES

ID: 3035

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: EXTRACELLULAR VESICLES EVALUATION IN DOGS WITH OVERWEIGHT AND OBESITY, BEFORE AND AFTER THE WEIGHT LOSS PROGRAM.

Introduction: The expansion of adipose tissue alters animal physiology and predisposes it to several comorbidities such as orthopedic, respiratory, and endocrine diseases. The extracellular vesicles (EVs) are nanoparticles surrounded by a lipid bilayer, which transport lipids, proteins, nucleic acids, and metabolites, and can be secreted by different cell types through exocytosis, budding or protrusion of the cell membrane. The adipocytes are capable of synthesizing, releasing, and transferring EVs to target cells modulating their regulation, thus playing a critical role in obesity pathogenesis and its metabolic complications.

Objective: The objective of this study was to evaluate the diameter and concentration of EVs in dogs with excess body fat, before and after the weight loss program.

Methods: A total of 19 neutered dogs (9 females and 10 males) of different breeds were evaluated at the university's veterinary hospital. The excess body fat was determined using the body condition score (BCS) and the dogs underwent a clinical evaluation to determine their health status. For EVs analysis, blood serum samples were initially subjected to three consecutive centrifugations (300G for 10 min, 2.000G for 10 min and 16.500G for 30 min) and stored at -80ºC. Afterwards, samples were thawed, filtered in a 0,20 µm, and subjected to two consecutive ultracentrifugation (120.000G for 70 min). The pellet resulting from the EVs isolation step was dissolved in PBS for the analysis of EVs diameter and concentration using NanoSight NS300®. After initial evaluation, dogs underwent a weight loss program with a standardized low-calorie diet (2990 Kcal/kg of metabolizable energy). The energy requirement for weight loss, in kcal/ day, was calculated using the formula: 70x(target weight)0.75. After 4 months of a low-calorie diet, the EVs diameter and concentration were reevaluate. Comparisons between groups were made by ANOVA ($p<0.10$). EVs were characterized by the expression of specific proteins by Western blot. The protocol was approved by the Animal Use Ethics Committee (n° 1940130519).

Results: In the initial evaluation, 2 dogs were overweight (11%) and 17 were obese (89%) and the mean values of body weight and BCS were 15.5±2.5 Kg and 8.2±0.2, respectively. The mean values of EVs diameter was 122.7±3.1 nm and EVs concentration was 1.1±0.1 x 1010 particules/ml. After the weight loss program, we observed a significant reduction of body weight (-10%), BCS (-17%), EVs diameter (-6%) and EVs concentration (-31%) ($p<0.10$). There was no difference in relation to sex in the evaluated parameters. EVs isolated from the dogs' serum samples were characterized by the expression of surface-marker protein CD9 and internal proteins Alix and HSP70 and absence of the cellular markers' proteins Cytochrome C and COX IV.

Conclusions and Support: The reduction in body weight and fat accumulation is accompanied by a decrease in the diameter and concentration of EVs in dogs. This result could indicate a reduction in the secretory activity of the adipose tissue in dogs, after 4 months of a low-calorie diet. FAPESP grants 2018/26547-0; 2014/22887-0 and 2015/21829-9.

ID: 3038

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: SHORT-TEM SUSTAINED HYPOXIA INCREASES EVOKED EXCITATORY TRANSMISSION IN THE NUCLEUS TRACTUS SOLITARY NEURONS OF MICE.

Introduction: Sustained hypoxia (SH) activates chemoreceptors to produce cardiovascular and respiratory responses to keep PaO2 within the physiological range. The first synaptic contact of peripheral chemoreceptor afferents in the central nervous system is located at the nucleus tractus solitarius (NTS) in the dorsal brainstem

Objective: To evaluate the effect of short-term sustained hypoxia [(SH) 24 hours, FiO2 0.10] on the synaptic transmission in the NTS neurons of mice.

Methods: Brainstem slices and whole-cell patch clamp were used to study the electrophysiological properties of NTS neurons from control (CON) and SH mice (C57Bl/6 mice). The experimental protocols were approved by the Institutional Ethical Committee Protocol #016/2018).

Results: The passive properties of NTS neurons of mice were not affected by SH when compared to control [input resistance, 0.69 ± 0.1 (n=9) vs 0.74 ± 0.19 MΩ (n=8)][RMP, -57.4 ± 3.3 (n=10) vs -61 ± 3.5 mV (n=7)]. SH also produced no changes in the spontaneous excitatory transmission in relation to control [sEPSC frequency, 1.13 ± 0.4 (n=5) vs 1.88 ± 0.7 Hz (n=6); amplitude, 29 ± 9 pA (n=5) vs 22 ± 9 pA (n=6); half-width, 2.3 ± 0.5 (n=5) vs 2.4 ± 0.3 ms (n=6)]. On the other hand, stimulation of afferent fibers in the tractus solitary of SH mice produced a significant increase in the excitatory transmission in NTS neurons, which amplitude of evoked excitatory currents was larger in NTS neurons from SH than in control mice [-62 ± 17 (n=8) vs -153 ± 30 pA (n=9)] with no changes in the kinetic of evoked current.

Conclusions and Support: The data are showing that SH produced no changes in the passive properties of NTS neurons but increases the evoked glutamatergic synaptic transmission in the NTS neurons of mice. We suggest that this effect of SH on the NTS neurotransmission can be related to the changes observed in the autonomic regulation in mice after SH. Financial support: FAPESP and CNPq

ID: 3294

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EUPHORBIA TIRUCALLI (AVELOZ) LATEX INTAKE MODIFIES CARDIAC FUNCTION IN RATS

Introduction: The use of medicinal plants as supporting treatment for different diseases is still a controversial issue due to few studies about them. In this regarding, Euphorbia tirucalli also known as Aveloz, is a popular plant used for several illnesses, including cancer treatment. Some studies have shown many benefic effects of Aveloz latex, but most of them were done in vitro and still there is a huge lack of information about its in vivo actions.

Objective: To evaluate the effects of Aveloz intake in the cardiovascular system of rats.

Methods: The present project was approved by the institutional Ethical Committee for Animal Research, CEUA-UFES number 09/2019. Sixteen, five months old, male Wistar rats were randomly divided in two groups: Aveloz treated (latex and water mixture,13.06 mg/kg) and Control group (water, 1 mL). The animals were treated by gavage for 15 days. Arterial blood pressure (BP) was measured before and after Aveloz treatment. Heart, lungs, blood cells and plasma were evaluated for cardiac function and hypertrophy, pulmonary congestion, oxidative stress, and inflammatory markers, respectively. Data were expressed as mean ± SEM and were considered significant when $p<0.05$.

Results: No differences were found in BP before and after treatment between experimental (118±3 mmHg and 122±4 mmHg) and control (109±83 mmHg and 129±3 mmHg) groups, respectively. Neither signs of cardiac hypertrophy (Aveloz: 16±1 mg/mm vs. Control: 17±1 mg/mm) nor lung congestion (Aveloz: 53±5 mg/mm vs. Control: 60±5 mg/mm) were found after mixture intake. On the other hand, cardiac function analysis results showed that dP/dtmax were significantly increased (8045±629 mmHg/s vs. 5221±1077 mmHg/s, $p<0.05$) and left ventricular relaxation time constant (Tau) constant were significantly decreased (0.01±0.002 s vs. 0.03±0.005 s, $p<0.05$) in the treated rats when compared with control animals, respectively. High levels of plasma and blood cells oxidative stress were observed in the Aveloz compared with the control group by the AOPP (31±2 µmol/L vs. 16±1 µmol/L, $p<0.05$), TBARS (0.04±0.02 µMol MDA/mg vs. 0.03±0.01 µMol MDA/mg, $p<0.05$), DHE (6892±712 a.u vs. 4444±712 a.u, $p<0.05$) and DCF assays (2366±317 a.u vs. 1624±53 a.u, $p<0.05$). Myeloperoxidase activity, an inflammatory marker, was also higher in the plasma of treated animals when compared to control group (0.14±0.011 a.u vs. 0.04±0.005 a.u, $p<0.05$).

Conclusions and Support: This is the first study to demonstrate in vivo Aveloz effects on the cardiovascular system and its effects on systemic oxidative stress. Our data demonstrated that Aveloz increases cardiac contractility, which seems good at first but could lead to a more cardiac energy spent and myocardial damage if the heart is overstressed. Additionally, Aveloz intake leads to high plasmatic reactive oxygen species levels, which could result in target-organ damage. In face of these preliminary results, further studies need to be designed to elucidated in which conditions Aveloz intake could have effective therapeutic actions. Support: CAPES and CNPq

ID: 2784

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: STEM CELL THERAPY IMPROVES CARDIAC FUNCTION AND AUTONOMIC MODULATION IN RATS WITH AORTIC REGURGITATION.

Introduction: Nowadays, studies demonstrate that stem cells (SC) paracrine factors improve cardiac performance in different cardiopathies. Aortic regurgitation (AR) is a valvopathy that causes volume overload followed by cardiac remodeling and dysfunction. Considering there is no specific and efficient pharmacological therapy for AR treatment, it becomes relevant to evaluate if cell therapy with SC can be a therapeutic alternative for AR.

Objective: We investigated the effects of mesenchymal stromal cells (MSC) on cardiac morphology and function, autonomic modulation, baroreflex control, inflammatory profile, and exercise capacity of Wistar rat with chronic AR.

Methods: MSC were obtained from whole bone marrow by ficoll gradient and it was separated by adherence to culture flask. The AR was surgically induced by leaflets laceration and it was confirmed by echocardiography (ECHO). False-operated animals (SHAM) were used as control. A week later, animals received an intramyocardial injection of DMEM culture media (SHAM group, n=15; AR group, n=14) or

MSC (106 cell/100 µL, AR MSC group, n=9). After three and seven weeks, the morphology (sphericity index, SI; left atrial diameter, LAD) and systolic (shortening fraction, SF) and diastolic function (E/A ratio) were measured by ECHO. The exercise capacity was measured by the time on exercise (TE) during the treadmill test. After that, animals were submitted to femoral arterial and venous catheterization for measurement of systolic blood pressure (SBP) and pulse interval (PI) on a beat-to-beat record in nonanesthetized rats. That record was used to evaluate baroreflex effectiveness (BEI) and calculate heart rate variability (HRV) in time (SDNN) and frequency domain (LF/HF). The left ventricular (LV) pressure register enabled us to acquire the LV end-diastolic pressure (LVEDP). The hearts were removed for fibrosis quantification and plasma was taken to analyze inflammatory profile by ELISA (TNF-α, IL-6 and TGF-β). Experimental procedures were approved by CEUA UNESP - 835. The data are expressed as media±SEM and statistical differences were assumed when $p<0.05$ after ANOVA one or two way followed by Dunnet post-test.

Results: After 8 weeks from AR, cell therapy preserved LAD (cm: AR+MSC= 5,65±0,16 vs SHAM=4,95±0,09; $p>0.05$) , although it did not prevent LV dilation caused by the volume overload (SI, cm: AR=0,89±0,03 and AR+MSC= 0,91±0,03 vs SHAM= 0,70±0,02; $p<0.05$). MSC treatment improved systolic (SF, Δ%: AR+MSC=9,2±1,7 vs AR=0,4±1,6; $p<0.05$) and diastolic function (animals percentual rescue back to normal range of E/A ratio, %: AR=29; AR+MSC=80) that may be related to LVEDP reduction (mmHg: AR+MSC= 8,8±1,3 vs AR= 13,5±0,16; $p<0.05$). Neither AR or treatment modified exercise capacity (TE, min: AR=25±2 and AR+MSC = 27±1 vs SHAM= 27±2; $p>0,05$). MSC therapy ameliorated BEI (%: AR+MSC=0,20±0,02 vs AR= 0,11±0,01; $p<0.05$) and did attenuate cardiac autonomic imbalance (LF/HF: AR+MSC= 0,34±0,04 vs SHAM=0,48±0,07; $p>0.05$) while no change was seen on HRV on time domain (SDNN: AR=7,1±0,1 and AR+MSC = 7,7±0,6 vs SHAM=8,9±0,7; $p>0,05$). AR didn't change the percentage of collagen deposition (CP, %: AR= 13±2 and AR+MSC = 14±2 vs SHAM= 9±2; $p>0,05$). TNF-α was reduced by MSC (pg/mL: AR+MSC=60,2±4,9 vs SHAM=36,4±8,0; $p<0.05$).

Conclusions and Support: MSC improves systolic and diastolic cardiac function preventing autonomic imbalance and baroreflex dysfunction. Supported by: CNPq and FAPESP

ID: 3297

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF RESVERATROL IN DIFFERENT DOSES ON AUTONOMIC CARDIOCIRCULATORY CONTROL OF RATS TREATED WITH ISOPROTERENOL

Introduction: The antioxidant action of Resveratrol (RESV), a polyphenol compound contained in red wine, is known to produce many beneficial effects in the cardiovascular system. Preclinical studies have shown satisfactory effects of RESV in animal models of myocardial ischemia and heart failure, preventing or reducing the disease progression. However, there is no evidence in the literature about the effect of different doses of RESV on autonomic modulation in isoproterenol(ISO)-induced cardiac dysfunction.

Objective: To assess the effect of different doses of RESV on autonomic and baroreflex function in awake rats with ISO-induced cardiac dysfunction.

Methods: Wistar rats were divided into the following groups: Controls (C); C+RESV (with 2.5 or 10 mg/kg, p.o., 14 days); ISO (5 mg/kg/day, i.p., 7 days); ISO+RESV (with 2.5 or 10 mg/kg, p.o., 14 days). RESV treatment started 1 week before ISO administration. At the end of the treatment, rats were anesthetized to insert catheters into femoral artery and vein for hemodynamic recordings and drug administration, respectively. After 24 hours, with animals recovered from anesthesia, basal arterial pressure (AP) and heart rate (HR) were recorded for 30 minutes. Thereafter, phenylephrine (4µg/Kg) and sodium nitroprusside (16µg/Kg) were administered for the analysis of baroreflex sensitivity, and the autonomic blockers methyl atropine (1mg/Kg) and propranolol (2mg/Kg) for the analysis of cardiac autonomic tone and intrinsic HR (iHR). CEUA-UNAERP Approval Nº02/2016.

Results: In basal parameters, 2.5 mg/kg of RESV reduced HR in ISO+RESV2.5, while at dose of 10 mg/kg increased basal mean AP in ISO+RESV10 compared to ISO group. Sympathetic tone was higher in ISO rats than controls, but RESV prevented this increase with greater effect at 2,5mg/kg (C: -26±4; ISO: -38±6; ISO+RESV2.5: -16±2; ISO+RESV10: -23±3). Parasympathetic tone was reduced in ISO group, but RESV hampered this effect in both doses (C: 112±8; ISO: 51±7; ISO+RESV2.5: 85±9; ISO+RESV10: 87±5). Although iHR was lower in all ISO groups compared to controls, ISO+RESV10 rats exhibited higher iHR than ISO and ISO+RESV2.5 (C: 406±5; ISO: 334±4; ISO+RESV2.5: 346±6; ISO+RESV10: 362±5). ISO administration attenuated the reflex bradycardia to phenylephrine (C: -2.5±0.2; ISO: -1.9±0.1), as well as the reflex tachycardia to sodium nitroprusside (C:-5.9±0.4; ISO: -4.0±0.3). RESV significantly improved such changes only at dose of 2.5 mg/kg, enhancing sensitivity to bradycardia (ISO+RESV2.5: -2.6±0.2; ISO+RESV10: -2.4±0.2) and to tachycardia (ISO+RESV2.5: -5.2±0.5; ISO+RESV10: -4.3±0.3).

Conclusions and Support: RESV in both doses prevented the harmful effects of ISO on cardiac autonomic function, counteracting sympathetic hyperactivation and improving vagal tone in this model of cardiac dysfunction. However, the dose of 2,5mg/kg seemed to be more effective since it had a greater effect on baroreflex sensitivity and sympathetic tone. CNPq and UNAERP.

ID: 3044

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: NEONATAL OVERNUTRITION IN FEMALE RATS PROMOTES CHANGES ON REPRODUCTIVE PARAMETERS IN THEIR MALE AND FEMALE OFFSPRINGS

Introduction: Recently, researchers have shown an increased interest in neonatal overnutrition induced by reduction in litter size. For this, on postnatal day (PND) 3, the litter size is adjusted, when 3 pups are kept, being 2 males and 1 female in the small litter (SL), or 10 pups, 5 males and 5 females, in the normal litter (NL) with each mother. Previous studies showed that, compared to female rats of NL, SL exhibited metabolic changes associated with reproductive dysfunctions. It has already been observed that neonatal overfeeding in females predisposes the development of obesity in their male offspring.

Objective: The aim of this study was to investigate if neonatal overfeeding in female rats promotes changes on metabolic and reproductive parameters in their male and female offsprings.

Methods: Offsprings of NL and SL Wistar rats were obtained by the mating of 25 females with males. Each offspring was maintained with 8 pups, 4 males and 4 females. After weaning, on PND 21,food intake and body weight were evaluated every 5 days until PND 60. Vaginal opening, first estrus, coefficient of each phase of estrous cycle, such as the regulation of the cycle were evaluated for females, and the preputial separation for males. On PND 59, animals were subjected to 6 hours of food restriction and Glucose Tolerance Test (GTT) was performed. At PND 60, Lee index was calculated, and after 6 hours of food restriction males were euthanized by decapitation. Females were euthanized on the first day of proestrus (afternoon of proestrus) starting from PND 60. After euthanasia, blood was collected for plasma evaluations of total cholesterol levels, triglycerides, free fatty acids, corticosterone, testosterone, estradiol, and progesterone. The weight of white adipose tissue, testicles, ovaries, uterus and adrenals was also measured. (CEUA 3457.2019.11).

Results: Males offspring of SL showed higher weight of retroperitoneal adipose tissue than offspring of NL. This group also presented higher glycemia after 15, 30 and 60 minutes of glucose overload, compared to control, as well as greater area under the curve of GTT. Male offspring of SL showed higher levels of triglycerides and lower testosterone levels. In addition, these animals also showed earlier preputial separation. On the other hand, females offspring of SL presented later regularization of estrous cycles and higher coefficient of diestrus I and II, in addition to higher levels of free fatty acids and lower estradiol levels, compared to offspring of NL. No significant differences were observed on the other evaluated parameters.

Conclusions and Support: Thus, it can be concluded that neonatal overnutrition in female rats predispose their male and female offspring to develop metabolic and reproduction disturbs. This work had the financial support of Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), Brazil.

ID: 3300

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: Sustained Hypoxia Decreases GABAergic Neurotransmission in the NTS of Sprague Dawley Rats

Introduction: In previous studies we documented that short-term sustained hypoxia (SH, 24hs, FiO2 0,1) in rats from Wistar-Ribeirão Preto (WRP) and Wistar Hannover (WH) strains leads to an increase in the magnitude of autonomic and respiratory responses to chemoreflex activation. In addition, it was observed an increase in the excitability of NTS neurons and in the glutamatergic transmission at the NTS. However, there is no experimental evidence about possible changes of GABAergic transmission in NTS neurons after SH protocol in rats from Sprague-Dawley strain.

Objective: To evaluate possible effect of SH on GABAergic neurotransmission in the NTS neurons projecting to ventrolateral medulla (VLM) of Sprague Dawley rats.

Methods: SD rats (25-30 days) were used in these studies (CEUA #136/2018). NTS neurons projecting to VLM (NTS-VLM neurons) were labeled with previous microinjection of Greenbeads into VLM. Brainstem slices containing caudal and intermediary NTS were obtained and the inhibitory postsynaptic currents (IPSCs) were recorded in labeled NTS-VLM neurons using whole-cell patch-clamp. The evoked IPSCs were induced by placing a concentric bipolar electrode onto the ipsilateral NTS area to the recorded neuron. The evoked and spontaneous GABAergic currents were confirmed by adding GABA receptor antagonist (picrotoxin-100 μM) in the bath perfusion at the end of experimental protocol.

Results: SD rats submitted to SH present a decrease in the amplitude of evoked IPSCs [-231.8 ± 33,95 (n=9) vs -48.83 ± 10,51 pA (n=6), p=0.0009] when compared to control. In addition, SH decreased the decay-time in the SD (25.42 ± 5,086 vs 9.23 ± 1.2 ms, p= 0.0247) and produced no significant changes in the rise-time parameter (2.810 ± 0.4638 vs 2.147 ± 0.1949 ms, p= 0.2864) in relation to control. SH produced significant decrease in the frequency of spontaneous IPSCs in relation to control [2.350 ± 0.1674 (n=5) vs 0.5086 ± 0.1344 ms (n=6), p<0.0001]. No significant changes were observed in the amplitude of sIPSCs (26.35 ± 2.232 vs 29.12 ± 6.557 pA, p= 0.6766) and in the half-width of sIPSCs (7.053 ± 1.181 vs 7.030 ± 1.804 ms, p= 0.9913) after SH.

Conclusions and Support: Conclusions: The data are showing that SH decreases: a) the GABAergic neurotransmission in NTS-VLM neurons; and b) the frequency of sIPSCs, suggesting that SH is affecting the pre-synaptic terminal. These findings, similar to that previously described in WH rats, indicate that changes in the GABAergic modulation in NTS-VLM neurons after SH may contribute to the increase in the magnitude of the cardiovascular and respiratory responses to chemoreflex activation observed in SD and WH rats. Financial Support: FAPESP, CAPES e CNPq.

ID: 3045

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: HEPATIC NORADRENERGIC FIBERS ACTIVATE GLUCONEOGENESIS THROUGH CREB/CRTC2 RECRUITMENT DURING THE COLD STATE

Introduction: The physiologic role of sympathetic innervation in the regulation of hepatic gluconeogenesis remains elusive. Understanding the mechanisms capable of regulating the hepatic glucose production is of great importance for new approaches in the treatment of diseases such as diabetes and obesity.

Objective: We aimed to investigate the role of sympathetic noradrenergic fibers in the activation of hepatic gluconeogenesis and the involvement of CREB and its coactivator CRTC2 in such effect.

Methods: Neonate male C57BL/6 mice (ethical committee nº183/2015) were submitted to pharmacological sympathectomy (6-OH-Dopamine). In adulthood, animals were exposed to cold stimulus (4ºC) for 3 and 6 h and blood glucose was measured each hour. Liver was harvested for enzymatic activity, western blot, and Rt-PCR analysis. The transcriptional activity of CREB in vivo was evaluated by an imaging system (IVIS) using mice reporter for CRE-luciferase. Catecholamines were estimate by HPLC and hormones by ELISA. The results were expressed as means ± SEM and were submitted to appropriate statistical analysis ($p<0.05$).

Results: Cold exposure (6h) of innervated mice increased plasma levels of glucose (1332±34 vs 899±26 in controls; AUC), glucagon (65.5±9.9 vs 10.5±1.3 in control; pg/dl) and corticosterone (13.5±3.5 vs 5.1±2.2 in control; µg/dl) but suppressed insulinemia, and did not affect plasma epinephrine. Cold also increased activity and mRNA levels of PEPCK and G6Pase, two key-enzymes of gluconeogenesis, the hepatic content of norepinephrine (185.4±13 vs 135.8±11 in control; ng/g) as well as the phosphorylation levels (1.45±0.03 vs 1±0.07 in control; AU) and in vivo transcriptional activity (3.1e9±1.5e9 vs 5.2e6±6.9e6 in controls; p/s) of CREB. All these effects were abolished or attenuated by sympathectomy. Moreover, cold stress increased dephosphorylation of the CREB co-activator CRTC2 at Ser171/275 in innervated mice, a covalent modification that activates CRTC2. The phosphorylation status of PKA and PKC substrates and their downstream targets were modulated by either cold and/or sympathectomy suggesting the involvement of both signalings in the activation of CREB and gluconeogenesis by noradrenergic fibers in response to cold stress.

Conclusions and Support: The data suggest that the hepatic sympathetic nerves acutely stimulate the gluconeogenesis in response to cold with the participation of CREB/CRTC-2 pathway. Support: FAPESP (2018/10089-2; 2019/05900-6; 2019/26583-9)

ID: 3052

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Instituições: Centro Universitário da Fundação Hermínio Ometto/FHO - Araras - Sao Paulo - Brasil

Title: ATTENUATION OF RENAL DAMAGE IN RENOVASCULAR HYPERTENSIVE AND OBESE RATS BY CALORIC RESTRICTION

Introduction: Caloric restriction (CR) reverses the overweight and obesity, but it can also be effective in renovascular hypertension. These pathologies can modulate the expression of intercellular communication proteins, mediated by Gap Junctions and cell adhesion.

Objective: To evaluate the effect of CR on the expression of cellular communication and adhesion genes in kidneys of hypertensive and obese rats.

Methods: This study was approved by the Ethics Committee on Animal Use (protocol no. 042/2016). Seventeen male Wistar rats (180 to 200g) were used and renovascular hypertension was induced by stenosis of the left renal artery, according to the 2-kidney, 1-clip (2K1C) model. The animals were divided into Sham, normotensive, fed a normolipidic diet ad libitum; Obese / Hypertensive (OH) with high-fat diet ad libitum for 12 weeks and Obese / Hypertensive / Restricted (OHR) with high-fat diet ad libitum for 8 weeks and after 40% CR of the high-fat diet for 4 weeks. The expression of genes associated with hypertension (Renin and Eca), cell communication (Cx37, Cx40 and Cx43) and cell adhesion (E-cad, N-cad and α-SMA), was analyzed by RT-PCR.

Results: Biometric parameters revealed that CR decreased the body weight of animals and improved their pressure indexes. Likewise, it reversed the atrophy of the stenotic kidney seen in the 2K1C model. Hypertension up-regulated the gene expression of Renin and Eca in the stenotic kidney, however, CR further stimulated the increase of Renin and attenuated of Eca expression. CR increased Cx37 and Cx40 gene expression in both kidneys but did not modulate Cx43 gene expression, being equal to the data observed in OH animals. CR selectively stimulated increased expression of E-cad and α-SMA in the stenotic kidney and restored the expression of the N-cad gene, decreased by the effects of hypertension and obesity.

Conclusions and Support: CR can recover renal weight and N-cad gene expression. By physiological adaptation mechanisms, CR increased Renin gene expression. However, to mitigate hypertension, CR decreased the Eca gene expression and stimulated the expression of Cx37 and Cx40, E-cad, and α-SMA. Together, these data suggest that CR was able to improve the systemic and local effects caused by stenosis of the left renal artery, contributing to the restoration of cell junctions in the kidneys and attenuating blood pressure and body weight gain. Such results contribute to a growing understanding of how CR is beneficial in reperfusion, suggestive of the resumption of renal homeostasis to restore blood pressure levels. This research was supported by Fundação Hermínio Ometto/FHO.

ID: 2797

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR PROFILE OF CONSCIOUS FREELY MOVING MICE AFTER SHORT-TERM SUSTAINED HYPOXIA

Introduction: Short-term sustained hypoxia (SH) induces hypertension in rats as a result of sympathetic overactivity, which is linked to changes in sympathetic-respiratory coupling. However, there is no consistent data about the effect of SH on mice due to the different protocols of hypoxia and difficulties associated with the handling of these animals under freely moving conditions.

Objective: To evaluate the effects of SH exposure on the baseline mean arterial pressure (MAP), heart rate (HR), and cardiovascular responses to chemoreflex activation of conscious freely moving mice.

Methods: C57BL/6 mice (7-8 weeks old) under anesthesia with Isoflurane had a catheter inserted into the femoral artery for recording pulsatile arterial pressure (PAP). Another catheter was inserted into the jugular vein for drug administration. Four days after the surgery, mice were submitted to normoxia or SH protocol (24h, FiO2 0.1). At the end of the protocol, cardiovascular parameters were recorded. Peripheral chemoreflex was activated by intravenous administration of KCN (0,16 mg/Kg, i.v.). Statistical analysis was performed by non-paired Student's t test. All experimental protocols were approved by institutional ethical committee (CEUA # 140/2019).

Results: SH mice (n=13) presented no significant changes in baseline MAP compared with the control (n=17) group (109 ± 2 vs 106 ± 2 mmHg). However, SH mice presented a significant decrease in baseline HR (510 ± 22 vs 633 ± 16 bpm; P = 0.002) in comparison with the control group. Mice from control (n=11) and SH groups (n=8) presented similar pressor responses to chemoreflex activation with KCN (27 ± 3 vs 22 ± 3 mmHg), but the magnitudes of bradycardic responses were greater in SH mice than in controls (-329 ± 36 vs -210 ± 30 bpm, P=0.02).

Conclusions and Support: The data are showing that the 24-h SH protocol produces no major changes in the baseline MAP of mice, which may be linked to increased parasympathetic tone to the heart, as revealed by a reduction in baseline HR and a large increase in the bradycardic component of the chemoreflex response. We suggest that the observed autonomic imbalance favoring the parasympathetic component to the heart may prevent the development of hypertension in mice submitted to SH. FAPESP, CAPES, CNPq.

ID: 3056

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: AEROBIC EXERCISE IMPROVES OBESITY-INDUCED CARDIAC REMODELLING IN COMPARISON TO ENALAPRIL TREATMENT

Introduction: The prevalence of obesity has increased over the decades and has become a public health problem as a consequence of nutritional habits and sedentary lifestyle. Obesity has being strongly associated with cardiovascular disease (CVD), and the relationship between both diseases has been attributed to dysfunctional changes in adipose tissues that contributes to homeostasis disturbance leading to activation of the classic axis of the renin-angiotensin system (RAS). Aerobic training is the first choice to treat and prevent obesity, and angiotensin-converting enzyme inhibitors have also demonstrated positive effects on CVD.

Objective: To compare the impact of aerobic training and/or enalapril on the heart in mice with diet-induced obesity (DIO) model.

Methods: C57BL/6 mice (3-mo-old) were fed a standard-chow (SC, n=10) or high-fat (HF, n=40) diet for 8 weeks. Then, HF group was randomly divided into: HF (n=10), HF-Training (HF-T, n=10), HF-Enalapril (HF-E, n=10), and HF-Exercise-Training (HF-ET, n=10). After another 8 weeks of either training and/or enalapril treatment, body mass (BM), systolic blood pressure (SBP), food and energy intake was evaluated periodically. Heart mass (HM), cardiomyocyte transverse area (CTA), and left ventricular lumen diameter (LD) and wall thickness (WT) were measured and morphometrical analyses were estimated for CV disease. Data presented as mean ± standard deviation and analyzed by one-way ANOVA with Holm–Sidak post-hoc test. P-value $\leq 0.05$ was statistically significant.

Results: HF group presented higher BM than SC, while HF-E and HF-T showed no difference in relation to SC group. HF-ET presented reduced BM than all experimental groups. All treated groups reduced SBP, while in HF groups was increased when compared to SC group. Food intake was constant in all groups, while HF group had higher energy intake in relation to SC group. HM was increased in HF group when compared with SC group. HF-E and HF-ET reduced the HM in relation to HF and HF-T groups, while HF-ET presented an additional reduction when compared to HF-E group. CTA was increased in HF group, while all groups with intervention remained similar to SC group. HF-T presented an increase in left ventricular LD in relation to other groups. SC and HF groups showed a similar LD, while HF-E and HF-ET reduced the LD when compared to SC. HF-T group presented left ventricular WT larger than all experimental groups, while in SC groups this measure was reduced in relation to all intervention groups. HF-ET group presented left ventricular WT larger than SC but smaller than HF-T, and there was no significant difference between HF and HF-E groups.

Conclusions and Support: Both enalapril and aerobic training decreased BM gain and SBP. In HF group there was increase in HM, but only HF-T was able to increase left ventricular LD and WT and maintain the CTA suggesting the aerobic training as a good alternative for obesity treatment and prevention when compared with enalapril treatment.Support: FAPERJ, CNPq, CAPES.

ID: 2801

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDAD DE LOS ANDES - - - Chile

Title: FUZZY TOPOGRAPHICAL STRUCTURE DIFFERENCES DUE TO THE SIZE AND SLIDING WINDOWING ON ELECTROMIOGAPHY MAPS

Introduction: Neuromuscular electrical activity of muscle contractions to study motor behavior may be acquired by non-invasive High-density surface electromyography (EMG) and be visualized their intensity through EMG maps using the root mean square as amplitude feature. However, 2D image representation of EMG requires signal processing parameters (window length and sliding for root mean square) which may change the own electrophysiology structure of map activations.

Objective: Therefore, here we determine the effect of size and sliding windowing on Fuzzy Topographical Structure of maps obtained through high-density electromyography technique.

Methods: This study was approved by the Bioethics Committee of the Universidad de los Andes (Santiago, Chile; # INV-IN201701) according to the principles of the Declaration of Helsinki. We analyzed 73008 topographic maps obtained from seven healthy participants (age 21.4 ± 1.5 year-old, body mass 74.5 ± 8.5 kg) performing isometric plantar flexion with the ankle at a neutral position. We used a rigid non-invasive array of 64 surface electrodes placed over the medial gastrocnemius muscle to collect monopolar data of muscle fiber depolarization. Size windows of 50, 100, 150, 250, 500 and 1000 ms with sliding of 0, 25, 50, 75, and 90% were used in a factorial design to create the EMG maps to compare how these parameters alter the neurophysiological information provided by muscles. A non-linear cross-entropy dimensional reduction of maps was applied to the data to obtain the own structure of them. Volume and entropy of reduced maps were studied. Intragroup behavior for volume and entropy of fuzzy topological structures were described by non-linear least square.

Results: The volume of fuzzy topographical structure increased under extreme sliding parameters (0, 25 and 90%) with R2 = 72.5%, and entropy of fuzzy topographical structure decreased under extreme sliding parameters (0, 25 and 90%) with R2 = 90,1%. The window length of 1000 ms decreased the entropy with R2 = 10,0% , and non-changes were observed in entropy under different widow length R2 = 16,9%.

Conclusions and Support: In conclusion, sliding to generate EMG maps cause the loss of fuzzy topographical structure and modifies its patterns, principally by the increasing of window sliding, but also small window length i.e. 50 ms creates the most different pattern of muscle activation.

ID: 2803

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: CBIOS- Universidade Lusófona - - - Portugal

Title: IMPACT OF KEFIR CONSUMPTION ON CUTANEOUS HEALTH ASSESSED USING A SLS-INDUCED LESION MODEL
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Introduction: The regular intake of probiotics has been associated with beneficial effects on cutaneous health and skin barrier function, but little evidence of such activity can be found in the literature. One of the most popular natural probiotic foods is kefir, a beverage produced by milk fermentation with kefir grains, which are formed by a symbiotic association of lactic acid bacteria, acetic acid bacteria and yeasts in a polysaccharide matrix. Its bioactive properties may be linked to the action of the microbiota or their metabolites, namely organic acids, released during fermentation.

Objective: The aim of this study was to evaluate, in vivo and in human volunteers, the differences in cutaneous health between healthy individuals consuming and not consuming kefir, thus contributing to the study of the benefits of the intake of kefir probiotic on skin health.

Methods: The study was approved by the local ethics committee (Process nº 1/2018). A group of 33 healthy male and female volunteers drank daily, for 8 weeks, 100ml of kefir (tfermentation=24h, T=20ºC). A control group of healthy volunteers without any probiotic ingestion was used. A model of induction of cutaneous irritation in the volar forearm using SLS (24h contact, 1% aqueous solution) was used to assess impact on skin barrier, at baseline and after 8 weeks. The impact of SLS on the barrier was evaluated using bioengineering equipment, namely transepidermal water loss (TEWL) measured by a Tewameter® TM300 (CK Electronics, Germany) and hydration measured by a Corneometer® CM825 (CK Electronics, Germany). Erythema was also evaluated by a ChromaMeter CR300 (Minolta, Japan) using the L*a*b system and the a* values.

Results: Using the SLS induced lesion model, we found a significant positive impact on the skin parameter TEWL, in the treated group after 8 weeks of consuming kefir daily, whereas no difference was detected in the control group for this parameter. No significant differences were found in both groups after SLS application in skin hydration and erythema at baseline and 8 weeks.

Conclusions and Support: Our results corroborate the hypothesis that the probiotic kefir may have a positive impact on skin health and that the utilization of the SLS model is a useful method to evaluate skin barrier status. Despite the limited number of volunteers in both groups, this study confirms the interest in continuing to assess the impact of the kefir consumption on skin health. Support: This work is financed by Portuguese national funds through the FCT - Foundation for Science and Technology, I.P., under the project UID / DTP / 04567/2020

ID: 2806

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Odontologia de Araraquara-UNESP - Araraquara - Sao Paulo - Brasil

Title: MUSCARINIC RECEPTORS OF THE MEDIAL SEPTAL AREA INVOLVED IN THE SALIVATION INDUCED BY PILOCARPINE INJECTED PERIPHERALLY

Introduction: Saliva is important for phonation and chewing, among other functions. Patients with xerostomia show signs of burns, infection in the oral mucosa, difficulties in feeding and periodontal diseases. Pilocarpine (muscarinic agonist) acts on salivary and sweat glands producing salivation and sweat. Although pilocarpine can stimulate salivary secretion by acting directly on salivary gland, it can cross the blood-brain barrier and activate central mechanisms that stimulate salivation. At least five genes encoding muscarinic receptors are recognized, subdivided into M1 to M5, with four of them (M1 to M4) being expressed in the rat brain. Besides salivation, pilocarpine binds to different central muscarinic receptor subtypes producing water intake and pressor responses. The cholinergic mechanisms of the medial septal area (MSA) are involved in the control of pressor, natriuretic and dipsogenic responses. A possible participation of the MSA in the salivation produced by pilocarpine was also suggested.

Objective: In the present study, we investigated the involvement of M1 and M3 muscarinic receptors in the MSA in the salivation and water intake induced by pilocarpine injected peripherally.

Methods: CEUA 07/2018. Male adult Holtzman rats (weighing 250-350 g, n = 7-11) with stainless steel cannulas previously implanted in the MSA were used. The saliva secreted was measured in rats anesthetized with ketamine (100 mg/kg of body weight), using previously weighed cotton balls placed in the oral cavity for 7 minutes. Water intake was measured for 1 hour using graduated tubes. Pilocarpine (1 mg/kg of body weight) was injected ip 15 min after the injection of pirenzepine (M1 antagonist), 4-DAMP (M1/M3 antagonist) or vehicle into the MSA.

Results: The injection of 4-DAMP (50 nmol/0.5 µl) into the MSA reduced ip pilocarpine induced salivation (313 ± 50, vs. vehicle into the MSA: 463 ± 35 mg/7 min, $p < 0.05$), but did not modify the dipsogenic response produced by pilocarpine (3.0 ± 0.7, vs. vehicle into the MSA: 4.3 ± 0.8 ml/1 h, $p > 0.05$). Pirenzepine (50 nmol/0.5 µl) injected into the MSA did not change salivation (580 ± 56, vs. saline into

the MSA: 552 ± 106 mg/7 min, p > 0.05) or water intake (2.9 ± 0.7, vs. saline into the MSA: 2.5 ± 0.5 ml/1 hour, p > 0.05) induced by ip pilocarpine.

Conclusions and Support: The results suggest that M3 receptors in the MSA are involved in the salivation induced by pilocarpine injected peripherally. It was not found involvement of M1 and M3 receptors in the MSA in the dipsogenic response and M1 receptors in the salivation to ip pilocarpine. CNPq (139587/2019-5), FAPESP.

ID: 2808

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Instituições: FCT UNESP, campus de Presidente Prudente - Presidente Prudente - Sao Paulo - Brasil

Title: THE EFFECTS OF OMEGA-3 ASSOCIATED TO AEROBIC PHYSICAL EXERCISE IN PROSTATE OF WISTAR RATS SUBMITTED TO HIGH-FAT DIET VERAS, A.S.C[1], GOMES, GOMES, R.L[2], Tavares, M.E.A[3], Correia, R.R[3], Batista, V.R.G[3], dos Santos, J.A.C[3], Lenquiste, S.A[2], Vanderlei

Introduction: It is known that excessive consumption of a high-fat diet (HFD) results in overweight, and the consumption of omega-3 (ω-3) is related to the reduction of some types of diseases and the association with physical exercise results in decreased risk of deaths.

Objective: The aim of study was verify the effects of HFD associated to ω-3 and aerobic physical exercise in ventral prostate of Wistar rats.

Methods: 49 Wistar rats were divided into 7 groups (n=7): CT- received the standard diet and water ad libitum; HF- received only the high-fat diet; HF+FO- high-fat diet and fish oil; HF+Ex- high-fat diet and performed aerobic physical exercise; HF+FO+Ex- received the high-fat diet, fish oil and performed aerobic exercise; HF+CO- the animals received high-fat diet and chia oil; HF+CO+Ex, received high-fat diet, chia oil and performed aerobic exercise. The protocol of aerobic physical exercise were performed 3 times per week, for 30 minutes in swimming water for 8 weeks, the fish and chia oils were applied 3 times per week, before exercise protocol. The study was approved by CEUA (protocol number 3962).

Results: The initial and final weight, and weight gain did not altered in groups, in other hand, the HF groups increased the mesenteric, retroperitoneal and epididimal fat and fat index, while trained and chia oil group reduced these fats. The exercise associated to fish and chia oil decreased the fat index of animals. From another perspective, the histologic parameters were possible to observed that the HF+Chia increased the mast cells and other groups do not statistical differences. To hormonal analysis in androgen receptor (AR) we analyzed the reduction caused by HFD in HF groups compared to HF+FO, HF+CO and HF+CO+Ex. The HF+CO+Ex were able to reduce the FAS/CD95 expression, and inflammatory cytokines as interleukin-6 (IL-6) were most reactive in HF compared to CT animals, HF+Chia compared to CT and HF+FO+Ex groups and finally high expression of IL-6 in HF+CO+Ex compared to CT and HF+Ex groups, while HF+FO minimized the expression of IL-6, the same happened in HF+FO+Ex group compared to HF+CO+Ex. The tumor necrosis factor-alpha (TNF-α) the exercise isolated did not able to reduce this expression, by the way, when associated to fish and chia oil (HF+FO+Ex and HF+CO+Ex) were most potent in reduction of this inflammation compared to HF group. When analyzing the antioxidant factor as superoxide dismutase (SOD), catalase (CAT), nuclear factor erythroid 2-related factor 2 (NRF-2), glutathione synthetase (GSS) and nitric oxide synthase-2 (NOS2), we observed that HF+CO+Ex animals reduced SABLOD-1 compared to HF+FO+Ex, the oppose happened in HF+FO+Ex that increased the CAT levels compared to HF group, the chia oil could improve the NRF-2 levels compared to HF, HF+FO and HF+CO+Ex groups. The GSS levels were enhanced by HF+CO in relation to CT group, and the high-fat diet reduced the NOS-2 gene levels compared to HF+FO+Ex and HF+CO+Ex animals, while the chia oil linked to exercise increased the NOS-2 levels in prostate of rats.

Conclusions and Support: However, to reduction of to reduce the disorders affected by the high-fat diet, the prostate disorders, inflammatory damages, and oxidative stress (induced by high-fat diet) it is necessary the association of aerobic physical exercise with fish and/or chia oils. This work was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior-Brasil (CAPES)-Finance Code-001.

ID: 3064

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: UFCSPA - Porto Alegre - Rio Grande do Sul - Brasil

Title: MICE DAMS AND THEIR OFFSPRING FED WITH A HYPERCALORIC OR RESTRICTIVE DIET PRESENT OXIDATIVE STRESS IN THE LIVER

Introduction: Pregnancy and lactation are important stages for the fetal development. During these phases the organism is able to react to adverse nutritional and behavioral situations for its normal development and to promote molecular, cellular and biochemical adaptations.

Nutrition during fetal life affects metabolic, cardiovascular, and endocrine function in the mature individual. It has been shown, from a study with rats, that the consumption of hypercaloric diets during pregnancy and lactation causes an increased risk of developing diseases in the offspring, such as metabolic syndromes, congenital abnormalities and obesity.

Objective: Assess oxidative stress parameters in the liver of dams and their offspring, which were fed with a hypercaloric or restrictive diet.

Methods: The Institutional Animal Care and Use Committee of UFCSPA (#388/15) approved this study. Thirty female BALB/c albino mice (60 days old) were separated in 3 different groups (n=10/group). The control group (CONT) received a standard mice chow ad libitum (total energy content of 3.4 kcal/g); the restrictive diet group (RD) had 30% reduction in the standard chow amount, compared to the consumption of CONT; and the hypercaloric diet group (HD) was fed with a special chow ad libitum (total energy content of 4.9 kcal/g). Diet adaptation lasted 25 days, after they were housed with males for mating. On the first postpartum day, litters were standardized at 6 pups. After weaning, the dams were euthanized, and hepatic tissue was collected for further analysis. After weaning, the female offspring of CONT, RD and HD dams was randomly divided into 2 groups: one fed with standard chow (CONT), and the other had a restrictive diet (RD). Thus, 6 experimental groups were generated (maternal diet/offspring diet): CONT/CONT, CONT/RD, RD/CONT RD/RD, HD/CONT, and HD/RD. The offspring diet (CONT or RD) was maintained along all their lives. The euthanasia, followed by tissue collection, was performed when they were 100 days old, and liver tissue was used for 2′,7′-dichlorofluorescein (DCF) and for thiobarbituric acid-reactive substances (TBARS) assays, and for the activities of superoxide dismutase (SOD) and catalase (CAT).

Results: In the liver tissue of the dams, we did not find changes in ROS formation among groups as measured by DCF assay. Nevertheless, MDA formation was higher in HD in comparison to RD group. SOD activity decreased in RD mice compared to CONT group ($F(2,17)=5.337$; $p=0.01$). In contrast, CAT activity was significantly increased in HD when compared to CONT ($F(2,14)=4.391$; $p=0.04$). We found a decreased SOD/CAT ratio in the RD and HD groups in comparison to the CONT group ($F(2,15)=13.53$; $p=0.0007$). The results for the offspring demonstrate differences in the oxidative stress parameters. There was a maternal diet effect ($F(2,12)=4.407$), and the SOD activity was increased in RD/RD compared to HD/RD ($p=0.036$).

Conclusions and Support: In the analyses in the liver of the dams and their progeny, we found parameters related to oxidative stress altered in the lipid peroxidation and in the activity of the antioxidant enzymes. These results indicate that the different diets can affect the balance of oxidative parameters in the livers of the dams and their adult offspring. Support: CAPES, CNPq, UFCSPA

ID: 3576

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Instituições: Unaerp - Ribeirão Preto - Sao Paulo - Brasil

Title: EFFICACY OF THE SOFTWARE "SNAPS" ON LEARNING CONSOLIDATION OF THE AUTONOMIC NERVOUS SYSTEM IN A PBL HYBRID CURRICULUM: A PILOT STUDY

Introduction: In order to assist students in learning physiology and pharmacology of the autonomic nervous system (ANS) and to replace physiology practical classes with animals, our group has developed the software "SNAPS" as a computer-assisted learning tool. This software simulates classical experiments performed on animals, in which substances were injected in dogs or rats to demonstrate physiological responses.

Objective: The aim of this study was to assess the efficacy of the software "SNAPS" on learning consolidation of the physiology and pharmacology of the ANS and the students' perception of this learning method.

Methods: This study was conducted in the Medical School of the University of Ribeirão Preto which employs a Problem Based Learning (PBL) hybrid curriculum. After the tutoring session and theoretical class about the ANS, sixty-two students were divided into 2 groups: 1) Group PRE (G.PRE, n=19), in which students answered 10 multiple-choice questions (MCQs) about the physiology and pharmacology of ANS before the practical class using the software "SNAPS"; 2) Group POST (G.POST, n=43), in which students answered the same 10 MCQs after the practical class using the software. The individual final score was the total correct answers of each one. At the end of the practical class, all students answered a Likert type questionnaire to evaluate their perceptions of the use of the software. We applied the Shapiro-Wilk test to verify data distribution (G.Pre p=0,061; G.Post p=0,004) and the non-parametric Mann-Whitney test to compare the medians from the two groups. UNAERP Ethics Committee approval no. 1.700.790.

Results: Students from the G.POST group obtained greater scores in the MCQ compared to G.PRE ($6\pm1.87$ vs. $5\pm1.3$, $p=0.049$). In students' perception, the software "SNAPS" helped in the learning process of the ANS (100%), assisted them in clarifying doubts (96.6%), and facilitated the correlation between theory and practice (100% ). In addition, most students agreed or totally agreed that the software "SNAPS" is interactive, dynamic and visually representative (100%) and it is effective as an alternative method to replace practical classes with animals (86%).

Conclusions and Support: This pilot study demonstrated that the software "SNAPS" was effective in consolidating learning of the physiology and pharmacology of the ANS. Moreover, in the perception of medical students, the software is interactive and representative, which assists in understanding and correlating the theoretical and practical content. Support: UNAERP and PET-Biotec. Keywords: Autonomic Nervous System. Physiology. Pharmacology. Computer-assisted Learning.

ID: 2809

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: USP - SAO PAULO - Sao Paulo - Brasil

Title: PREVENTION OF RESPIRATORY FUNCTIONAL AND NEUROANATOMICAL CHANGES IN TNFR1-/- MICE SUBMITTED TO THE 6-OHDA MODEL OF PARKINSON'S DISEASE

Introduction: Parkinson's Disease (PD) is a neurodegenerative disease well known for its classical motor symptoms. Nevertheless, non-classical symptoms, such as respiratory deficits, are also present and responsible for considerable deaths in PD patients. Previous studies have already shown brainstem degeneration which is probably linked to respiratory function impairment in a rat model of PD induced by 6-hydroxydopamine (6-OHDA) injection in caudate-putamen nucleus (CPu). Many mechanisms are responsible for neuronal death, including neuroinflammation which is present in many neurodegenerative diseases.

Objective: The aim of this study is to investigate the role of neuroinflammation mediated by glial cells, such as astrocytes and microglia, in respiratory functional and neuroanatomical deficits observed in the animal model of PD induced by 6-OHDA.

Methods: C57BL/6 or tumor necrosis factor receptor 1 knockout mice (TNFR1-/-) (CEUA:8760150318) were anesthetized with isoflurane 2.5% and received bilateral injection of 6-OHDA (10 µg/µl) or vehicle in CPu. To investigate the time-course of degeneration and respiratory deficits, 5, 10 or 20 days after surgery, C57BL/6 mice were submitted to whole body plethysmography to assess respiratory parameters under normal, hypercapnic (7% CO2) and hypoxic (8% O2) conditions. In TNFR1-/- mice respiratory parameters were assessed just 20 days after surgery. At the end of protocol, animals were perfused and the brains were removed to further immunohistochemical analysis.

Results: In C57BL/6 mice, 6-OHDA bilateral injections in CPu massively destroyed TH+ neurons in SNc in all times analyzed (5 days: 75%; 10 days: 77%; 20 days: 74%). Neuroanatomical assessment reveal degeneration in the preBotzinger complex (preBotC) (10 days: 44%, and 20 days: 43%) and in the retrotrapezoid nucleus (RTN) (5 days: 41%, 10 days: 35%, 20 days: 56%). Astrocytes density is enhanced in SNc (10 days: 112%, 20 days: 122%), tends toward a reduction in preBotC ($p<0.05$) and is reduced in RTN 10 days after surgery (46%). Microglia morphological analysis indicates for a possible neuroinflammation only in SNc and RTN. Respiratory parameters assessment reveal reduction in basal respiratory frequency 10 and 20 days after surgery (10 days: 29%; 20 days: 24%) associated with enhanced inspiratory and expiratory times. TNFR1-/- mice also present massive degeneration of TH+ neurons in SNc (77%), however, neurodegeneration was prevented in RTN. Moreover, there is no change in respiratory parameters between TNFR1-/- mice that received 6-OHDA injections and animals from vehicle group, indicating prevention of respiratory deficits.

Conclusions and Support: In this model of PD, respiratory deficits are clearly present and can be associated with neurodegeneration in important brainstem areas involved with neural control of breathing. Abolishing TNF-α inflammation pathway, respiratory rate is restored, indicating the involvement of this pathway in the neurodegeneration of brainstem nucleus in PD animal model. Support: FAPESP, CNPq, CAPES and Serrapilheira Institute.

ID: 2810

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade de São Paulo - São Paulo - Sao Paulo - Brasil

Title: NEUROVASCULAR GLIA INTERACTION IN VENTRAL MEDULLA SURFACE IN A RAT MODEL OF PARKINSON'S DISEASE

Introduction: Parkinson's disease (PD) is a progressive motor disorder characterized by selective and progressive loss of dopaminergic neurons in the substantia nigra (SNpc). Patients afflicted with PD experience several symptoms, which include orthostatic hypotension and sleep apnea, highly correlated with peripheral and central chemoreflex dysfunction, both of which maintain arterial PCO2 and PO2 within very narrow ranges. Blood flow is a fundamental determinant of tissue CO2/H+, yet the extent to which blood flow regulation within chemoreceptor regions contributes to respiratory behavior and delineating such regulation during neurological disease such in PD remains unknown.

Objective: We tested the hypothesis that impaired respiratory chemoreflex noted in PD-induced rats through treatment with 6-hydroxydomanine was correlated with dysfunctions in vascular homeostasis within the retrotrapezoid (RTN) region.

Methods: 45 adult male Wistar rats (Vehicle or 6-OHDA intrastriatal-injected previously, CEUA: 9674120619) were used under urethane anesthesia (1.2 g/kg iv.). Diaphragm (DiaEMG) and abdominal (AbdEMG) muscles were recorded in electrophysiological experiments and pial vessels video recorded for posterior analysis through the functional experiments.

Results: First, in order to validate our PD model, TH expression in SNpc reduced 84% in the 6-OHDA striatum-injected animals compared to vehicle-injected. In the electrophysiological experiments, we found that the pial vessels present a higher contraction in response to CO2

in PD-induced animals (5.5 ± 0.2 vs. Sham: 3.2 ± 0.2 %, p<0.001). Using pharmacological tools, ATP in the VMS is able to contract this particular vessel, which presents a more expressive contraction in PD-induced animals (4.5 ± 0.5, vs. Sham: 3.2 ± 0.5%, p<0.001). Those effects are attenuated by PPADS (a purinergic P2-receptor blocker) administration in both groups. We also found a very clear and similar contractile response by CO2 after ARL67156 (an ectonucleotidase antagonist) in VMS in both groups (Sham: 6.2 ± 0.2 % and PD-induced: 6.9 ± 0.2 %). We also quantified the number of GFAP and IBA-1 positive cells in the RTN, and then we performed morphometric assays, including skeletonization and fractal analysis. However, we report that in this PD-induced animal model, glial (GFAP) and microglial (IBA-1) cells do not show important morphological changes.

Conclusions and Support: These data indicate that dysfunction in purinergic signaling, potentially through altered ATP bioavailability in the VMS, compromises the RTN neuroglial vascular unit during PD. Financial support: FAPESP, CAPES, CNPq.

ID: 2815

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Medicina de Ribeirão Preto - Ribeirão Preto - Sao Paulo - Brasil

Title: CALCITONIN GENE-RELATED PEPTIDE MODULATES CARDIAC AUTOPHAGY IN MOUSE. Schavinski, A.Z1; Morgan, H1; Silva, N.L.E2; Kettelhut, I.C1,2; Navegantes, L.C.C1. 1Department of Phisiology, and 2 Departament of Biochemistry and Immunology, Ribeirão Preto Medical

Introduction: Introduction: Calcitonin Gene-Related Peptide (CGRP) is a potent vasodilator peptide widely distributed in the central nervous system and various peripheral tissues, including skeletal and cardiac muscle. We have previously shown CGRP plays an important role in protein metabolism in skeletal muscle through autophagy inhibition. However, its role in heart protein metabolism is still unknown.

Objective: Objective: The main objective of this study was to evaluate the in vivo acute effects of CGRP on cardiac autophagy.

Methods: Methodology: Male C57Bl6 mice were fed or fasted and treated with CGRP (100 µg/Kg) or saline 0,9% for, 15, 30 and/or 60 min. CGRP effects on autophagic flux was estimated by means of colchicine treatment in 24h-fasted mice sacrificed at 15 min (CEUA, 184/2010, FMRP-USP). After treatment, the animals were anesthetized, blood was collected for biochemical analysis, and the hearts were excised for western blot and Rt-PCR measurements. The results were expressed as mean ± SEM, the ANOVA test was applied, and the level of significance was 5%.

Results: Results: In fed mice, CGRP increased glycemia (~55%) and decreased insulinemia (~79%) without altering the content of hepatic glycogen. In heart, the treatment with CGRP increased phosphorylation levels of CREB (~3x) and sensitive hormone lipase (~50%) suggesting activation of cAMP/PKA signalling. The CGRP-induced CREB phosphorylation effect coincided with an elevated expression of SIK1 (~2x), a well-known CREB target. At 15 min, CGRP increased p62 and tended to decrease the LC3II:LC3I ratio (an index of autophagy). In parallel, the treatment with CGRP decreased phosphorylation levels of Akt, at both residues (Thr308 and Ser473; ~60%), did not alter phosphorylation of Foxo1 (Ser256), but transiently increased phosphorylation levels of mTOR (Ser2448) (~2x), S6 (Ser235/236) (~4x) and Ulk1 (Ser757) (~2x). In fasted mice, CGRP decreased the autophagic flux in heart as indicated by the lower level LC3II (~50%) at 15 min.

Conclusions and Support: Conclusion: These data suggest that CGRP acts through the cAMP pathway in mice heart leading to inhibition of autophagy via activation of mTORC1 independently of insulin/Akt signaling. Support: CAPES, CNPq, FAPESP (18/10089-2).

ID: 3662

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Santa Catarina - Florianópolis - Santa Catarina - Brasil

Title: EFFECTS OF VITAMIN D ON THE CENTRAL SEROTONERGIC NEUROTRANSMISSION OF FEMALE RATS PRENATALLY EXPOSED TO DEXAMETHASONE

Introduction: Dexamethasone (DEX) is a synthetic glucocorticoid (GC) that alters the neurochemistry of fetal brain, which can lead to emotional disorders in adulthood. Vitamin D (VitD) has been used to reduce the harmful effects of GC, mainly by stimulating fetal brain development.

Objective: We investigated whether the gestational supplementation of VitD can improve emotional responses by altering components of the serotonergic neurotransmission in the female offspring exposed to fetal programming induced by DEX. We also aimed to test whether the effects of VitD occur in a time-dependent manner.

Methods: Pregnant Wistar rats were treated with DEX or vehicle in drinking water (0.1 mg / kg) during the final third of pregnancy + VitD (500 IU / day) or vehicle during the whole pregnancy. Pups were evaluated at 3, 6 and 12 postnatal months (PNM). Female offspring were divided into 4 groups (n = 7-10/group): CTL, DEX, VitD and DEXVitD. Anhedonia and depressive behaviors were assessed in the sucrose preference test (SPT) and the forced swimming test (FST), respectively. In addition, the protein expression of tryptophan hydroxylase (TPH), serotonin receptor (5-HT1A), serotonin transporter (SERT) and glucocorticoid receptor (GR) were evaluated in the dorsal raphe nucleus (DRN) by Western Blotting. Procedures were approved by the Ethics Committee on Animal Use, Federal University of Santa Catarina, nº 7174170417.

Results: Prenatal treatment with DEX led to a decrease in the preference for sucrose in females at 12 PNM. This response was reverted when VitD was administered concomitantly, indicating an anti-anhedonic effect of VitD. Regarding the FST, gestational supplementation with VitD, decreased immobility time at 3 and 12 PNM, indicating an anti-depressive effect of VitD. However, the concomitant treatment of VitD+ DEX reverted this effect at 12 PNM. Regarding the latency to immobility, VitD and DEX also exhibited time-dependent opposite effects: prenatal use of VitD increased the latency to immobility at 6 PNM, an anti-depressive effect, while DEX treatment led to a decrease of the latency for immobility at 12 PNM, a depressive effect. VitD was able to increase the duration of proactive swimming at 12 PNM, but this response was impaired when VitD and DEX were used concomitantly. Neither DEX nor VitD affected the proactive behavior of climbing. Prenatal treatment with DEX reduced the protein expression of TPH and 5-HT1A in the DRN of females at 6 PNM, but this effect disappears at 12 PNM. Interestingly, this reduction was not attenuated by the gestational supplementation with VitD, indicating that although the deleterious effects of DEX involve alterations in the serotonergic system, the protective effect of VitD does not. The protein expression of GR was not affected by neither DEX nor VitD.

Conclusions and Support: Altogether, these results suggest that the emotional changes induced by prenatal exposure to DEX might be resulted from disruptions in serotonergic components and are time-dependent. Also, although the gestational supplementation with VitD seemed to be protective against some of the negative emotional outcomes from prenatal exposure to DEX, this effect might not involve the serotonergic system. Support: CAPES and CNPq.

ID: 3435

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Alfenas - Alfenas - Minas Gerais - Brasil

Title: EFFECTS OF TEMPOL ANTIOXIDANT ON RENAL CHANGES INDUCED BY METALOPROTEINASE-2

Introduction: Matrix Metalloproteinase-2 (MMP-2) is a protease with important roles in the development of glomerular and renal tubular injury in rodent models of kidney diseases. However, the mechanisms of MMP-2 induced kidney alterations are not fully elucidated. A recent study showed that human recombinant MMP-2 administration in vivo activates pro-oxidant pathways that result in vasoconstriction.

Objective: To evaluate if the administration of recombinant human MMP-2 causes renal dysfunction and oxidative stress, and if the antioxidant Tempol prevents these changes

Methods: MMP-2 mas expressed in E. coli bacteria and the protein was purified on a gelatin sepharose chromatographic column. For in vivo treatment, C57BL-6 mice [Wild type (Wt)] were treated with MMP-2 (150 ng/g, i.p.) for 4 weeks. Animals were also treated with the antioxidant Tempol (18mg/g by gavage). Control mice received vehicle or Tempol. Blood and kidney were collected for analysis. Plasma creatinine, kidney catalase (CAT) activity, superoxide dismutase (SOD) activity and glutathione (GSH) levels were measured. Reactive oxygen species (ROS) generation was accessed in situ with the fluorescent dye dihidroethidium (DHE). Statistical analysis was performed using two-way ANOVA, followed by Sidak's post-test. Ethics Committee Approval (6175230518 -ID 000990)

Results: Increased ROS formation was observed in the MMP-2 and MMP-2+Tempol groups ($p<0.05$; C: 7.997±2.389, C+T: 10.32±1.807, MMP: 11.44±0.9090, MMP: 12.47±2.648). Plasma creatinine levels was increased only in MMP-2+Tempol group, ($p<0.05$; C: 0.4071±0.2864, C+T: 0.3970±0.5026, MMP: 0.7617±0.1855, MMP+T: 1.300±0.4050). There was a decrease in CAT activity in MMP-2 group, and a normalization of the enzyme activity was observed in the MMP-2+Tempol group ($p<0.05$, C: 0.05143±0.02360, C+T: 0.02067±0.01027, MMP: 0.03080±0.01610, MMP+T: 0.07729 ±0.02321). GSH levels were increased in the MMP-2 and MMp-2+Tempol groups ($p<0.05$; C: 0.3145±0.2125, C+T: 0.3176±0.1618, MMP: 0.9754±0.4040, MMP+T 0.9385±0.3019). No difference was observed in SOD activity in all groups ($p>0.05$; C 0.1459±0.1235, CT 0.03517±0.01902, MMP-2 0.07517±0.07483, MMP-2T 0.1434±0.1020).

Conclusions and Support: Conclusion: Our data suggest that the administration of MMP-2 increased ROS formation and decreased the antioxidant defense in the kidney. Tempol treatment did not reverse the changes, yet the concomitant administration of the antioxidant and MMP-2 led to impaired renal function in the animals. Support: CAPES, CNPq, FAPEMIG

ID: 3691

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidad de O'Higgins - - - Chile

Title: Associations Between Leptin Levels and DNA Methylation on Cord Blood Cells: Leptin as a Modulator of Early Epigenetic Programming

Introduction: Increased leptin levels have been associated with disease in adults. High levels of cord blood leptin have been found in cord blood of newborns developed in conditions of high risk to disease in adult life, such as maternal obesity. Recently, our group found in a cohort study that the offspring of women with pre-gestational obesity with high leptin levels have an increased risk to develop asthma at age 3. DNA methylation is a major epigenetic mechanism involved in developmental programming and altered methylation patterns mediate early origins of disease. These findings suggest that leptin plays a role in the early epigenetic programming of immune cells that might contribute to increased risk to disease later in life.

Objective: Hypothesis: high and low levels of leptin at birth are associated with a differential DNA methylation signature in cord blood cells.

Methods: Cord blood monocyte DNA methylation was analyzed using the Infinium MethylationEPIC BeadChip (n = 29) and quantitated as beta values (methylated/total cytosine ratio). Samples were categorized as "low-leptin" (1st tercile) and "high-leptin" (3rd tercile). Leptin/DNA methylation correlation was evaluated using the Spearman correlation method and DNA methylation differences between low- and high-leptin groups were determined by 2-way ANOVA with FDR correction. Differentially methylated CpG sites (DMC) that also showed a correlation with leptin levels were collected and two subsets were subsequently selected: a) top 10 DMC with the largest difference in average methylation levels (Δbeta values) and b) top 10 DMC with the largest correlation coefficients. A stepwise logistic regression method was used to create a model with the best area under the ROC curve (AUC), Negative (NPV) and Positive Predictive Values (PPV). Whole cord blood DNA methylation data generated with the Illumina HumanMethylation450 BeadChip was obtained from the GEO repository for validation (n = 111, GEO accession: GSE129841). A FDR-adjusted p-value cutoff of 0.05 was used for statistical significance.

Results: Comparisons of monocyte DNA methylation revealed 3,588 DMC of which 2,480 (69.1%) correlated with cord blood leptin levels. Regression analysis of the DMC subsets produced Model A (AUC = 0.9667, NPV = 90.0%, PPV = 88.9%) and Model B (AUC = 0.9889, NPV = 100%, PPV = 90.0%). Because our data and the GSE129841 dataset were obtained using different platforms, the probes used to build model A and B are not present in the latter. The probe lists were compared and the matching probes were submitted to the previous analysis strategy using our data. The analysis of the new top 10 Δbeta value subset produced Model C (AUC = 0.9778 , NPV = 90.9%, PPV = 100%) and Model D (AUC = 0.9889, NPV = 90.0%, PPV = 88.9%); the new top 10 correlation coefficient subset was used to build Model E (AUC = 0.9778, NPV = 90.0%, PPV = 88.9%). The GSE129841 dataset was used for validation: Model D had the best performance when applied (AUC = 0.7385, NPV = 70.3%, PPV = 70.3%).

Conclusions and Support: Monocyte DNA methylation data can discriminate between high- and low-leptin levels at birth with outstanding performance. The use of these models of prediction on cord blood data did not achieve comparable results. This could be explained by the use of different methods and biological sources (monocytes vs. whole cord blood cells). The results suggest that early exposure to high leptin levels contribute to modifications in blood cell DNA methylation that might lead to functional changes.

ID: 3436

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Estadual de Londrina - Londrina - Parana - Brasil

Title: CYCLOSPORIN EXPOSURE IMPAIRS SPERM PARAMETERS AND INFLUENCES SERUM TESTOSTERONE AND TESTICULAR CYTOKINE LEVELS

Introduction: Cyclosporin (Cs) has immunosuppressive properties and is used in prophylaxis and treatment of transplant rejection and autoimmune diseases. This molecule exerts its therapeutic effect by inhibiting T-cell activation and IL-2 production, culminating in immunosuppression and affecting the production of several cytokines. Studies have related Cs with male fertility impairment and with testicular and epididymal morphological alterations. Besides its immunoregulatory properties, cytokines have direct effects on physiologic functions on male genital system and sperm production. Accordingly, the cytokine imbalance can affect sperm morphology and function.

Objective: The aim of this study was to evaluate whether Cs affects the sperm parameters, testicular cytokines and the serum testosterone levels.

Methods: OF. CIRC. CEUA Nº 68/2017. Swiss mice were distributed into Cs group, which received 10mg/kg of Cyclosporin (Sandimunn Neoral®, Novartis, gavage) and Control (Ctrl) group, which received only the vehicle (water) for the same period. Twenty mice of each group were treated during 10 days: ten of each group were euthanized immediately after the end of the treatment and ten went in a recovery period of 10 days, without any treatment. Other twenty mice of each group received Cs or the vehicle for 50 days: ten of each group were

euthanized immediately after the end of the treatment and ten went in a recovery period of 50 days, without any treatment. At the end of the experimental period of each group, mice were anaesthetized with Isoflurane (1mL/mL) and euthanized by decapitation. Testis were used for TNFα, IL-1β and IL-10 quantification. Spermatozoa from the vas deferens were used to evaluate sperm morphology and acrosome integrity. Serum was used to testosterone levels quantification.

Results: Cs-treated mice during 10 days showed an increase on acrosome defects ($p = 0.037$) and serum testosterone ($p = 0.028$). No alterations on sperm morphology and cytokines levels in testicular tissue was observed after 10 days of treatment with Cs. After the 10-day recovery period, both the levels of acrosome-disrupted spermatozoa and serum testosterone levels in Cs-treated mice were restored to Control's. No alteration on sperm morphology and testicular cytokines was observed. Cs-treated mice during 50 days showed an increase on acrosome defects ($p = 0.017$), while serum testosterone levels ($p = 0.021$) and testicular TNFα levels ($p = 0.020$) were decreased. Sperm morphology, and testicular IL-1β and IL-10 levels were not altered in Cs-treated mice after 50 days of exposure. After the 50-day recovery period, the number of abnormal sperm is increased in mice previously treated with Cs for 50 days ($p = 0.0001$). Additionally, testicular IL-1β ($p = 0.001$) and TNFα levels ($p = 0.005$) were decreased. No changes were observed in the number of disrupted acrosome, serum testosterone levels and IL-10 levels in the testis.

Conclusions and Support: Short-term administration of Cs in adult mice resulted in reversible impairment of acrosome integrity and increased testosterone levels, suggesting effects on epididymal sperm maturation and testicular steroidogenesis. However, long-term Cs treatment affected testicular cytokine production and sperm morphology; effects there were not reversible after 50 days. The long-term effects of Cs underscore the need of fertility assessment of reproductive-age men undergoing treatment with this drug. Support: CAPES - PROEX - AUXILIO 690/2018 PATOLOGIA EXPERIMENTAL

ID: 3437

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR AND AUTONOMIC EFFECTS ON OBESE ANIMALS: MODULATION BY PHYSICAL TRAINING AND L-ARGININE SUPPLEMENTATION

Introduction: Obesity is a chronic disease where there is an excessive accumulation of adipose tissue in the abdominal area and is the biggest risk factor for the development of cardiovascular diseases. Nitric oxide (NO) has an important role in cardiovascular and autonomic function, in regulating energy balance such as hunger and satiety, and also in the inflammatory process, both as an antioxidant and as a pro-oxidant. Therefore, there are different effects proposed for the action of NO on biological functions. A decrease in NO production or in its bioavailability has been associated with several cardiometabolic disorders. L-arginine is considered a fundamental substrate for NO synthesis, and food supplementation with l-arginine present similar effects to physical exercise in promoting positive changes in the cardiovascular system through vasodilation and in the prevention of cardiovascular diseases. In addition, the regular practice of aerobic exercise is capable of promoting several beneficial effects to the body, especially to the cardiovascular system, modulating the bioavailability of NO, increased vagal activity, among other effects. However, just a few studies have evaluate the effects of these association in obesity.

Objective: Evaluate the cardiovascular and autonomic effects in obese rats submitted to physical exercise associated or not with supplementation with l-arginine.

Methods: The protocols for the experiments of this study were approved by the Ethics Committee on Animal Use (CEUA / UEL: 130/2017) of the State University of Londrina. Obesity was induced by subcutaneous administration of 4 mg / g monosodium glutamate (MSG) from the 1st to the 5th day of life and equimolar saline was used for the control animals. The animals were divided into eight experimental groups. Physical training on a treadmill and supplementation with l-arginine occurred concurrently for 8 weeks. After this period, the animals were submitted to catheterization of the femoral artery to record cardiovascular parameters and calculate blood pressure variability, pulse interval and baroreflex sensitivity. After cardiovascular registration the animals were euthanized to collect and store tissues for body composition and nitrite analysis.

Results: Obese animals showed an increase in perigonadal fat that was not reduced by physical training, but was reduced by supplementation with l-arginine. As well as, sedentary obese animals treated with water presented tachycardia in relation to sedentary obese animals supplemented with l-arginine and physical training promoted bradycardia in obese animals in relation to obese sedentary animals water. With respect to heart rate variability, sedentary obese animals showed decreased variance but physical training and supplementation with l-arginine did not show significant improvements in this parameter. The nitrite concentration is increased in various peripheral tissues and the plasma of the animals in the experimental groups, showing that supplementation with l-arginine as well as physical training and physical inactivity can increase the concentration of nitrite in control and obese animals.

Conclusions and Support: Supplementation with l-arginine associated or not with exercise training is beneficial for cardiometabolic dysfunctions of obese individuals. Financial support: CAPES (fellowship) and CNPq (Edital Universal 2016/process number: 408474/2016-5)

ID: 3693

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: Gestational Obesity and Swimming training Effects on Newborn Rat's Offspring: A Preliminary Study

Introduction: Adverse condition in maternal environment, such as obesity and type 2 diabetes mellitus, especially in critical stages of life development of its babies/pups, can program metabolic disorders as long-term consequence. Herein we were interested on to evaluate the effect of maternal gestational obesity and swimming training on biometrical parameters at birth and feeding behavior of the newborn rat's offspring.

Objective: Evaluate the effect of obesity and maternal swimming on biometric parameters at birth and feeding behavior of the offspring.

Methods: At 40-days-old, female rats began feed an obesogenic diet (hypercaloric diet plus 20% sucrose), three weeks later they were began to swam (30 minutes/day, 5 days/ week, with the addition of 2.5% of body weight). At 75-days-old, female rats were mated and the pregnancy detected through the presence of sperm in a vaginal smear. At birth, body weight, naso-anus length, number of living birth and the male and female ratio were recorded and litter size adjusted to 8 pups per nursing mother. Milk consumption, after 4 hours of fasting, was performed at ages 6th, 11th and 16th of the rat offspring. The body weight of rat offspring was assessed every two days throughout lactation. All parameters in the study were approved by the Ethical Committee (protocol number 2108.017073/2019-56).

Results: The reproductive parameters were not statistically different between groups (number of living birth and the male/female ratio ($P>0.05$). Comparing rat offspring from Co-Sed mothers with Ob-Exe rats, we observed a smaller body weight (–16.7%) and reduced naso-anal length (–5.4%) in Ob-Exe rat offspring ($P<0.001$). Despite a reduction of 21.6% in the body weight evolution of the Ob-Exe rats ($P<0.001$), it was possible to observe a prominent catch-up growth from 12-days-old in the Ob-Exe rats. Regarding milk feeding, at 6th and 11th days of age, Ob-Exe rats were normophagic, but at 16th days of age the milk consumption by Ob-Exe rats was observed to be 87.9% higher than Co-Sed rat offspring ($P<0.001$).

Conclusions and Support: Our data, although at the beginning, show that gestational obesity was able to induce low birthweight and hyperphagia in suckling phase, which is a strong risk factor for the onset of several other metabolic diseases. In addition, swimming training was not able on to mitigate these parameters in offspring. CAPES, CNPq, FAPEMAT

ID: 3438

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF EXCESSIVE CHRONIC OMEGA 3 AND OMEGA 6 SUPPLEMENTATION IN FEMALE WISTAR RATS BREAST MILK SERUM PARAMETERS

Introduction: Excessive chronic n-3 and n-6 PUFA supplementation in female pregnant Wistar rats are related to cause nutritional and metabolic injuries to their offspring. Few studies have validated this effect on the breast milk serum parameters, though.

Objective: Here is presented an experimental analysis (CEUA 1303) of these parameters along with the supplementation effect on the main metabolic tissues relative to total body weight.

Methods: After offspring weaning (21-day old), mothers were left for a 12-hour resting period before breast milk collection. The milk was diluted with saline solution (0,9% NaCl) and then destined to serum parameters and total protein measurement. All data underwent a statistic analysis by ANOVA testing.

Results: Comparing total cholesterol and soluble proteins were seen that both parameters levels of n-3 PUFA supplemented mothers were higher than control, and n-6 PUFA supplemented group values were intermediate. In the case of total triacylglycerols, supplemented mothers showed higher mean rather than control. However, Total Glucose presented no difference between groups. 24-hours post milk collection, rats were weighed and euthanized by decapitation, using a rodent guillotine, and the blood sample was collected to serum parameters measurement. As a result, a higher Total Cholesterol level in n-6 PUFA supplemented females in comparison to n-3 and control group was observed. Total Triacylglycerol levels, though, were related lower in n-3 PUFA supplemented group than n-6 and control group. Total Glucose levels related no difference between groups. Comparing body weight and liver weight, all groups showed no disparities. Although, adipose tissue deposits, both retroperitoneal and mesenteric were higher in n-3 and n-6 PUFA supplemented females when compared to the control group.

Conclusions and Support: Therefore, indeed, excessive chronic supplementation not only affects mainly metabolic systems but also nutritional conditions of the offspring during the lactational period due to the proven metabolic imbalance effect on the breast milk of these mothers. This research was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

ID: 3439

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: Cardiac Remodeling in Fish: Strategies to Maintain Cardiac Function in the Face of Climate Change

Summary: Temperature is capable of affecting the rate of virtually all physiological and biochemical processes, thus influencing the performance and biogeography of many ectothermic organisms, including fish. Some fish remain active throughout the year, thus being subject to wide temperature variations (e.g. chronic variations) between summer and winter. Although temperature affects the functioning of various body functions, the interaction between the respiratory and cardiovascular systems is particularly important since both work synchronously on the maintenance of oxygen ($O_2$) transport, and can be altered to meet the body's metabolic aerobic demand. Thus, many fish have mechanisms capable of preserving heart function in the face of annual temperature changes, a process known as cardiac remodeling, and which includes temporal and reversible changes in the morphology and physiology of the heart (e.g. phenotypic plasticity). However, cardiac remodeling can result in dysfunction (pathological remodeling), compromising the ability of the cardiovascular system to maintain body functions. For example, adult and reproductive-stage salmonids in nature have a high prevalence of coronary arteriosclerosis. Although the causes of the high prevalence of arteriosclerosis are still unknown, the experimental occlusion of coronary blood flow in rainbow trout (Oncorhynchus mykiss) compromises the capacity of the fish to face situations of high metabolic demand, such as those observed when exposed to high temperature and physical activity. Many species of salmonids travel long distances during their migratory route, mostly facing strong currents upstream. This scenario is usually associated with a certain mortality rate, however, recent increases in river temperatures associated with climate change events have been a complicating factor in the survival of some salmonid species.

Conclusions and Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (#2019/12311-7) Swedish Research Council for Sustainable Development (#2019-00299)

ID: 3440

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: INFLUENCE OF THE HYPOTHALAMUS-HYPOPHYSIS-ADRENAL (HPA) AXIS IN THE ANIMAL MODELS OF CHRONIC DIFUSE HIPERALGESY.

Introduction: Considered clinical condition difficult to threat, chronic pain is described as emotional and cognitive sensation with durability above to the considered normal. Commonly diagnosed in women in menopause, fibromyalgia, an example of it, have been studied through the years. Possible excitability mechanisms of the stimulatory paths sensible to P substance and Glutamate are speculated as a possible cause of development of the syndrome, as call for initiating some symptoms associated as anxiety and depression. Furthermore, it is presumed that functional changes in Hypothalamus-hypophysis-adrenal axis (HPA axis) could contribute with mechanisms of chronic pain, although it isn't clear how. Today,the use of animal models of fibromyalgia, one of these consisted in double injection of acid saline solution on gastrocnemius, with an interval of 5 days between the injections, already can replicate the chronic hyperalgesia. Thus, evaluating the relationship between fibromyalgia and HPA axis becomes important to better understand this disease whose etiology is still unclear and influences in patients' quality of life.

Objective: Evaluating the influence of HPA axis modulation on female rats induced to model of chronic and diffused hyperalgesia.

Methods: Female Wistar rats weighing 200–300g were acclimated for 5 days to a 12 h light-dark cycle and maintained at ambient temperature with free access to food and water. All protocols were approved by the Ethics Committee for Experiments on Animals of Federal University of Sergipe(CEUA/UFS:7031290519). Animals were divided in 5 groups with 6 animals each: control group(CONTROL); group induced to model of fibromyalgia(FIBRO); group subjected to surgery(SHAM), group with bilateral adrenalectomy procedure(ADX), and group with adrenalectomy treated with a unique dose of 2.5% of dexamethasone(DEX). The groups SHAM, ADX and DEX were, also, induced to fibromyalgia model, and the first injection was given 5 days after surgery. For group DEX, dexamethasone was given at 18pm in the same day of the second acid saline injection. Following tests were performed to compare the animals' behavior before and after model induction and the surgery: Activity monitor, Hot Plate and Von Frey. The data collected was analyzed by paired T test for intragroup behavior, and by one-way ANOVA for intergroup.The significance level considered was 95%.

Results: For surgical groups, the distance coursed reduced significantly after 5 days of procedure, and this could explain also the significant difference between these groups with CONTROL and FIBRO before model induction, only on this test. Experimental groups demonstrated significant difference in all tests after hyperalgesia when compared to CONTROL. Behavioral analysis showed same significant reduction on ADX and DEX response in all tests after model induction, invalidating the proposed acute treatment with dexamethasone. In SHAM

group, this reduction was observed in latency time and paw withdrawal threshold. For FIBRO group, there was a reduction only in the paw withdrawal threshold.

Conclusions and Support: The results confirm the important influence of corticosteroids on modulation of chronic hyperalgesia, since the ADX animals displayed an expressive hyperalgesic response even when compared to others experimental groups. The acute treatment with dexamethasone didn't provide any change in the behavioral feedback, suggesting that protocol could be inefficient to promote behavioral changes in animals submitted to the model. Support: CnPq

ID: 3441

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: MUDANÇA AMBIENTAL, BIODIVERSIDADE E FISIOLOGIA: SÍNTESE SOBRE UMA CONVERGÊNCIA DISCIPLINAR - Online Symposium: "Fisiologia Animal sob Mudanças Climáticas"

Introduction: A mudança climática constitui um dos mais complexos problemas da atualidade. Se trata de um problema multifacetado que não pode ser estudado adequadamente pela a ótica de qualquer disciplina isolada. No campo da biologia, um dos problemas mais intensamente abordados é o do impacto das mudanças climáticas e ambientais sobre a biodiversidade, tema que tem sido tratado sob múltiplas perspectivas. O problema é complexo porque envolve inúmeros fatores que atuam simultaneamente, incluindo clima, poluição, fragmentação de hábitat, doença emergente, e espécies invasoras, entre outros. Além disso, existem diferenças fundamentais na enorme variação fisiológica associada à biodiversidade, com contrastes entre contextos aquáticos e terrestres, a relação clima-escala e o impacto ainda não bem entendido do tamanho corpóreo, e a variação fenotípica e ontogenética que pode existir dentro de uma população. Entretanto, mesmo se tratando de um problema de altíssima complexidade, avanços fundamentais têm acontecido, com um papel notadamente importante dos estudos fisiológicos.

Objective: Por isso, nesta palestra gostaria salientar alguns aspectos da confluência entre fisiologia e ecologia, uma proposta que tem raízes no início do século 19, e que tem integrado diferentes disciplinas tentando entender os padrões, processos, e mecanismos associados à perda contemporânea da diversidade.

Methods: O papel da fisiologia é preponderante justamente no entendimento de mecanismos, e as raízes históricas remontam à proposta de Victor E. Shelford, que propôs um vínculo essencial entre ecologia e fisiologia com consequências altamente relevantes na distribuição das espécies. De acordo com este modelo, haveria condições ambientais particularmente adequadas para o estabelecimento de populações de diversas linhagens. Assim, na medida em que variáveis ambientais determinantes mudassem, o potencial de tolerância poderia diminuir, criando assim zonas ótimas e zonas de estresse ecológico/fisiológico. Visões posteriores deixaram claro que haveria um certo potencial de resposta mediante ajustes fisiológicos, tanto evolutivo ou individual (aclimatização), mas que tal potencial seria limitado e divergiria entre linhagens, criando-se assim o conceito de "resiliência" à mudança ambiental.

Results: Este simpósio apresenta algumas perspectivas dentro deste tipo de raciocínio, pesquisas aplicadas a diversos modelos de pesquisa, entre eles corais recifais e outros contextos marinhos, peixes e anfíbios. Trataremos justamente de padrões reportados, investigação fisiológica sobre mecanismos de impacto, propostas de mitigação, e modelos de vulnerabilidade vinculados a cenários de mudança.

Conclusions and Support: O comum denominador das palestras é justamente que todas apresentam um tipo convergência da fisiologia com outras disciplinas, visando entender o impacto da mudança ambiental sobre a biodiversidade.

ID: 3442

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: "INTERFERENCE WITH THE RENIN-ANGIOTENSIN SYSTEM REDUCES THE PALATABILITY OF 0.3 M NaCl IN SODIUM-DEPLETE RATS"

Introduction: Renin-angiotensin system (RAS) controls hypertonic NaCl intake driven by sodium appetite.

Objective: We investigated whether the antagonism of RAS interferes with hedonic and aversive orofacial motor responses, or palatability, to intraoral infusion of 0.3 M NaCl (hNaCl).

Methods: Adult male rats (n = 6 - 9) were depleted of sodium by combined sc injection of furosemide and 24 h removal of ambient sodium.

Results: In experiment 1, losartan (AT1 angiotensin II receptor antagonist, intracerebroventricular, 200 mg/ml), produced a three-fold (60 ± 11 vs. vehicle 16 ± 10/min) increase in aversive orofacial motor responses to hNaCl. Losartan also suppressed hNaCl intake recorded

immediately thereafter. In experiment 2, each animal had repeated recordings of hNaCl intake and orofacial responses to hNaCl distributed for 180 minutes. Paired recordings of intake and orofacial responses occurred within five successive blocks after the recordings of only orofacial responses when the animals were still sodium deplete (block zero). Depletion increased the number of hedonic responses, but injection of captopril (angiotensin converting enzyme blocker, intraperitoneal, 30 mg/kg) inhibited by 75% these hedonic orofacial responses to hNaCl in blocks zero and 1. The hedonic responses to captopril remained the same throughout blocks, but became similar to vehicle (14 ± 8 vs. vehicle 16 ± 7/min) from blocks 2 to 5. There was no difference in aversive responses to 0.3 M NaCl between captopril and vehicle. Captopril produced a 70-100% inhibition of hNaCl intake in blocks 1 to 5.

Conclusions and Support: The results suggest that angiotensin II acts in the brain increasing the palatability of hypertonic sodium during the consummatory phase of sodium appetite. CEUA FOAr: 42_2017. Support: CAPES, CNPq, FAPESP, PIPGCF UFSCar/UNESP.

ID: 3445

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: RESPIRATORY ANATOMOFUNCTIONAL CHANGES FOLLOWING APOCYNIN TREATMENT IN A PARKINSON’S DISEASE MODEL

Introduction: Parkinson's Disease (PD) is the second most common neurodegenerative disease with unknown etiology. There are several motor and non-motor symptoms, being the loss of tyrosine hydroxylase (TH) neurons in substantia nigra (SN) the main hallmark of the disease in animal model. Regarding the respiratory deficits (reduction in respiratory frequency (FR) and minute ventilation (VE) at normoxia and hypercapnia), it was already observed that PD causes neurodegeneration in the respiratory column and it is probably due to a dysregulated free radical production. The precise involvement of the oxidative stress seems like to be caused by a high reactive oxygen species production, mainly due to the overactivation of NADPH oxidase (NOX), which is highly expressed within the respiratory column region.

Objective: Evaluate the effects of the NOX non-specific inhibitor, apocynin, preventing the neurodegeneration of respiratory nuclei and reverting the respiratory deficits.

Methods: Wistar male rats (n=19, 250-300 g) were set up in four experimental groups: I) Vehicle-injected, II) 6-OHDA-injected, III) Vehicle-injected treated with apocynin and IV) 6-OHDA-injected treated with apocynin (CEUA nº 2740200319). Vehicle or 6-OHDA (24 µg/µl) were injected bilaterally into the caudate-putamen region to achieve SN neurons and provoke a PD model in 6-OHDA rats. Groups III and IV were treated with apocynin (10-15 mg/ml/kg, water intake) starting at 20 days after the surgery, for the next 20 days, then euthanized and its brains were dissected for immunohistochemistry analysis. At 40 days after PD induction, respiratory parameters were recorded by whole body plethysmography in all groups. SN slices were evaluated for TH to verify the PD model.

Results: 6-OHDA reduced ~70% TH+ neurons in SN (I: 66 ± 38, II: 11 ± 7, III: 71 ± 13, IV: 15 ± 4 %, $F_{1,17}$ =32.16; $p<0.0001$), although apocynin treatment did not reverse it, as expected. At normoxia, 6-OHDA animals (group II) showed reduced fR (II: 66.7 ± 1.9 vs. I: 101.8 ± 12.5 bpm, $F_{1,15}$ =7.951; $p=0.0129$) and VE (II: 113.4 ± 10.2 vs. I: 327.5 ± 80.9 ml/min/kg, $F_{1,15}$ =8.188 $p=0.0119$) with an increased inspiratory time (Ti) (II: 584.1 ± 21.9 vs. I: 269.0 ± 43.6 ms, $F_{1,15}$=47.97; $p<0.001$) compared to vehicle-treated animals (group I). Apocynin reverted increased Ti in 6-OHDA animals (group IV) (IV: 308.5 ± 84.9 ms, $F_{1,15}$=29.98; $p<0.0001$). During hypercapnia, 6-OHDA rats treated with apocynin (group IV) showed an improvement in fR (III: 119.5 ± 5.0 vs. IV: 151.8 ± 6.2 bpm, $F_{1,14}$=13.85, $p=0.0023$), Te (II: 258.8 ± 23.7 vs. IV: 211.5 ± 10.7 ms, $F_{1,14}$=5.591, $p=0.033$) and Ti (II: 249.6 ± 41.5 vs. IV: 185.5 ± 4.5 ms, $F_{1,14}$=15.05, $p=0.0017$) compared to 6-OHDA non-treated rats (group II). We did not observe changes in other respiratory parameters.

Conclusions and Support: Treatment with apocynin improved respiratory parameters in PD animal models and NOX is a great candidate to be involved in respiratory nuclei degeneration. SUPPORT: FAPESP 2019/00065-1 and 2019/19810-9.

ID: 3447

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Goiás - Goiânia - Goias - Brasil

Title: CARDIAC EFFECTS OF THE PARA-AMINOBENZAMIDINE IN NORMOTENSIVE AND HYPERTENSIVE RATS

Introduction: Para-aminobenzamidine (PAB) is known as a serine protease inhibitor. The Diminazene Aceturate (DIZE), an Angiontesin Converting Enzyme 2 (ACE2) activator, is a molecule consisting of two benzamidine moieties linked via a triazene that is susceptible to cleavage resulting mainly in the formation of PAB. Similar to DIZE, some serine protease inhibitors also have vascular effects. However, it is unknown whether PAB has a direct effect on cardiac function.

Objective: Thus, the aim of this work was to evaluate the acute effects of PAB in the cardiac function in normotensive and hypertensive rats.

Methods: Wistar and spontaneously hypertensive rats (SHR), weighing 280-300g were used. The animals were euthanized by decapitation, the hearts were extracted and isolated by the Langendorff technique with constant flow. After a basal period (20-30 min), the hearts were perfused with either: PAB (1 nM), PAB + L-name (10nM, an inhibitor of Nitric Oxide Synthase). All protocols were approved by the Animal Use Ethics Committee of the Federal University of Goiás (#039/2017).

Results: PAB promoted a reduction in the Left ventricular End-systolic Pressure (LVESP, Emáx: -26.17 ± 4.9%, p<0,05), Maximal Rate of Left Ventricular Pressure Rise (dP/dtmáx, Emáx: -25.12 ± 5.4%, p<0,05), Maximal Rate of Left Ventricular Pressure Decline (dP/dtmín, Emáx: -35.54 ± 6.9%, p<0,05) and Perfusion Pressure (PP, Emáx: -28, 68 ± 7.4%, p<0,05). These effects were significantly reduced in SHR (Emáx: LVESP: -19.59 ± 4.1%; dP/dtmáx: 20.16 ± 4.7; dP/dtmín: 29.10 ± 6.6; and PP: 13.25 ± 5.0 %, p<0.05). Pretreatment with L-name blocked all of the PAB-induced effects in Wistar hearts.

Conclusions and Support: These results demonstrate that PAB reduces cardiac contractility and promotes coronary vasodilation more effectively in normotensive than hypertensive rats through a mechanism mediated by the nitric oxide release. Support: Higher Education Personnel (CAPES), National Council for Scientific and Technological Development (CNPq), Goiás Research Support Foundation (FAPEG).

ID: 3448

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Santa Catarina - Florianópolis - Santa Catarina - Brasil

Title: IMPACT OF THE TREATMENT WITH MOMETASONE FUROATE OVER PANCREATIC BETA CELLS MASS IN RATS

Introduction: Synthetic glucocorticoids (GCs) are anti-inflammatory and immunosuppressive drugs, commonly used for treating asthma, rheumatoid arthritis, and multiple sclerosis as well as after organ transplants to prevent possible immune responses against the newly transplanted organ. GCs efficacy is undeniable but depending on the degree of drug exposure adverse effects will be present such as skin and muscle atrophy, osteoporosis, and delayed growth. Excess of GCs also result in significant alterations over the glucose metabolism including reduction in the peripheral insulin sensitivity and impairment of glucose tolerance. Glucose intolerance is possibly due to an uncouple between beta-cell function or mass with the metabolic demand, as observed in rats treated with dexamethasone. Most of undesirable metabolic effects of GCs occurs through upregulation of genes containing glucocorticoid responsive elements. An already existing GC, mometasone furoate (MF), could be a candidate for maintaining the GC efficacy with lesser adverse effects, due to its preferential binding in vitro to the Farsenoid X receptors. MF is applied for topic/inhaled purposes and there is no study evaluating its systemic effects due to its low bioavailability.

Objective: We aimed to evaluate the impact of MF administration on pancreatic beta-cell mass and to compare these findings with those obtained in rats treated with DEX.

Methods: The experimental protocol was approved by the institutional Committee for Ethics in Animal Experimentation (5012250518). Three-month-old Wistar rats received daily injection of the following compound during seven consecutive days: corn oil (1 ml/kg b.m., o.g.) or NaCl 0.9% (1 ml/kg b.m., i.p.) as controls, DEX 1 mg/kg b.m. i.p or o.g. diluted in saline and MF 1 mg/kg b.m. i.p. or diluted in corn oil. After the last day of treatment, the animals were euthanized, and their pancreas was processed for insulin immunofluorescence. Morphometric analyses were done using ImageJ software. One-way ANOVA followed by post hoc Tukey test (GraphPad Prism 8.0.1.) was applied for multiple comparisons of parametric data. The significance level adopted was $P < 0.05$.

Results: Preliminary data indicate rats treated with MF through i.p. exhibited higher beta-cell mass (32,95 mg) compared with their control group (corn oil-treated), in contrast with the o.g. group which did not exhibit modification of beta-cell mass. DEX treatment resulted in higher absolute beta-cell mass for both i.p. (32,82 mg) and o.g. (44,23 mg) groups than in the control group (saline-treated).

Conclusions and Support: Treatment with MF through o.g. is not associated with change in beta-cell mass. This data may indicate rats treated with the anti-inflammatory MF through o.g. have either unaltered insulin sensitivity and glucose tolerance or this unaltered beta-cell mass is not sufficient to avoid glucose metabolism disturbances, a matter to be investigated. MSA receives a PIBIC/CNPq scholarship, PLZ receives a CAPES scholarship, AR is funded by a CNPq research grant.

ID: 3705

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Estadual de Maringá - Maringá - Parana - Brasil

Title: LOW PROTEIN DIET DURING LACTATION PROGRAMS TO HPA-AXIS ACTIVATION AND ALTERATIONS IN MILK

COMPOSITION

Introduction: An environment of nutritional imbalance in early life is associated with an increased risk of developing metabolic diseases in adulthood, according to DOHaD concept. The suckling period make up a window of susceptibility to metabolic programming. In rodents, the development and maturation of the major organs and tissues, such as the endocrine system and central nervous system, occurs mainly during the first weeks after birth. During this period, postnatal undernutrition exposure can affect the development of neural circuitry involved in metabolism and energy expenditure. Severe caloric and/or protein restriction is considered a stressful insult that can shape hypothalamic-pituitary-adrenal (HPA) axis. Moreover, stressful insults during lactational period can affect milk composition of macronutrients and hormones.

Objective: Therefore, we evaluated the short-term impact of a low-protein diet during lactation on milk composition and plasma hormones and macronutrients.

Methods: After mating, pregnant Wistar rats were separated in individual cages. At birth, litters were divided into two groups: NP; dam received normal protein (20%) diet at lactation and LP; dam received low-protein (4%) diet in the first two weeks of lactation. Offspring and mother body weight (bw) were measured through lactation and area under curve (AUC) were calculated. Milk samples and offspring plasma were collected at postnatal day (P) 7, 14 and 21 days of life to perform biochemical analysis.

Results: Through lactational period, LP dams and offspring presented a reduction of 17% and 40% ($P<0.001$) in bw gain, respectively. LP milk protein content was elevated by 135% at P7 ($P<0.01$), equal to control at P14 and reduced by 53% ($P<0.05$) at P21. Total carbohydrate content in the milk was increased by 53% in LP group at P7 ($P<0.01$), equal to control at P14 and reduced by 68% ($P<0.0001$) at P21. Milk total fat was increased in LP group at P7 and 14 by 83% ($P<0.01$) and 113% ($P<0.0001$) respectively. This parameter showed reduction at P21 (42%, $P<0.05$). Corticosterone concentration in milk at P14 was elevated 133% in LP group ($P<0.05$). Analysis in offspring plasma showed that protein content was reduced at P7 and 14 by 12% ($P<0.05$) and 26% ($P<0.0001$), respectively. We observed an increase in triglycerides (35%, $P<0.01$) and in glucose (54%, $P<0.01$) concentration in LP offspring plasma at P21. LP animals presented elevated corticosterone at P7 (92%, $P<0.05$).

Conclusions and Support: Low-protein during lactation promotes altered milk macronutrients composition and activates HPA-axis in early life. Finnacial Support: CNPq and CAPES

ID: 3450

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Goiás - Goiânia - Goias - Brasil

Title: CHRONIC ANTAGONISM OF GHRELIN RECEPTOR GHS-R1A PROMOTES ITS HYPOTHALAMIC DOWNREGULATION AND MODIFIES BAROREFLEX REACTIVITY BUT NOT AUTONOMIC TONE IN NORMOTENSIVE RATS.

Introduction: Ghrelin is a gastric peptide hormone involved in the control of several physiological functions, including those relying on gabaergic synapses, such as the autonomic balance governing cardiovascular system. Although ghrelin effects are triggered from its binding to GHS-R1a receptor, this cognate also displays a ghrelin-independent constitutive activity.

Objective: We next investigated the effects of chronic antagonism of GHS-R1a on: i) baroreflex reactivity; ii) heartbeat autonomic control; iii) hypothalamic GHS-R1a and GAD65/67 protein expression.

Methods: For this purpose, Wistar rats (10 weeks of age) were anesthetized ketamin (10 mg/kg, i.p.) and xylazine (4 mg/kg, i.p.) and were implanted with osmotic pumps (Alzet 2004) filled with the GHS-R1a antagonist PF-04628935 (280mg/kg/28days; n=5) or vehicle (NaCl 0.9%; n=3). At the 26th day, rats were again anesthetized for catheterization of femoral artery and vein. At 27th day, phenylephrine and sodium nitroprussiate were injected i.v. (5mg/mL 0.1mL) to test baroreflex reactivity. Subsequently, in order to assess chronotropic autonomic control, we injected atenolol (4mg/Kg) followed by methylatropine (3mg/kg) with 15min intervals. At the 28th day, the orderliness for atenolol and methylatropine injections was inverted. At the end of experiments, animals were euthanized; brains were removed for GHS-R1a and GAD65/67 protein expression analyses. All experimental procedures were approved by ethics committee (CEUA-UFG 087/19).

Results: We found that: i) bradycardic reflex and baroreflex sensitivity were greater in animals treated with GHS-R1a antagonist; ii) there were no differences in the cardiac autonomic control between groups; iii) chronic GHS-R1a antagonism reduced its expression in the hypothalamus but not in the midbrain; iv) GAD65/67 levels were increased in midbrain of animals treated with PF-04628935.

Conclusions and Support: Our preliminary data suggest that chronic GHS-R1a antagonism promoted its hypothalamic downregulation, increased GAD65/67 in midbrain and modified baroreflex reactivity. However, basal (non-reactive) autonomic control of cardiac chronotropy seems to be preserved. Findings resulting from the chronic treatment with PF-04628935 may rely on a reduction in hypothalamic GHS-R1a constitutive activity. Support: CNPq, CAPES and FAPEG.

ID: 3451

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal Rural do Rio de Janeiro - Seropédica - Rio de Janeiro - Brasil

Title: PHARMACOLOGICAL MODULATION OF SEROTONERGIC SYSTEM DURING PERINATAL PERIOD BY PAROXETINE HYDROCHLORIDE AND ITS PSYCHOBIOLOGICAL CONSEQUENCES

Introduction: Serotonin (5-HT) plays an important role in the embryogenesis of central nervous system of mammals. It modulates the ontogenesis of different neuronal system, including those involved in the regulation of humor and the response to stress. In this context, changes in the 5-HT signaling in the early life may compromise the mental health and increase the susceptibility to humor and anxiety disorders in the adulthood.

Objective: Our aim in this study was to evaluate the influence of perinatal exposure of swiss female mice offspring to paroxetine hydrochloride (PARO) and its consequences on behavioral profiles in the adulthood.

Methods: To reach our aim we used two groups of swiss couple mice (n = 8 each, body weight ~ 35 g). They were mated and kept together up to the delivery of the offspring. The offspring mice were then treated subcutaneously (sc) by either NaCl 0.9% (control – CTL) or paroxetine hydrochloride 1 mg/kg (PARO 1 mg/kg) from day 5th to day 15th post-natal. The female offspring were used for molecular biology protocols and male were kept up to day 70th and then submitted to the following behavioral methods: Open Field (OF), Elevated Plus Maze (EPM), Light-Dark Box (LDB), Social Interaction (SI) and Tail Suspension (TS). Statistical analysis was performed by SPSS software and GraphPad Prism 8.0 and the results were expressed as mean ± standard error of mean (s.e.m) and we considered statistical difference between groups when p value was smaller than 0.05. All the experimental protocols were approved by the local Animal Welfare Committee (CEUA-ICBS-UFRRJ) under the protocol 005/2017.

Results: In the OF method among the parameters analyzed we observed an increase of 435% in the rearing (CTL - 2.60 ± 0.93 vs PARO – 13.90 ± 4.12; $p<0.05$). In the LDB, we observed an increase of 163% in fecal pellets (CTL - 1.90 ± 0.71 vs PARO - 5.00 ± 0.93; $p<0.05$). In the SI method, we observed an increase of 47% in grooming behavior in the session 1 (CTL - 3.40 ± 0.43 vs PARO - 5.00 ± 0.49; $p<0.05$) and 40% in session 2 (CTL - 5.00 ± 0.76 vs PARO - 7.00 ± 0,45; $p<0.05$). We also found an increase of 162% in the rearing behavior in session 1 (CTL - 2.10 ± 0.35 vs PARO – 5.50 ± 1.22; $p<0.05$) and 108% in session 2 (CTL - 3.60 ± 1.27 vs PARO – 7.50 ± 1,78; $p<0.05$) and an increase in the central chamber time of 69% in the session 2 (CTL - 67.00 ± 11.37 sec vs PARO - 113.30 ± 16.66 sec; $p<0.05$).

Conclusions and Support: We did not find any changes in the others behavioral parameters when compared to the control group in the EPM or TS methods. Therefore, the results presented here in the OF as well as SI sessions 1 and 2 which reveal an increase rearing behavior suggest an increase in anxiety-like behaviors. The decrease in social motivation, novelty interest and possibly sociability due to the increase in time of central chamber. We believe that these changes are due to the possible modulation of the serotonergic system development during the postnatal time exposure to PARO. Also, once at this level of dosage no changes were observed in the EPM or TS methods and we did not observe any changes in depression-like behaviors between CTL and PARO groups. However, to elucidate the molecular mechanism of it is necessary to investigate the changes in quantity of proteins (TPH2, SERT, 5-HT1a/1b, 5-HT2 e 5-HT3) directly related to serotonin function. Financial support: FAPERJ

ID: 3709

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Instituições: Unicesumar - Maringá - Parana - Brasil

Title: BODY MASS INDEX AS ESTIMATED ASSESSMENT OF FAT LOSS IN OBESE INDIVIDUALS

Introduction: The sedentary lifestyle is disturbing; it is directly associated with obesity and it's increasingly. The Mundial Healthy Organization (WHO) classifies the nutritional status of people based on the Body Mass Index (BMI) – correlation between weight and height. In addition to being a disease, obesity is a risk factor for several other pathologies. That said, many people pursue diets and physical exercises in order to improve life quality and reduce fat levels. However, the fat should not always be the sole focus – increasing lean mass is also essential. A good approach would be to focus on maintaining lean muscle mass as fat mass is decreased, which is achieved with physical exercise. BMI relates height to body mass, although, it is necessary to understand better the process of changing body composition in obese people.

Objective: Compare the changes between before and after 6 weeks of physical training, in order to verify the correlation between BMI, body weight, lean mass and fat mass of obese individuals.

Methods: The sampling consisted of 4 voluntary men bearers of type 2 and 3 obesity. They were submitted by 6 weeks of physical training (1 hour, 3 times a week), consisted by a combined circuit of resisted training and endurance. The assessment of the body composition was estimated by multifrequency bioimpedance in the weeks before and after training.

Results: After the six weeks of physical training, the volunteers I and II got an increment on the BMI values of 0,9 and 0,1, respectively. In the first case, there was a decrease of the fat mass (-1,8%) and an increase of the body weight (2,1%) and of the lean mass (5%). For the volunteer III, the lean mass (-1,6%) was reduced and there was a rise on the body weight (0,2%) and on the fat mass (0,9%). About the others volunteers, the BMI reduced 2,3 and 0,9, respectively. The volunteer II got all the values lower: body weight (-5,5%), lean mass (-1,8%) and fat mass (-14,5%). At last, the volunteer IV, besides have been a decrease of the BMI, there was an increase of the lean mass (0,3%), whereas its body weight and fat mass were reduced (-2,1% e -5,3%, respectively). All BMIs values have been changed according to the body weight, as expected, however, it was noticed great influence by the type of body composition, given that 75% of the volunteers exhibited reduction of fat mass.

Conclusions and Support: It should be noted the importance of the combination between BMI and other rates in order to monitor the loss of weight in obese, since factors like lean mass and fat mass modified during the weeks have influence on the body weight. Furthermore, it's possible to conclude that the training applied turn up efficient to overweight people who seek for fat loss.

ID: 3711

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Medicina de São José do Rio Preto - FAMERP - São José do Rio Preto - Sao Paulo - Brasil

Title: Head and neck cancer patients with characteristics of cancer stem cells have important clinical comorbidities.

Introduction: A small population of cells inside the head and neck cancer (HNC) knowledge as cancer stem cells (CSCs) exhibit self-renewal ability. They are responsible for tumor initiation, invasion and migration, origin of relapse and metastases as well resistance to treatments. It has been reported that tumor cells have a great capacity to promote invasion perineural which can be related with changes in sympathetic systems.

Objective: To identify head and neck cancer stem cells (HNCSCs) and non-HNCSCs and to relate with smoking and alcoholic habits, clinical and histopathological characteristics.

Methods: All patients signed consent term that was approved by the Institutional Research Ethics Committee of the Medical School São José do Rio Preto-FAMERP (nº 903.775; CAAE: 37632114.9.0000.5415). Six samples of HNC were obtained after surgical resection. They were cultured in DMEM with 10% FBS and 1% AB/AM, at 37°C and 5% CO2. Cells were immunophenotyped by flow cytometry using CD44, CD117 and CD133 markers. Migration (scratch assay) and invasion (matrigel) assays was performed to evaluate the tumorigenic and aggressive potential.

Results: The six patients with HNC presented a median of the 57 years old and 83% was male and 17% was female. About smoking and alcoholic habits 83% smoking more than 1 pack/day of the cigarettes for more than fifteen years and 50% drunk more than 400ml/day for more than 35 years. The tumors of the patients evaluated had a median of 0.3% of CSCs and 11% non-CSCs. CSCs presented increased rate of migration (61.47%) and invasion (46.75%) and these characteristics enable perineural invasion. The primary site most frequent was oral cavity (50%), larynx (33%) and pharynx (17%). These 83% was in Stage I/II and 17% was in Stage III. The number of the patients that presented relapse or pulmonary metastasis was 50% this was related to less than 2-year survival in 33% of all cases. The treatment most common was surgery (50%) or radiotherapy (50%) plus chemotherapy with platina (33%) or taxol (17%). The patients frequently present diabetes mellitus II (33%), low weight (50%), respiratory (17%) or cardiovascular (50%) comorbidities highlights to hypertension in 50% of the cases.

Conclusions and Support: Patients with HNC who present CSCs usually have important comorbidities, such as low weight and hypertension associated with aggressive radiotherapy. These association need to be investigated in more detail, as this combination leads to resistance to treatment, relapse, metastasis and low survival. Therefore, it is important to study the mechanisms that link cancer to cardiorespiratory diseases to design more effective treatment protocols. Support: Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brazil (CAPES) - Finance Code 001, The Brazilian National Council for Scientific and Technological Development (CNPq), grant #310987/2018-0, and grants #2015/04403-8 #2014/15009-6, São Paulo Research Foundation (FAPESP). Support was also provided by FAMERP/FUNFARME.

ID: 3712

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Estadual de Maringá - Maringá - Parana - Brasil

Title: ADOLESCENCE AS A PROGRAMMING WINDOW TO METABOLIC OUTCOMES FROM DOPAMINERGIC IMBALANCE IN WISTAR MALE RATS

Introduction: Methylphenidate is a psychostimulant used in the treatment of Attention Deficit Hyperactivity Disorder that inhibits the reuptake of dopamine mainly in the striatal nucleus and prefrontal cortex. Adolescence, as well as pregnancy and lactation, is considered a sensitive period of development, since neural connections, including dopaminergic system, are still being formed in the brain. Therefore, stressful insults in this phase can permanently modulate the development of systems, programming metabolic diseases and behavioral changes in adult life.

Objective: We evaluated the effect of Methylphenidate treatment during adolescence on biometrical and biochemical parameters of offspring adult male rats.

Methods: From weaning, Wistar male rats received Methylphenidate (Ritalin) by gavage (MPH; 1 mg/kg/day) for 30 days, whereas control rats received saline (SAL; NaCl 0.9%) in the same volume. From 51 to 110 days-old both groups were untreated. At 51 and 110 days-old intraperitoneal insulin tolerance test (ipITT) and intravenous glucose tolerance test (ivGTT) were performed. After this, euthanasia was realized, fat pad stores were removed and weighted, and plasma were collected to perform biochemical analysis.

Results: During treatment, MPH reduced 12% of food intake ($P<0.01$), however there was no difference in body weight. At 51 days-old fat tissue stores were equal between groups and fasting insulinemia was decreased in 50% ($P<0.05$). Glucose tolerance and insulin sensitivity showed no differences between groups. After treatment, MPH group showed an increase of 23% in body weight ($P<0.01$). Fat tissue stores were increased by 20% ($P<0.05$) in treated animals. ivGTT showed higher glucose levels in MPH group at 15 ($P<0.05$), 30 ($P<0.05$) and 45 minutes ($P<0.01$) and these animals are insulin resistant, as demonstrated in Kitt ($P<0.05$).

Conclusions and Support: Dopaminergic imbalance at adolescence programs male rats to overweight and metabolic alterations at adulthood. Financial l Support: CNPq and CAPES

ID: 3713

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

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Title: Sodium glucose co-transporter 2 (SGLT2) inhibitor, Dapagliflozin, potentiate metabolic dysfunction in adult offspring submitted to early overfeeding.

Introduction: Obesity and type 2 diabetes mellitus (T2D) can be programmed during the early stages of life, mediated by epigenetic changes. The growing prevalence of overweight and obesity among children and adolescents worldwide is worrying, considering that both significantly increase susceptibility to chronic diseases such as T2D in adulthood. The animal model of litter reduction supports the hypothesis that overnutrition during lactation permanently affects metabolic homeostasis, leading to a picture of insulin resistance, fasting hyperglycemia, hyperinsulinemia and overweight. Studies indicate that Dapagliflozin (DPG), a hypoglycemic drug, acts effectively in the treatment of T2D.

Objective: Evaluate the effect of DPG on metabolic disorders presented by overweight rats, induced by reduced brood.

Methods: The experimental protocol was approved by the Animal Use Ethics Committee of UEM (nº 6245030919). Pregnant Wistar rats were kept in individual boxes until the birth of the offspring, then the newborns were divided into 2 experimental groups: Litter Control (LC) ($n = 3$) and Small Litter (SL) ($n = 8$). The LC animals comprised litters of 9 lactating mothers, while the SL animals composed litters of 3 lactating mothers. Upon completing 90 days, the groups were subdivided into treaties and control, forming a total of 4 groups ($n = 10$). The treatment was performed with DPG administration (0.1 mg / kg B.W., diluted in water), daily, orally. Body weight, fat stores and fasting blood glucose were evaluated. Data were expressed as mean ± se and submitted to test t-student and applied after Bonferroni test with significance level when $p < 0.05$.

Results: A significant difference in body weight was observed when comparing the SL and NL groups. The SL-Saline group showed an increase of 13.6% ($p<0.05$) compared to NL-Saline, while SL-DPG showed an increase of 16.8% ($p<0.05$) compared to NL-DPG. Such results show that DPG was not effective in reducing the animals' body weight. There was also a significant increase in retroperitoneal fat in the SL group compared to the LC group. The periepididymal fat of the SL-Saline group was significantly higher (24.2%, $p<0.01$) compared to NL-Saline; however, no difference was observed to treated groups. Mesenteric fat did not show significant changes between groups. The fasting blood glucose values of the SL groups showed a significant increase (9.3%, $p<0.05$) compared with the LC groups. However, the SL group treated with DPG showed a significant increase (4.6%, $p<0.05$) in the blood glucose level compared to the untreated SL group, which contradicts the effects expected by the treatment of the drug.

Conclusions and Support: Treatment with dapagliflozin was not effective to improve metabolic dysfunctions of animals programmed to develop obesity, besides drug caused hyperglycemia.

ID: 3459

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RENAL

Forma de Apresentação: Ê-POSTER

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Title: HIGH-FAT DIET DECREASES WATER DEPRIVATION-INDUCED WATER INTAKE, WITHOUT CHANGING SODIUM INTAKE IN FEMALE RATS

Introduction: In recent decades, obesity has become a worldwide epidemic. In obesity condition, the activity of the renin-angiotensin system (RAS) increases, resulting in increased plasma angiotensin II, which may act in the central nervous system (CNS) causing thirst and sodium appetite. In male rats, water deprivation for 24-36 h (WD) followed by 2 h of access to only water (partial rehydration-PR) induces sodium intake that depends on RAS activation. The ingestion of high-fat diet (HFD) causes changes in the hydroelectrolytic balance, such as a decrease in daily water intake (Sa et al, Behavioral Brain Res, 373: 112075, 2019). In addition, obese Zucker female rats have an increase in daily hypertonic saline intake, whereas sodium depletion was not highly effective to induce sodium intake (Oumoessi et al., Physiology and Behaviour, 89: 576, 2006).

Objective: Therefore, the present study was aimed to verify the dipsogenic responses and sodium intake in female rats fed with HFD submitted to 24 or 36 h of water deprivation-partial rehydration protocol.

Methods: (CEUA 26/2016) Female Holtzman rats (260–280 g) were fed with standard diet (SD, 11% calories from fat; n=5) or HFD (46% calories from fat; n=6) for 6 weeks, and daily intake of water and 0.3 M NaCl and body weight (b.wt.) were measured. The female rats underwent 24 h WD and thereafter had access to only water for 2 h (PR). After this period, 0.3 M NaCl was also available and the intake of both 0.3 M NaCl and water was recorded for an additional 2 h (salt appetite test). A week later, the same protocol was repeated after 36 h of water deprivation. At the end of the experiments, the retroperitoneal, ovarian, and mesenteric adipose tissues were removed and weighed.

Results: Female rats that ingested HFD had an increased daily 0.3 M NaCl intake from the 3rd week of the HFD (6.3 ± 0.9, vs. SD: 3.9 ± 1.5 ml/100 g of b.wt./24 h; $p < 0.05$) and a decrease in daily water intake since the 1st week of the HFD (5.2 ± 0.3 ,vs. SD: 10.8 ± 0.9 ml/100 g of b.wt./24 h; $p < 0.05$). After 24 h of WD, during the PR, animals fed with HFD had a reduced water intake (3.5 ± 0.3, vs. SD: 4.5 ± 0.3 ml/100 g of b.wt./2 h; $p < 0.05$), without differences in 0.3 M NaCl intake (HFD: 1.0 ± 0.4, vs. SD: 0.2 ± 0.1 ml/100 g of b.wt./2 h; $p > 0.05$). After 36 h of WD, the HFD group had again a reduced water intake (4.4 ± 0.2, vs. SD: 5.6 ± 0.6 ml/100 g of b.wt./2 h; $p < 0.05$), without difference in 0.3 M NaCl intake during sodium appetite test (HFD: 3.5 ± 0.3, vs. SD: 3.4 ± 0.6 ml /100 g of b.wt./2 h; $p > 0.05$). The retroperitoneal (HFD: 1.05 ± 0.12, vs. SD: 0.38 ± 0.04 g/100 g of b.wt.; $p < 0.05$), and the ovarian (HFD: 1.28 ± 0.20, vs. SD: 0.52 ± 0.07 g/100 g of b.wt.; $p < 0.05$) adipose tissues increased in the group fed with HFD, but not the mesenteric adipose tissue (HFD: 0.44 ± 0.05, vs. SD: 0.31 ± 0.02 g/100 g of b.wt.; $p > 0.05$).

Conclusions and Support: The results suggest that female rats fed with a HFD have a decreased water intake daily or after 24 or 36 h of water deprivation. In addition, HFD increased daily 0.3 M NaCl intake, but not after 24 or 36 h of water deprivation. Future studies are necessary to reveal the mechanisms involved. Support: CAPES, FAPESP, CNPq

ID: 3460

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: CYCLIC GMP-SPECIFIC PHOSPHODIESTERASE TYPE 5 INHIBITOR DECREASES KIDNEY OXIDATIVE STRESS AND SYSTEMIC INFLAMMATION IN DIABETIC RATS.

Introduction: High levels of blood glucose are a hallmark sign of Type 1 Diabetes Mellitus (T1DM). Over time, hyperglycemia will trigger a permanent damage in target organs mainly due to the generation of reactive oxygen species (ROS) and inflammatory cytokines. Kidney is important for blood filtering, volume homeostasis and to remove waste products from the body. It is known that nephron can become damaged in T1DM and this could contribute to aggravate an already compromised body function in this disease. Some studies have shown that a cyclic GMP-specific phosphodiesterase type 5 inhibitor, sildenafil (SIL), has a potential for treat other conditions besides erectile dysfunction and pulmonary hypertension with beneficial widespread actions in several organs.

Objective: To investigate the effects of sildenafil treatment on oxidative stress and inflammation of T1DM rat's kidney.

Methods: Experimental T1DM was induced through penile vein one injection of streptozotocin (STZ, 50 mg/kg) in Wistar rats weighing about 300 g. Three days after STZ injection, animals had their blood collected for glucose evaluation. Animals with less than 250mg/dL blood glucose (BG) were withdrawn from the study. Seven days later, rats were randomly divided in two groups and treated via gavage with water or sildenafil, 3 mg/kg, for 14 days: Diabetes-vehicle (DV, N=6) and Diabetes-sildenafil (DS, N=6), respectively. An additional group of rats without any treatment were used as a Control non-diabetic (CT, N=6). After sildenafil or vehicle treatment, all animals, including CT rats, were euthanized for blood and kidney collection to glycemia, oxidative stress and inflammatory damage analysis. Data were expressed as mean ± SEM and considered significant when $p<0.05$. The project was approved by the institutional Ethical Committee for Animal Research, CEUA-UFES number 14/2017.

Results: As expected, BG was higher in DV when compared to CT group (403 ± 26 mg/dL vs. 158 ± 8 mg/dL, $p<0.05$, respectively). SIL was not able to decrease BG in DS animals (DS: 440 ± 34 mg/dL, $p>0.05$ vs. DV group). As verified by Dihydroethidium assay, ROS was increased in the renal cells of DV compared to CT group (644 ± 37 a.u. vs. 516 ± 32 a.u. $p<0.05$, respectively). SIL decreased ROS in the kidney cells of DS group (468 ± 34 a.u. vs. DV group, $p<0.05$). The result above was also confirmed with 2',7' – dichlorofluorescin diacetate assay (DV: 1229 ± 216 a.u. vs. CT: 740 ± 29 a.u., $p<0.05$) and (DS: 714 ± 45 a.u. vs. DV, $p<0.05$). T1DM caused an increase in plasma inflammatory marker myeloperoxidase in the DV (0.1600 ± 0.0077 a.u.) compared to CT rats (0.1150 ± 0.0071 a.u., $p<0.05$). Sil treatment was highly effective decreasing MPO activity in DS (0.1017 ± 0.0054 a.u. vs. DV group, $p<0.05$).

Conclusions and Support: Ours results confirm previous studies that showed a potent antioxidant and anti-inflammatory sildenafil effects. Considering that in T1DM, kidney dysfunction could negatively affect the disease progression, our findings could contribute to ameliorate body and organ function. CAPES and CNPq.

ID: 3716

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: PROTEOMIC ANALYSIS INDICATES OBESITY-INDUCED CHANGES ON ENERGY METABOLISM AND SYNAPTIC FUNCTION OF THE RAT HYPOTHALAMUS

Introduction: Obesity, characterized by increased adiposity resulting from positive energy balance, is associated with physiological and psychological problems which impact health-related quality of life. High intake of saturated fat is commonly referred as an important environmental factor leading to obesity, a disease highly related to hypothalamic deregulation.

Objective: To better understand hypothalamic molecular mechanisms affected by high-fat feeding-induced obesity, we analyzed the proteome of this brain region in rats.

Methods: This study was approved by the Research Ethics Committee of the Universidade Federal de São Paulo – UNIFESP/EPM (CEUA N 2172030315). Three-months-old female Wistar rats received either balanced chow (2.87 kcal/g, 15% of energy from fat; control group, n = 6) or high-fat diet (3.6 kcal/g, 45% from fat; obese group, n = 6) for 12 weeks. After harvesting, the hypothalami were processed and analyzed by data independent acquisition MS-based proteomics. Data were analyzed by unpaired Student's "t" test. Differentially expressed proteins were submitted to pathways enrichment analysis based on binomial test followed by Bonferroni correction for multiple testing. Significance was set at $p < 0.05$.

Results: The intake of high-fat diet induced obesity, with increased abdominal fat and hyperleptinemia. Increased HOMA-IR and leptin/adiponectin ratio evidenced the presence of insulin resistance and inflammatory activation in the obese group. A total of 624 proteins comprised the present hypothalamic proteome database. A differential profile was observed in the hypothalamus of obese rats: while 49 proteins were down-regulated, 53 proteins were up-regulated. The dataset presents alterations in proteins which have not yet been described in the hypothalamus under obesity conditions, such as increased expression of trifunctional enzymes subunit alpha (Hadha, which participates in mitochondrial beta-oxidation), up-regulation of toll-interacting protein (Tollip, which may act as both positive or negative regulator of inflammation depending on its subcellular localization), and down-regulation of neural cell adhesion molecule L1 (L1cam, which mediates axon elongation and neuronal migration), among others. Pathway-enrichment analysis evidenced that altered proteins are mainly related to energy metabolism (pyruvate metabolism, TCA cycle and respiratory electron transport), cellular responses to stress, innate immune system, membrane trafficking (including Golgi-to-endoplasmic reticulum transport), axon guidance and signaling by receptor tyrosine kinases (TRKs).

Conclusions and Support: Changes on hypothalamic bioenergetics observed in the present study indicate impaired mitochondrial function, a feature interconnected with innate immunity and cellular response to oxidative stress, pathways that also showed statistical enrichment. Modulation of proteins associated to synaptic plasticity, evidently important to hypothalamic function, was also observed. The findings provide new insights on obesity-induced hypothalamic imbalances and warrant future investigations. Research relating to this abstract was supported by CAPES, CNPq and FAPESP.

ID: 3461

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: BAROREFLEX RESPONSES TO TEMPERATURE VARIATION AND ACTIVITY IN SOUTH AMERICAN RATTLESNAKES

Introduction: The baroreflex mechanism controls beat-to-beat arterial pressure (P). Intramural mechanoreceptors monitor P changes through arterial wall stretching, triggering heart rate and vascular compensatory responses. In reptiles, baroreflex gain at the operating point (Gop) reduces when body temperature (Tb) increases, as well as the time constant for pressure decay (τ: the product of arterial resistance and compliance), such that P and the oscillatory power fraction (OPF: a measure of proportional cardiac energetic waste) remain unaltered. In mammals, the metabolic increment related to activity resets baroreflex gain. If the same mechanism works for reptiles, activity at high Tb will lead to conflicting baroreflex adjustments. Here, we used the South American rattlesnake, Crotalus durissus, to study how reptiles comply with those adjustments during physical activity at different Tb.

Objective: To analyze baroreflex-related adjustments of the cardiovascular system during activity at different Tb.

Methods: Rattlesnakes (n=8) had their vertebral artery cannulated (PE50) for arterial pressure recording at different temperatures (15, 20, and 30°C). Snakes were allowed to recover for 24h before the experimental protocol. Chamber temperature was randomly altered each 24h. In each day, we recorded blood pressure at resting conditions and induced snakes to forced activity for five minutes. A 24h resting interval for animal recovery followed each activity trial. Systolic pressure (Ps), diastolic pressure (Pd), and pulse interval (PI) were derived from the pressure signal. Pulse pressure (Pp) is Ps–Pd, and OPF, 1–(Ps+2Pd)/3Ps. τ was assessed by fitting the last 70% of the Pd wave to the Windkessel equation: $P(t)=(P0–A)e^{-t/\tau}+A$ (A=asymptote; t=time). τ/PI indicates how fast pressure decays in relation to PI. Gop and baroreflex effectiveness index (BEI) were assessed with the sequence method. Gop was normalized as Gnorm = Gop × [(Ps+2Pd)/3]/PI. We used a two-way ANOVA for repeated measurements and a Tukey test ($P<0.05$) to test effects from temperature and activity.

Results: Both Ps and Pd increased with Tb and activity. Pp increased from 15 to 20°C, and was reduced at 30°C. Activity elevated Pp at all Tb. OPF did not change from 15 to 20°C but decreased at 30°C in resting snakes. During activity, OPF remained constant at 15°C, but increased at 20 and 30°C. Increased Tb reduced τ, although τ/PI remained unchanged. Activity reduced τ at all Tb, and τ/PI at 20 and 30°C. Gop was lower at higher Tb at both resting and active animals, although Tb did not affect Gnorm. Activity reduced Gop and Gnorm at all Tb tested. BEI was unaffected by any treatment.

Conclusions and Support: The cardiac energy “wasted” at each cycle (OPF) is reduced at resting snakes at 30°C, whereas it is similar at 15 and 30°C during activity, indicating that energy usage is optimized at the preferred Tb of C. durissus (30°C). Although both τ and Gop are reduced with increased Tb, the unchanged τ/PI and Gnorm indicate τ and Gop are actively optimized to work at different heart rate and pressure conditions imposed by various Tb at rest. Increased Pp during activity indicates that arterial compliance decreases, affecting both τ and Gop. Support FAPESP: #2016/20158-6; #2018/05035-0

ID: 3717

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: METABOLIC ACIDOSIS AND NEUROMUSCULAR FATIGUE DEVELOPMENT DURING HIGH INTENSITY INTERVAL EXERCISE

Introduction: High-intensity interval exercise (HIIE) is an exercise-type characterized by shorter (< 2 min) or long (> 2 min) bouts performed at high intensities with passive or actives recoveries between them. The increase of bout duration during HIIE may evoke higher metabolic acidosis, compromising the neuromuscular function when compared with shorter bouts. However, the effect of bouts duration on the central and peripheral neuromuscular fatigue development remains an unsolved question.

Objective: The present study investigated the effect of bouts duration of HIIE on the metabolic acidosis, and neuromuscular fatigue development.

Methods: Fourteen physically active participants (mean ± SD) age 23 ± 4 years; height 1.77 ± 0,10 m; body mass 71 ± 8 kg; “V” ̇O2¬max. 47 ± 6 mL.kg-1.min-1; and peak power output 256 ± 5 W performed two HIIE protocols with matched total workload duration: 1 - 4 x 4 min., 3 min. recovery - HIIE4 and; 2 - 16 x 1 min., 45 s of recovery - HIIE1. Bouts and recoveries intensities were set at 90 and 50 % of “V” ̇O2¬max, respectively. Blood samples from the capillary lobe and brachial venous were obtained immediately before and 3 minutes after exercise to determine the blood lactate and pH, respectively. Maximum voluntary contraction (MVC), voluntary activation (VA) and evoked quadriceps twitch force by electrical stimuli at 100, 10 and 1 Hz (Qtw100, Qtw10, and Qtw, respectively) were evaluated before and 30 s after exercise. The study was approved by the Ethics Committee for Human Research at the Federal University of Pernambuco – CAAE 10324019.2.0000.5208.

Results: Capillary lactate increased from pre- to post-exercise similarly under both conditions (HIIE1: 2.0 and 5.9 mmol.L-1 vs. HIIE4: 2.1 and 6.4 mmol.L-1,respectively, $p<0.05$). Blood pH decreased from pre- to post-exercise similarly under both conditions (HIIE1: 7.3 and 7.2 vs. HIIE4: = 7.3 and 7.2, respectively, $p<0.05$). MVC decreased from pre- to post-exercise in all conditions ($p<0.05$), however, this

reduction was higher in the HIIE4 (500 ± 66 and 379 ± 76 N, respectively) than in the HIIE4 (503 ± 67 and 412 ± 82, respectively). VA evoked force at 100, 10 and 1 Hz declined similarly after HIIE, regardless of the condition (HIIE1: -6 ± 8%, -26 ± 24%, -41 ± 21%, and -42 ± 21% vs. HIIE4: -4 ± 8%, -20 ± 11%, -44 ± 16%, and -38 ± 15%, respectively, $p<0.05$).

Conclusions and Support: Increasing the high-intensity interval exercise bout duration caused a higher global fatigue development, but not central and peripheral isolated components fatigue. Such alteration cannot be explained by exercise-induced metabolic acidosis. This study was funded in parts by the National Council for Scientific and Technological Development (CNPq).

ID: 3462

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF INTENSE CALORIC RESTRICTION SINCE BIRTH ON COGNITION AND BEHAVIOR OF ADULT RATS

Introduction: Caloric restriction (CR) has been the most widely used non-pharmacological intervention to investigate mechanisms related to aging and longevity. This intervention has shown beneficial results in the reduction and incidence of several chronic diseases and functional declines related to aging such as age-related cancers, immunological and neuroendocrine disorders, motor dysfunctions and the development of diseases such as Parkinson's and Alzheimer's. The effects of caloric restriction on cognition present ambiguous results, since its effects vary according to its intensity and the period in which it is performed. According to a recently published review, moderate calorie restriction can lead to beneficial effects on cognition when started early in life.

Objective: Thus, the objective of this work was to investigate the effects of an intense caloric restriction protocol (50%) since birth on the cognition and behavior of adult male Wistar rats.

Methods: The experimental procedures were approved by the Ethics Committee on the Use of Animals at the Federal University of Jequitinhonha and Mucuri Valleys (CEUA-UFVJM), under registration number 053/2019. The animals were divided into a control group (C) (n = 24) fed ad libitum, and a restricted group (R) (n = 24) that started the 50% calorie restriction protocol from birth and were breastfed in mothers already restriction regime. After weaning, the puppies received the same diet as their mothers until 90 days of age. At 90 days, the animals underwent behavioral tests to assess exploratory behavior, learning and memory, spatial memory and anxious behavior using the Open Field, Novel Object Recognition, Barnes Maze and Elevated Plus Maze tests, respectively. After the behavioral tests, the animals had their tissues collected and frozen for further analysis.

Results: Our preliminary results suggest that even an intense caloric restriction when initiated shortly after birth, can lead to beneficial effects on the cognition of rats.

Conclusions and Support: Our results may contribute to a better understanding of the mechanisms related to the beneficial effects of caloric restriction on cognition and in improving the quality of mental health.

ID: 3719

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: METABOLIC ACIDOSIS AND NEUROMUSCULAR FATIGUE DEVELOPMENT DURING HIGH-INTENSITY INTERVAL EXERCISE WEARING AIRFLOW RESTRICTION MASK

Introduction: INTRODUCTION. Elevated Training Mask®, an airflow restriction mask (ARM), has been a practical and less expensive strategic used to increase high-intensity interval exercise (HIIE)-induced training adaptations. Part of these changes is related to the increased workload of the inspiratory muscles, reducing O2 saturation (SaO2), and exacerbated lactate accumulation. The higher homeostatic control challenges imposed by the ARM might compromise neuromuscular function but remains an open question.

Objective: OBJECTIVE: The main aim of this study was to investigate the effects of wearing ARM on blood pH, capillary lactate, and neuromuscular fatigue development during a HIIE.

Methods: METHODOLOGY: Fourteen physically active men (mean ± SD) age 24.1 ± 6.5; height 1.72 ± 5.5 m; body mass 70.1 ± 8.7 kg; “V” ̇O2¬max. 39.4 ± 5.1 mL.kg-1.min-1; and peak power output (PPO) 225 ± 33W performed two HIIE (4 x 4min, 3min recovery) sessions with and without ARM. Bout and recovery intensities were set at 90 and 50 % of maximal heart rate respectively. SaO2 was obtained at the last of each bout and recovery throughout HIIE. Blood pH and lactate were measured immediately before and 3 minutes after HIIE. Maximal voluntary contraction (MVC), voluntary activation (VA), and evoked 100 Hz force twitch was measure immediately before and 30 s after the HIIE. This study was approved by the Ethics Committee for Human Research at the Federal University of Pernambuco - CAAE: 10488319.7.0000.5208.

Results: RESULTS: SaO2 decreased ~1% throughout HIIE under both conditions ($p < 0.05$), but mean SaO2 over the HIIE was lower in the ARM (94 ± 2%) than in the control (97 ± 1%) condition ($p < 0.05$). Blood pH decreased from pre- to post-exercise in all conditions ($p < 0.05$), but decreased further in ARM than in the control condition (Control: 7.33 ± 0.03 and 7.26 ± 0.03 vs. ARM: 7.34 ± 0.03 and 7.17 ± 0.06, respectively, $p < 0.05$). Capillary lactate increased from pre- to post-exercise in all conditions ($p < 0.05$), but increased further in the ARM than in the control condition (Control: 2.33 ± 1.11 and 4.45 ± 1.29 mmol.L-1 vs. ARM 2.11 ± 0.68 and 6.34 ± 1.72 mmol.L-1, respectively, $p < 0.05$). MVC decreased from pre- to post-exercise in all condition, but decreased further in ARM than in the control condition (ARM: -32 ± 13% vs. control: -22 ± 12%, respectively, $p < 0.05$).VA decreased from pre- to post-exercise in the ARM, but not in the control condition (ARM: -19 ± 10% vs. control: -9 ± 6%, respectively, $p < 0.05$). Evoked force at 100 Hz declined similarly after HIIE, regardless of the condition (ARM: -22 ± 14% vs. control: -22 ± 12%, $p < 0.05$).

Conclusions and Support: CONLUSION: The use of an airflow restriction mask increases metabolic disruption during a HIIE session. Such alterations seem to carry for greater post-exercise central but not peripheral fatigue. SUPPORT: This work was funded by the Foundation Support Science and Technology of the Pernambuco - FACEPE.

ID: 3464

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: RELATING HUMAN PHYSIOLOGY CONTENT TO COVID-19: A STRATEGY TO KEEP STUDENTS IN TOUCH WITH PHYSIOLOGY IN TIMES OF SOCIAL DISTANCE DUE PANDEMIC

Introduction: Introduction: Due to the context of social distancing imposed as a result of COVID-19 pandemic, universities are looking for emergency remote education alternatives.

Objective: Objective:To propose and evaluate the students’ perception of a teaching-learning model using online platforms to review physiology contents relating them to COVID-19 physiopathology and consequences.

Methods: Methods: We organized a web course entitled “Special Topics in Human Physiology”, which aimed to review relevant physiology topics and relate them to COVID-19 with undergraduate students at the Federal University of Pampa. The course was held in May / 2020. The activities were carried out through synchronous meetings that took place through the Zoom platform twice a week, and asynchronous activities, using articles, case studies and online tools for active learning. After making the materials on the interaction between COVID-19 and physiological systems available, the most important points were discussed and the students’ doubts were resolved in synchronous meetings. It was also proposed that students use their creativity to create flyers, schemes and drawings for publication on their social networks such as Instagram and or / Facebook in order to contribute to the dissemination of information about COVID-19 and to avoid the divulgation of “fake news”. This proposal was approved by the Institutional Education Committee (Research Ethics Committee No. 10,069. 20).

Results: Results: 37 students that participated in the course answered our evaluation questionnaire (a response rate of 74%), students were asked if they ever had thought about the relationship of the different systems studied in Human Physiology course with the COVID-19 previously, 75.7% said “no”. Besides, 94.6% of the students affirmed that they shared information related to COVID-19 with their social group (family, friends, co-workers, etc...), yet, 97.3% said that the information discussed in the course helped them to select better sources of News and all the participants consider that establishing this relationship contributed and will impact their academic formation. Still, 86.5% said that their concern about the seriousness of the pandemic had increased after the course, 97.3%of students affirmed that studying the interactions of Sars-CoV-2 with the different body systems helped to understand better the CoViD-19. In addition, 75.7% of students considered that they learned “much” with this strategy of making relationships between physiology and COVID-19. We also asked if the course contributed to making the participants able to identify fake news about COVID-19 easily; 94.6% said that contributed a lot. Besides, 81.1% of the participants thought that studying the action mechanisms of soap and hand sanitizer helped them much to understand the importance of hygiene care. Regarding the way in which the physiology topics related to CoVID-19 were worked, 59.5% considered it excellent, and 40.5% good.

Conclusions and Support: Conclusion: We conclude that contextualizing physiological content with daily life situations, such as COVID-19, has a significant impact on the students’ learning, and this type of method can be adopted in the web teaching, using online platforms. Additionally, this practice has an impact in the daily life of students, influencing their decisions and practices. Support: UNIPAMPA, CAPES, CNPQ.

ID: 3465

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: BIOINFORMATIC DATABASES AS A TOOL TO ANALYZE ALTERATIONS IN CELL PHYSIOLOGY IN CARCINOGENESIS: A COMPARATIVE ANALYSIS OF OPEN ACCESS DATA ANALYSIS PLATFORMS

Introduction: The development of genomics and transcriptomics and the potential associated with sharing data led to a growing understanding of cell physiology. In particular, the comparative analysis of gene expression in normal and cancer tissues allows the dissection of the impact of certain genes or gene networks in carcinogenesis. For that purpose, it is essential to use user-friendly platforms, where it is easy to analyze, compare and collect information for a certain set of genes.

Objective: To compare five open access online platforms for tumor gene expression and patient survival analysis from TCGA datasets – cBioPortal, USCS Xena, GEPIA, UALCAN and ONCOLNC.

Methods: We explored these platforms from the point of view of a lay user, assessing their applicability to study differences in gene expression in tumor vs normal tissues, or according to cancer stage, and the impact of such expression patterns on patient survival.

Results: The platforms analysed allow an easy access to data and explore individual and multiple gene expression patterns. Some platforms relate gene expression to disease stages and analyse survival associated with the under and overexpression of a given gene. Some platforms also allow the user to filter data by selecting specific attributes, such as the type of cancer, molecular alteration, recurrence, histological aspects, etc. The data can be visualized through graphs, showing the distribution of the expression of a given gene or set of genes, also allowing the quantification of expression levels and establishing statistical relationships.

Conclusions and Support: Although all five platforms are very intuitive and access to the data is simple, they vary in the information available, results visualization, and statistical tests performed. Therefore, the choice of a given platform must take in consideration the type of information sought for each purpose. Additionally, if one platform does not provide all the information/recourses needed, it is possible to combine analysis obtained from more than one platform, regarding the same database is selected as source. The diversity of available information contributes in a very relevant way to the study of the complex mechanisms involved in cancer cell physiology, since the investigative approaches can be multiple. Support: Fundação para a Ciência e a Tecnologia (FCT) through grant UIDB/04567/2020 to CBIOS. Universidade Lusófona/ILIND (Grant Programme FIPID 2019/2020).

ID: 3721

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: ANALYSIS OF DIFFERENT REPRODUCTIVE PERIODS OF WISTAR FEMALES RELATED TO ANTIOXIDANT ENZYMATIC ACTION AND LIPOFUSCINE DEPOSITION IN THE HIPPOCAMPUS

Introduction: Population aging tends to triple in the coming years, signaling the need for research on the physiology of aging. In humans, the female reproductive system is the first to age, in a process characterized by the gradual transition from regular reproductive cycles to irregular cycles and the cessation of fertility in the period of acyclicity. During normal cell metabolism, lipid peroxidation occurs, increasing the formation of reactive oxygen species (ROS) and depletion of antioxidants, such as vitamins C and E and the consequent deposition of lipofuscin. Excessive deposition of lipofucsin occupies a large area of cytoplasm, which can alter the normal functioning of the neuron. Experimental studies with rodents have shown that lipofuscin can be identified as a marker of aging, its presence being related to the response to oxidative stress and irregularity in the mitochondria. The design of neuronal and hormonal signaling changes that occur throughout life and the exploration of possible corrective interventions will contribute to improving the quality of life of women, in favor of healthy aging.

Objective: Considering that the oxidative stress associated with the gradual decrease of estrogen in the female reproductive system are factors that contribute to aging, the objective of this study was to evaluate in the period of the regular estrous cycle and in the period of acyclicity (stropause) the concentration of lipofuscin in the hippocampus of the Wistar rats.

Methods: After confirmation of cyclicity of the estrous cycle (6 months - 10 rats) and acyclicity (30 months - 10 rats), the hippocampus was collected and processed for histological analysis of lipofuscin deposition. The experimental protocol was approved by the Ethics Committee for the Use of Animals (CEUA) of the Faculty of Dentistry of Araçatuba (2019 / 10943-6).

Results: As a main result, there was an increase in the accumulation of lipofuscin in pyramidal cells of CA1 and CA3 in the formation of the hippocampus in rats at 30 months compared to rats at 6 months.

Conclusions and Support: The lipofuscin pigment found in the cytoplasm of neuronal cells is an important biomarker of cell lesions that contribute to determine cell senescence. This high concentration of lipofuscin in the senescence period suggests a neural environment conducive to the occurrence of neurodegeneration.

ID: 3466

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Rio Grande do Sul - Porto Alegre - Rio Grande do Sul - Brasil

Title: THE IN VITRO INFLUENCE OF PLEUROTUS ALBIDUS EXTRACT ON AORTIC TONE REGULATION

Introduction: Oxidative stress is explained as an imbalance between oxidant and antioxidant molecules, being associated with several cardiovascular diseases. The literature describe that antioxidants used as pretreatment may protect the cardiovascular system from oxidative damage, then Pleurotus albidus (P. albidus) extract emerges a therapeutic alternative, because his in vitro antioxidant potential is already known. This mushroom is native from Latin America and has few reports about his pharmaceutical properties.

Objective: The aim of this study was to evaluate if the antioxidant P. albidus capacity influences on aortic tone regulation.

Methods: Male Wistar rats weighing 230 – 250g were used, where hearts and thoracic aortic arteries were removed for use in vascular reactivity and biochemical analysis. The homogenates were exposed to P. albidus extract at different concentrations for 30 minutes and then exposed to the free radical generation model for 30 minutes. In the biochemical analysis of the heart, we evaluated the lipid peroxidation, the activity of the enzymes superoxide dismutase, catalase and glutathione peroxidase. In aortas, we evaluated the lipid peroxidation, sulfhydryl levels, and the activity of NADPH oxidase and nitric oxide synthase enzymes. In the analysis of vascular reactivity, were evaluated the P. albidus influence on functional thoracic aortic rings tone regulation in 2 analyses: when pre-incubated with 1.5mg/mL of this extract; and in a dose-concentration curve of P. albidus. Ergothioneine levels was quantified in the extract by HPLC. All animal care procedures were approved by the Animal Research Ethics Committee of the Universidade Federal do Rio Grande do Sul (No. 34651).

Results: In the cardiac tissue, the dose of extract 1.5mg/ml was able to reduce lipid peroxidation and increase the activity of enzymes catalase and glutathione peroxidase. In the aorta, the dose of extract 0.3mg/mL was able to reduce the lipid peroxidation and the activity of NADPH oxidase, as well as increase the activity of nitric oxide synthase and the sulfhydryl levels. On vascular reactivity analysis, the P. albidus pre-incubated aortic rings showed a significant reduction in the maximum response to acetylcholine concentration-effect curves. The dose-concentration P. albidus curves showed a progressive vasodilatory response, achieving a maximum relaxation of 35.57% with 0.3mg/mL, which was reduced with increasing concentrations. It was also possible to verify the presence of ergothioneine in the extract, this molecule is described on the literature as an antioxidant molecule and can be the major influencer of extract vasodilator effect.

Conclusions and Support: Pleurotus albidus extract emerge as a future therapeutic alternative for mitigating the damage of oxidative stress and vascular disorders. However, further studies are necessary to verify the mechanisms of action of the extract and to verify his potential in vivo. Support: CNPq and CAPES

ID: 3722

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de São Paulo - Sao Paulo - Sao Paulo - Brasil

Title: ACYLATED GHRELIN LEVELS INFLUENCES POSTMENOPAUSAL DEPRESSION

Introduction: The postmenopause-associated symptoms impact negatively women quality of life. We have previously found clinical and experimental evidence of a connection between the lack of ovarian hormones and increased rates of obesity and depression. Ghrelin involvement on modulation of mood disorders has also been investigated but its role in depression is still ambiguous.

Objective: To investigate the relationship between depression symptoms with anthropometric and biochemical parameters in postmenopausal women.

Methods: This was an observational, prospective and cross-sectional study, which was approved by the Ethics Committee of the Universidade Federal de São Paulo (CEP #921394/2014), and was conducted according to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines. All participants signed the written consent. Fifty-five postmenopausal women with depression symptoms were included in the study and were allocated into three groups according to the classification of depression symptoms, assessed by the Beck Depression's Inventory (BDI): mild (n=26), moderate (n=22) or severe depression group (n=7). FSH levels and amenorrhea for at least 1 year confirmed menopause status. Anthropometric, blood biochemical and hormonal determinations, and depression symptoms (by BDI and Patient Health Questionnaire - PHQ-9) were conducted. Data were analysed by either Anova (and post-hoc Tukey) or Kruskall-Wallis. Significance was set at $P<0.05$. Pearson's correlation and linear regression model were applied.

Results: The severe depression group had higher levels of total and acylated ghrelin than those of the mild depression group. All other clinical parameters failed to show significant differences. All groups were identified with overweight (measured by body mass index [BMI]), abdominal obesity (waist/hip ratio [WHR]) and high percentage of body fat. Correlations analysis showed total ghrelin ($P<0.001$), acylated

ghrelin (P<0.001), BMI (P=0.05) and WHR (P=0.01) to correlate positively with BDI scores. Additionally, total ghrelin (P=0.016), acylated ghrelin (P=0.017), WHR (P=0.002) and HOMA-IR (P=0.002) correlated positively with PHQ-9 scores. Multivariate regression analysis for BDI as the dependent variable showed that active ghrelin (P<0.00001) and BMI (P<0.02) correlate positively with depression symptoms. The multivariate regression analysis for PHQ-9 as the dependent variable showed that active ghrelin (P=0.008) and HOMA-IR (P=0.005) correlate positively with depression symptoms.

Conclusions and Support: Among all the overweight postmenopausal women, the depression symptoms were strongly correlated with BMI, WHR, HOMA-IR and ghrelin levels, indicating that total and acylated ghrelin, insulin resistance and total and abdominal obesity are associated with mental health disorders in postmenopausal women. To the best of our knowledge, this is the first report that analysed the relationship between ghrelin levels and depression symptoms in postmenopausal women. We have shown an important association between the levels of acylated ghrelin and the severity of the depression symptoms in this population. Further investigations are warranted to assess if the levels of acylated ghrelin may be used as a criterion describing depression prognosis as well as treatment effectiveness in postmenopausal women. Research relating to this abstract was funded by CAPES and CNPq.

ID: 3467

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal de Pelotas - PELOTAS - Rio Grande do Sul - Brasil

Title: PLEUROTUS ALBIDUS SUPPLEMENTATION PRESENTS PROMISING POTENTIAL FOR THE CONTROL OF BODY WEIGHT AND FOOD INTAKE IN HEALTHY C57BL/6 MICE

Introduction: Mushrooms have been used for centuries because they present promising proprieties for the health. In these sense, the mushrooms of the genus Pleurotus stand out for being the most popular and cultivated worldwide. Among others species of this genus, Pleurotus albidus (P. albidus) presents nutritional and medicinal properties in vitro. Besides that, P. albidus specie has not been tested in vivo.

Objective: The aim of this study was to evaluate the influence of P. albidus hydroalcoholic extract supplementation for 20 days on body weight, food intake, blood glucose, triglycerides, total cholesterol, high density lipoprotein, and urea levels.

Methods: Healthy male C57BL/6 mice were divided into two experimental groups: control and P. albidus. The supplementation was performed by gavage (500 mg/kg) for 20 uninterrupted days. During this period, all animals received food and water ad libitum and had their food intake and body weight monitored daily. After 20 days, the mice underwent the insulin sensitivity test, followed by euthanasia and biochemical analysis. All animal procedures were reviewed and approved by the Institutional Animal Care and Use Committees at the Universidade Federal de Pelotas (No. 28614-2019).

Results: The food intake and body weight were significantly decreased with P. albidus supplementation in healthy mice. However, lipids, urea, and insulin sensitivity were not changed after 20 days.

Conclusions and Support: Pleurotus albidus hydroalcoholic extract showed capacity to reduced the body weight and food intake in healthy mice. Support: CNPq and CAPES

ID: 3468

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE FEDERAL DE GOIÁS - GOIÂNIA - Goias - Brasil

Title: TREATMENT WITH ANGIOTENSIN-(1-7) DURING CHILDHOOD PREVENTS CARDIOVASCULAR DYSFUNCTIONS IN ADULT HYPERTENSIVE RATS.

Introduction: The exposure to adverse factors in the early stages of life can be a determinant factor for the development of diseases in adulthood. Previous studies have shown that changes in the activation of genes regulated by the Renin-Angiotensin System may contribute to the development of hypertension. Besides, it is broadly known that Angiotensin-(1-7) [Ang-(1-7)] presents cardioprotective effects.

Objective: We here postulate that treatment with Ang-(1-7) during childhood may attenuate the development of cardiovascular dysfunction in adult hypertensive rats.

Methods: It was used normotensive (Wistar) and spontaneously hypertensive (SHR) rats (Ethical committee approval #110/19). Osmotic mini-pumps containing Ang-(1-7) (24 µg/Kg/h) were implanted in the SHRs at 4 weeks of age and removed after 3 weeks. The systolic blood pressure (SBP) was monitored by tail plethysmography (from the 6th to16th weeks of age). Echocardiography and vascular reactivity in isolated aortic ring preparation was assessed ate week 16th. The heart and kidneys were collected for analysis. Results are mean±SEM; Wistar vs. SHR vs. SHR Ang-(1-7), and compared using one-way ANOVA with Tukey (n=6/group, $P<0.05$).

Results: The treatment with Ang-(1-7) did not change the SBP in adult SHRs. There was no difference between the groups in the aortic vascular reactivity. Ang-(1-7) prevented the increased intraventricular septum thickness in systole (0.19±0.009 vs. 0.23±0.009 vs. 0.19±0.005 cm) and in diastole (0.148±0.002 vs. 0.164±0.005 vs. 0.152±0.006 cm). Ang-(1-7) also prevented left ventricular (LV) cardiomyocyte hypertrophy (10.38±0.08 vs. 11.48±0.09 vs. 10.08±0.10 µm), interstitial fibrosis (4.63±0.30 vs. 6.85±0.35 vs. 4.48±0.31%), and perivascular (3.98±0.24% vs. 6.88±0.72% vs. 5.06±0.41%). The LV protein expression of the ACE2, ACE, AT1, AT2, collagen I, GSK3B, and calcineurin in the heart were not different. pAKT was decreased in both SHR control and SHR Ang-(1-7) (1±0 vs. 0.54±0.03 vs. 0.53±0.1). The treatment leads to an increase in MMP9 (1±0 vs. 0.98±0.09 vs. 1.6±0.27) and a decrease in caspase (1±0 vs. 0.83±0.07 vs. 0.71±0.04) and procaspase (1±0 vs. 1.14±0.18 vs. 0.65±0.09) levels. The ratio pERK/ERK was also reverted by the treatment (1±0 vs. 1.57±0.09 vs. 1.16±0.07), and calmodulin levels were decreased (1±0 vs. 0.75±0.09 vs. 0.56±0.09). Furthermore, the Ang-(1-7) increased the SOD-1 LV protein expression (1±0 vs. 1.04±0.16 vs. 1.89±0.32) and catalase activity (24.56±1.42 vs. 19.27±2.96 vs. 29.27±2.15 U CAT/mg of protein) and reduced the level of Tbars (7.77±0.24 vs. 6.45±0.39 nmol/mg). The Ang-(1-7) also prevented the thickening of the renal capsule (6509±229.9 vs. 7666±159.8 vs. 6853±127.0 µm2) and glomerulus (5161±150.1 vs. 5949±130.6 vs. 5550±111.2 µm2).

Conclusions and Support: These data show that the treatment with Ang-(1-7) in childhood can prevent the development of the cardiac and renal injuries caused by hypertension through mechanisms involving the activation of antioxidant pathways and this effect is independent of changes in the blood pressure. Support: CAPES, CNPq, and FAPEG

ID: 3469

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF PU ERH (Camelia sinensis) EXTRACT ON MORPHOMETRIC PARAMETERS AND GLUCOSE TOLERANCE IN WISTAR RATS FEEDING ON A HYPERLIPIDIC DIET

Introduction: Obesity is one of the main risk factors for chronic non-communicable diseases, such as type 2 Diabetes Mellitus, cardiovascular diseases and dyslipidemia. Many substances extracted from plants are used to treat obesity or prevent its onset. Among the various teas consumed in the world, Pu Erh extract (red tea - Camelia sinensis) has been associated with decreased levels of triglycerides and total cholesterol in rats and with improved insulin sensitivity in mice.

Objective: Evaluate the effects of Pu Erh extract (Camellia sinensis) on morphometric parameters and the sensitivity to insulin through the glucose tolerance test, in adult, male Wistar rats, fed a high-fat diet.

Methods: This study was approved by the Animal Use Ethics Committee of UFRGS (nº 38712). Sixty male Wistar rats (60 days old) were divided into 6 groups: SDW- standard diet and water; SDP1-standard diet and Pu Erh P1 (2g/Kg body weight/day); SDP2- standard diet and Pu Erh P2 (4g/Kg body weight/day); HDW- high-fat diet and water; HDP1- high-fat diet and Pu Erh P1; HDP2- high-fat diet and Pu Erh P2. The animals received this treatment for 12 weeks. The Pu Erh extract was prepared by infusing water (95°C, 3') and offered daily. The animals were fed ad libitum with a standard or a hyperlipidic diet. Body weight was estimated before the beginning and at the end of treatment and weight gain was calculated. The Glucose Tolerance Test (GTT) was performed after fasting (8 hours) at 4, 8 and 12 weeks of treatment. After the first blood collection, a 50% glucose solution was administered by gavage. Blood was collected from the tail at times 0, 15, 30, 45, 60, 90 and 120 min and blood glucose was measured with glucometer. At the end of the experimental period, the animals were killed by decapitation and the tissues were removed and weighed. The fatty somatic índices (FSI, tissue weight/animal weight) of white adipose tissues (epididimal- eWAT, retroperitoneal -WATr and subcutaneous -WATs) and brown adipose tissue (BAT), as well as the hepatossomatic index (HI) were estimated.Statistical Analysis: The normality of the data was verified by the Kolmogorov-Smirnov test. Area under the curve (AUC) was calculated by GTT. The data were submitted to two-way ANOVA analysis followed by Bonferroni post hoc. The accepted significance was $P<0.05$ and the tests were performed using the Prisma software version 8.0.

Results: Weight gain was greater ($p<0.05$) in animals fed a high-fat diet compared to control animals (standard diet). The aqueous extract of Pu Erh did not alter body weight gain. However, it caused a decrease ($p<0.05$) in the FSI of rWAT, sWAT and BAT in control animals in the two studied doses (P1 and P2). In contrast, the high-fat diet caused an increase in the indexes ($p<0.05$) of rWAT, sWAT, eWAT and BAT compared to the control animals. In addition, the high-fat diet impairment of glucose tolerance at 8 and 12 weeks of treatment. Nevertheless, the Pu Erh treatment had no impact on the GTT.

Conclusions and Support: Pu Erh extract did not prevent the effects caused by the high fat diet in weight gain and GTT. However, the red tea reduced body fat reserves in animals treated with a control diet. Further studies are needed to clarify these findings. Support: CNPq; CAPES and PROPESQ (Pró-reitoria de Pesquisa from UFRGS, Brazil); Tea Shop® (Brazil).

ID: 3470

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EVALUATION OF CALORIC RESTRICTION TO ATTENUATE INTERMITENTE HIGH-FAT HIGH-SUCROSE DIET-INDUCED INSULIN RESISTANCE IN C57BL6/J MICE

Introduction: According to the World Health Organization (WHO), obesity has more than doubled since 1980, arguably it is a global problem of global public health. Obesity is directly linked to insulin resistance (IR), cardiovascular diseases, dyslipidemia, type 2 diabetes mellitus, and thus, a set of factors characterizing Metabolic Syndrome (MS). Calorie restriction (CR, 30% to 40%) has been shown to counteract the damage caused by obesity, including weight loss, decrease serum glucose and insulin levels and improve insulin sensitivity in many experimental models and also clinically, mainly as diverse models of intermittent CR. On the other hand, obesity has been experimentally mimicked by administering long-term high-fat diet, which triggers several markers of MS. However, recent studies have shown many of these markers using intermittent high caloric diets.

Objective: Here, we used a high-fat high-sucrose (HFHS) diet once a week for 12 weeks and compared mice that received ad libitum chow diet or CR (40%) in intervals between HFHS diet (6 days a week)

Methods: For this 48 C57BL/6 mice that were divided into four experimental groups: Chow: fed a standard diet, HFHSw: received HFSH diet once a week and ad libitum chow diet in invervals, ChowR fed continuously with standard diet in a CR protocol (40% CR) and HFHSwR: received HFHS diet once and 40% CR in intervals. Insulin tolerance test (ITT), intraperitoneal glucose tolerance test (ipGTT) were performed in different times during the protocol, and at the end of twelve weeks, the animals were euthanized 24h after the last challenge of HFHS and blood and different tissues and organs were collected for analysis (Ethics committee: CEUA/CCS/UFRJ/FARMACIA08-115/18).

Results: During the ITT, the HFHSw group showed a higher curve between the groups and a significant increase in blood glucose at times 60 and 120 compared to Chow. The CR groups showed a decrease in the glycemic curve confirmed by the area under the curve (AUC). During ipGTT, the HFHSw group showed a higher confirmed glycemic curve in AUC compared to Chow; this is an indication of RI and the HFHSwR group showed a reduction in AUC compared to HFHSw. When evaluating the lipidogram, an increase in serum triglyceride (TG) levels was observed in the HFHSw and HFHSwR groups, again indicating IR. By Western blot, we observed increased phosphorylation of AMP-activated protein kinase (AMPK) at Thr172 (pAMPK-T172) in ChowR and HFHSwR groups as compared to their counterparts, indicating activation of this enzyme. This activation is confirmed by increased phosphorylation of Acetyl-CoA Carboxylase (ACC) at Ser79 (pACC-S79), a substrate for AMPK. Moreover, pACC-S79 is indicative inhibited lipogenesis, which is confirmed by downregulation of key transcription factor in lipogenesis Sterol Regulatory Element-Binding Protein 1c (SREBP-1c), evaluated by qPCR. Histological analysis liver tissues suggests an increase of steatosis in HFHSw group was compared to Chow group, which is not observed in HFHSwR group.

Conclusions and Support: So far, our results are indicative that CR is able to prevent intermittent HFHS diet-induced damages on C57BL6/J mice, but more analysis will be carried out to deepen these results. Funding: FAPERJ/CAPES/CNPq

ID: 3471

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: REVERSAL OF GENOTOXICITY AND CELL DEATH IN AORTA OF DIABETIC RATS AFTER SILDENAFIL CITRATE TREATMENT

Introduction: Diabetes Mellitus (DM), is a metabolic disease that can induce significative vascular alterations leading it to a functional dysfunction. Aorta is the largest artery in the body and its main function is to provide arterial blood to the major organs through the smaller arteries that arise from it. Collagen is one of the most important components of the aortic wall and its concentration plays a significant role

in the aorta function and mechanical properties. Growing evidence suggest a pleiotropic effect of Sildenafil (SIL), a phosphodiesterase-5 inhibitor, however it´s not known if SIL can avoid vascular DNA damage.

Objective: To investigate SIL effects on DM rat's aorta.

Methods: Eighteen male Wistar rats, were used in this study. In twelve animals Diabetes Mellitus (DM) was induced through streptozotocin (50 mg/kg) injection in the penile vein. After confirmation of DM, rats were divided in Diabetes Vehicle (DV) and Diabetes Sildenafil (DS) treated via gavage with SIL (3 mg/Kg) for 14 days. An additional six rats without any treatment were used as control (CT). After treatment, rats were euthanized, and blood was collected for glycemia evaluation and aorta were removed for DNA damage, oxidative stress, and histological analysis. Data were expressed as mean ± SEM and considered significant when $p<0.05$. This project was approved by the institutional Ethical Committee for Animal Research, CEUA-UFES number 14/2017.

Results: Aorta comet assay through tail DNA analysis revealed greater DNA damage in the DV group (78 ± 4 %) compared to CT group (57 ± 2 %). In the DS group this damage was significantly decreased (63 ± 2 % vs. DV, $p<0.05$). In addition, comet assay also showed an increased tail moment in DV compared to CT (61 ± 4 a.u. vs. 41 ± 3 a.u., $p<0.05$). Sil treatment also decrease tail moment in DS (48 ± 2 a.u. vs. DV, $p<0.05$). DV showed an increase in aorta collagen (25 ± 2 %) compared to CT (14 ± 1 %, $p<0.05$). Collagen amounts decrease in DS (15 ± 1 % vs. DV, $p<0.05$). Thickness of aorta intima-media layer increased in DV (15849 ± 209 μm) compared to CT (13046 ± 100 μm, $p<0.05$). Sil treatment prevented this increase in DS (10156 ± 969 μm vs. DV, $p<0.05$). Aorta cell viability did decrease in DV (1818 ± 175 %) compared to CT (1413 ± 25 %). Treatment with SIL avoid aorta cell death (DS: 1338 ± 47 % vs. DV, $p<0.05$). Interesting, the SIL effects was independent of glucose blood levels: CT (158 ± 8 mg/dL), DS (440 ± 34 mg/dL) vs. DV (403 ± 26 mg/dL, $p>0.05$). Oxidative stress evaluated in aorta cells, showed an increase in reactive oxygen species (ROS) in DV (1502 ± 38 a.u.) compared to CT (1332 ± 13 a.u., $p<0.05$). ROS levels did decrease after SIL treatment in DS (1374 ± 22 a.u., vs. DV, $p<0.05$).

Conclusions and Support: In DM aorta lesions caused by high ROS levels and DNA damage can affect severely its functions and compromise organ and tissue adequate blood perfusion. The antigenotoxicity and antioxidant effects of sildenafil can be an option to ;minimize and treat vascular lesions in broad spectrum of diseases. Support: CAPES and CNPq

ID: 3473

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF LITTER SIZE EXPANSION-INDUCED NEONATAL MALNUTRITION ON REPRODUCTIVE PARAMETERS OF FEMALE RATS

Introduction: Epidemiological studies and animal models show that early disbalanced nutritional supply, both in intrauterine and postnatal periods, can predispose individuals to deseases throughout life. The data in the literature concerning neonatal undernutrition by expansion of litter size are controversial. Some results show that neonatal malnutrition programmed both male and female Wistar rats to remain small and lean in adult life, with lower food intake. On the other hand, others say that after weaning, animals exposed to postnatal underfeeding have increased food consumption and they can even reach the body weight of control rats. Moreover, it is known that changes in energy suppply in early periods of life can negatively affect the organization of neural circuits involved in the control of reproduction. However, the results on this topic are also controversial, since postnatal malnutrition in females may result or not in decreased growth related to delay in puberty. Therefore, more studies are necessary to elucidate the effects of litter size expansion on the development and reproductive parameters of female rats.

Objective: To evaluate body weight gain, food intake, Lee index, ano-genital distance, vaginal opening, first estrus, cyclicality, glucose tolerance, weights of visceral white adipose tissue, ovaries, uterus and adrenals of female adult rats from normal (NL) and large (LL) litters.

Methods: On the birth, litter size was manipulated to large (LL - 16 pups) and normal (NL - 10 pups) litters. Pups were weighed on postnatal days (PND) 3, 7, 10, 14, 17, 21 (weaning), and then every 5 days until PND 90. The ano-genital distance was also measured at PND 0 and 21. Starting on PND 21, female pups were daily evaluated for vaginal opening and, thereafter, vaginal smears were daily examined until the regularization of estrous cycles. From PND 75 to 90, body weight and food intake were measured, and vaginal smear was daily performed. At the first proestrus after PND 90, female rats were fasted for 6 hours and were euthanized by decapitation. Retroperitoneal and perigonadal visceral adipose tissues, adrenal glands, ovaries and uterus were removed and weighed. This study was approved by the Ethics Committee on the Use of Animals of the State University of Londrina (18310.2019.03).

Results: On the weaning day, LL females had significantly lower ano-genital distance than NL females. From PND 3 to 90, LL females showed reduced body weight compared to NL females. Mean daily food intake during the analyzed period (PND 21 – 90) was higher in LL group than NL animals. There was delay on the first estrus in LL females, without differences on vaginal opening and cyclicality. LL animals showed glucose intolerance, lower weight of retroperitoneal fat pad and higher weight of adrenal glands than NL animals, with no differences on perigonadal fat pad, uterus and ovaries weight.

Conclusions and Support: It was possible to observe that the expansion of the litter size promoted decresaed ano-genital distance on PND 21, associated with glucose intolerance, higher food intake and weight of adrenal glands. On the other hand neonatal undernutrition reduced body weight gain and the amount of retroperitoneal adipose tissue, associated with delay on the onset of puberty as observed by later occurrence of first estrus, without changes in the cyclicity.

ID: 3474

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Odontologia de Araraquara- FOAR (UNESP) - Araraquara - Sao Paulo - Brasil

Title: A POSSIBLE INHIBITORY ROLE FOR ALPHA2-ADRENOCEPTORS ON THE SALTY TASTE OF SODIUM-DEPLETE RATS

Introduction: Activation of alpha2-adrenoceptors mediates the actions of antihypertensive therapeutic drugs and inhibits NaCl intake in the rat. Preliminary results from our laboratory suggested that an intraperitoneal (ip) injection of clonidine (40 µg/kg) might not affect the orofacial responses to an intraoral infusion of 0.3 M NaCl (hNaCl) of sodium-deplete rats.

Objective: The objective of the present work was to investigate whether clonidine affects orofacial motor responses after the animals have access to hNaCl to ingest.

Methods: Adult male Holtzman rats (n = 15) were depleted of sodium by combined subcutaneous (sc) injection of a natriuretic/diuretic (furosemide) and 24 h removal of ambient sodium, with free access to water and sodium-free food. Then, they received a counterbalanced ip injection of either clonidine or vehicle. Fifteen minutes after injection, a recording of orofacial motor responses of the sodium-deplete animals was immediately followed by a 15-min hNaCl intake test (block zero). The paired recordings of orofacial motor responses and intake were repeated within each block of a series of five successive blocks during a total period of 240 minutes.

Results: Clonidine inhibited the hedonic orofacial responses to intraoral hNaCl in block zero (56 ± 18, vs. vehicle: 156 ± 22/min). Similar effect persisted in block 1 and 2, when clonidine reduced hNaCl intake to zero versus the 9 ± 1 ml of the vehicle group. The effect of clonidine on the hedonic orofacial responses disappeared as the animals began to ingest hNaCl progressively at block 3 reaching similar intake to vehicle at block 5.

Conclusions and Support: Contrary to the preliminary results, the present results indicate that clonidine may inhibit for at least one hour the hedonic orofacial responses to hNaCl. This suggests that the inhibition of hNaCl intake by clonidine is a result of the reduced rewarding effect of salty taste. Supported by: CAPES, CNPq, FAPESP, PIPGCF UFSCar/UNESP.

ID: 3475

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: RELATIONSHIP BETWEEN EXERCISE-INDUCED MUSCLE SORENESS AND SKIN TEMPERATURE IN MEN AND WOMEN

Introduction: Delayed onset muscle soreness (DOMS) leads to strength loss, reduced range of motion, and pain. Biochemical tests quantify muscle damage, but these analyses are invasive and expensive. In this context, the use of technological tools to quantify physiological responses to training has gained prominence. Infrared thermography is a non-invasive and easy to use imaging technique that allows measuring the skin temperature in different contexts. Considering that the inflammatory process associated with DOMS can influence the blood flow and lead to local hypothermia, the use of thermography to monitor DOMS would be of great practical applicability. However, the relationship between skin temperature, muscle damage, and DOMS still is unclear.

Objective: To determine the relationship between exercise-induced muscle soreness and skin temperature in men and women performing physical exercise.

Methods: Twenty-two healthy participants (10 men and 12 women) completed a squat exercise protocol with maximal voluntary repetition to induce DOMS in the quadriceps muscle. Muscle soreness, and skin temperature were evaluated in three moments (pre-exercise, post, and 48h post-exercise). The mean skin temperature of the anterior thigh was measured using an infrared thermography camera with a resolution of 320 x 240 pixels (FLIR model E-60, Flir Systems Inc., Wilsonville, Oregon, USA). DOMS was assessed using a visual analog scale (VAS, considering 0 = no pain and 10 = extreme pain) and the pressure pain threshold (PPT) using an algometer (Digital Dynamometer Model DD-200) for sites in the distal, medial, and proximal portions of rectus femoris and vastus lateralis. The Shapiro-Wilk teste confirmed the normality of data, the VAS data were compared by the Friedman teste with Wilcoxon post-hoc, differences between sexes using U of Mann-Whitney. Repeated measures ANOVA with Bonferroni post-hoc were applied to compare values of PPT at each region measured. The same analyzes were performed to compare skin temperature data. Finally, stepwise multiple linear regressions were performed using the variations of Δ skin temperature (differ between post and pre-exercise), and ΔT 48h (between 48h post-exercise and pre-exercise), and variation of VAS and PPT. The R2 value was provided for the regressions models and the significance level was set at 0.05. The

local University's ethics committee approved this research (CAAE: 26037119.9.0000.5323) and all procedures established in the Helsinki Declaration were respected.

Results: DOMS increased post, and 48h post-exercise for both sexes, but without difference between men and women ($p>0.42$). PPT in men decreased only in post 48h ($p < 0.01$). For woman, PPT was stable in all moments and remained always lower than men ($p < 0.05$). Skin temperature did not differ between pre and 48h post-exercise ($p > 0.05$). Moreover, skin temperature did not predict DOMS and PPT for men ($p > 0.05$). For women, $\Delta T48$ of the mean skin temperature from anterior thigh showed a direct relationship with the absolute values of the $\Delta 48h$ pain threshold of the vastus lateralis ($R2 = 0.43$ and p-value = 0.02).

Conclusions and Support: We conclude that changes in skin temperature in exercised muscle are related to pain threshold 48h after exercise in women.This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior - Brasil (CAPES) - Finance Code 001 granted to WS. A research fellow of CNPq-Brazil supports FPC.

ID: 3476

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: RELATIONSHIP BETWEEN AESTHETIC OCCUPATIONS AND HEALTH INDICATORS

Introduction: Professions based on body standards for daily performance are identified in the literature as non-conventional occupations with health risks (such as models, athletes and dancers). They have a greater emphasis on the female audience and in addition to a professional career, these professions become a lifestyle. The common and individual peculiarities of each profession and the daily demands on young women can modify daily behaviors, which can lead to increase risk for health if not identified early.

Objective: To identify the relationship among professions with aesthetic demands and quality of life, level of physical activity and self-image of models, athletes and dancers.

Methods: The study was approved by the local Ethics Committee (number 67847317.5.0000.5347). This cross-sectional study recruited 41 female adolescents and young adults aged between 14 and 24 years, who were allocated in 4 groups: control/university group (UG=11), model group (MG=11), dancers group (DG=11) and athletes group (AG=8). The allocation was due to the professional performance of each participant. Variables of general quality of life (and physical, psychological, social and environmental domains), level of physical activity and self-image were evaluated.

Results: No differences were found among groups for quality of life variables ($p>0.05$). Social domains values were considered below the normal range for AG and DG. For the level of physical activity, all groups reached the recommendations for daily physical activity. However, significant difference was found for vigorous physical activity and physical activity between groups, with AG presenting higher values than the others groups ($p<0.05$). For self-image, all groups presented values considered below the cut-off of image distortion, thus, no significant differences were found between groups ($p>0.05$).

Conclusions and Support: The professions analyzed do not seem to interfere in quality of daily life, levels of physical activity and the perception of self-image. However, even achieving satisfactory results, we believe they are at risk public, since daily habits continue throughout of life, being interesting a constant monitoring given the particularities and daily pressures imposed not only by professions, but also on the female public. Support: The authors SDCL, AFV, JBF were supported by Capes, RRC by PNPD/Capes, and JLT, ARO supported by CNPq.

ID: 3477

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

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Title: THE ROLE OF OXIDATIVE STRESS ON THE DEGENERATION OF MEDULLARY RESPIRATORY NEURONS IN AN ANIMAL MODEL OF PARKINSON'S DISEASE.

Introduction: Parkinson's disease (PD) is a progressive and irreversible neurodegenerative disease characterized by the loss of dopaminergic neurons in the Substantia Nigra (SN) region. It consists of classical motor symptoms and non-classical symptoms such as respiratory problems. It is known that there are several causes for injuries in SN dopaminergic neurons, from genetic factors to environment-individual interactions, andoxidative stress directly related to the neurodegeneration suffered by individuals who develop PD, already described in the SN region. The oxidative stress is also developed in respiratory medullary regions after 30 days of 6-hydroxydopamine (6-OHDA) induced rat models, which may be due to increased enzymatic activity of NADPH oxidase (NOX). It results in a high loss of medullary respiratory nuclei leading to respiratory dysfunction at 40 days.

Objective: Evaluate the time course of oxidative stress in the respiratory control nuclei such as nucleus of solitarytract (NTS), retrotrapezoid nucleus (RTN), pre-Bötzinger (pre-BötC) and rostral ventral respiratory nucleus (rVRG) in PD animal model.

Methods: Bilateral injections of vehicle or 6-OHDA (24 µg/µl) in male Wistar rats (250-300 g) striatum were done and after 20 and 40 days dihidroetidium (DHE) assay was performed to evaluatethe superoxide anion production in respiratory nuclei(CEUA n°2740200319).

Results: After the induction of PD model, immunohistochemistry for tyrosine-hydroxylase (TH) confirmed the neurodegeneration of 6-OHDA-injected rats with a substantial reduction in SN population (~80%) (6-OHDA 20: 104 ± 26; 6-OHDA 40: 91 ± 29 vs. vehicle: 501 ± 72, F(2,11)==22,42, p=0.0001). It was possible to determine that the imbalance in the redox signaling in respiratory nuclei of 6-OHDA-rats, did not begin at 20 days after the PD model induction, nor was presented at 40 days: NTSc (6-OHDA 20: 87.6 ± 14.3%; 6-OHDA 40: 363.6 ± 570.6% integrated density), NTSi (6-OHDA 20: 105.8 ± 23.1%; 6-OHDA 40: 165.40 ± 112.7% integrated density), rVRG (6-OHDA 20: 98.0 ± 48,5%; 6-OHDA 40: 146.7 ± 71.3% integrated density), preBotC (6- OHDA 20: 112.3 ± 61.4%; 6-OHDA 40: 123.0 ± 36.3% integrated density) and RTN (6-OHDA 20: 112.7 ± 35.2%; 6-OHDA 40: 193.7 ± 166.9% integrated density).

Conclusions and Support: Our data showed that there are no changes in the redox balance at 20 or 40 days after 6-OHDA injection in the respiratory control nuclei, and that may happen due to the continuous death of cathecolaminergic neurons. However, the previous data of our laboratory showed an increase in oxidative stress in those nuclei at 30 days. Because of that, it is plausible to start treatment against oxidative stress at 20 days after PD model induction to try to reverse the damage on breathing. Financial support: FAPESP 2019/00065-1 and 2020/01831-7.

ID: 3478

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF MINOCYCLINE ON MICROGLIA CELLS IN THE LOCUS COERULEUS REGION IN A SPORADIC MODEL FOR ALZHEIMER'S DISEASE

Introduction: Alzheimer's disease (AD) is the most common neurodegenerative dementia in the world. Inflammation of the central nervous system in AD is the result of activation of the microglia cells in response to the formation of amyloid plaques (o extracellular accumulation of βA1-42 peptide) and/or hyperphosphorylation of the tau protein (NFTs), which may promote a chronic state neuroinflammation that worsens and accelerates the progression of the disease. In our previous study, we demonstrated the increased expression of beta amyloid peptide in the Locus Coeruleus (LC) region that can trigger a initial neuroinflammatory process in AD. Thus, we investigate a pharmacological intervention of the treatment with minocycline in the microglia cells in the LC an sporadic model for AD. All experiments was conducted according to the guidelines of the Brazilian College of the National Council for the Control of Animal Experimentation (CONCEA, MCT, Brazil) and with the approval of the the Faculty of Agricultural and Veterinary Sciences and Animal Care, Use Committee (CEUA, FACV-UNESP, Jaboticabal campus; Protocol no. nº 05796/19).

Objective: Based on the evidence, the aim of our study was to evaluate the effect of minocycline treatment on microglia cells in the Locus Coeruleus region.

Methods: For this, we performed 5 days treatment with minocycline a sporadic AD model induced by intracerebroventricular injection of streptozotocin (STZ; 2 mg / kg). After the 5 days of treatment, the animals were perfused and the brains were collected and cut into a cryostat in coronal sections 40 µm containing the LC region and the marking of the cells of the microglia was made by labeling the molecule-adapter-binding 1 (Iba-1) to compare the density and morphology of microglia in the LC. The analysis parameters were the cell density, morphological index that consists of the division of the arborization area by the area in the cell body and the measurement distance for the neighbors (nnd) to verify the proximity of each cell.

Results: In the analyzes it was seen that minocycline treatment decreased the cell density of microglia in the AD model (P = 0.0001). In addition, the treatment did not alter the proximity of the microglia cells in the STZ model (P = 0,0392). Likewise, after treatment with minocycline, arborization of cells in the STZ-AD group increased (P = 0.0001) and the cell body decreased (P = 0,0006) indicating the return of the microglia to its reactive form. The data confirm with the decrease in the morphological index (P = 0.0001), that reflects the inactivation of the microglia cells in the AD model. We did not observe changes in the locomotion (nnd, p = 0,0392) of the microglia cells in the STZ-AD model after treatment.

Conclusions and Support: In summary, all our data show that treatment with minocycline was effective in decreasing the activation of microglia. This way, minocycline is a promising drug in the treatment of AD neuroinflammation caused by microglia cell activation.

ID: 3480

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: ANXIOLYTIC LIKE EFFECT OF 7,8-DIHYDROXY-4-METHYLCOUMARIN IS ASSOCIATED WITH IMPROVED FASTING GLUCOSE LEVELS AND HYPOTHALAMIC VEGF GENE EXPRESSION IN MICE

Introduction: The search for strategies to develop resilience against metabolic and neuropsychiatric disorders has motivated the clinical and experimental assessment of early life interventions such as lifestyle-based and use of unconventional pharmacological compounds. Coumarins are polyphenols that constitute a large class of heterocyclic oxygen compounds and demonstrated therapeutic potential in several diseases, including obesity, diabetes and neurological disorders. The 7,8-Dihydroxy-4-methylcoumarin (DHMC) is a coumarin synthetized by relatively simple with possible neuroprotective effect, mainly related to its antioxidant and anti-inflammatory properties.

Objective: To determine the effects of voluntary physical activity and coumarin DHMC, independently or in combination, over mice physiological and behavioral parameters, adult hippocampal and hypothalamic neurogenesis, and neurotrophic factors expression in the hypothalamus.

Methods: Adult male mice C57Bl/6J were submitted to a 29-day treatment with DHMC and allowed free access to a running wheel. Fasting blood glucose data, voluntary physical activity, locomotion and anxious behavior were collected. For analysis of anxious behavior and locomotion, we use the Elevated Plus Maze (EPM). BrdU (5-bromo-2'-deoxyuridine) was used in the first 10 days to evaluate cell proliferation and neurogenesis. After euthanasia and extraction of the brain, hypothalamus was subjected to molecular analyzes of cell proliferation and neurotrophic markers. Statistical analyses were carried out using unpaired two-tailed Student's t-test, two-way analysis of variance (ANOVA) or ANOVA with repeated measures when appropriate. Data was presented as means ± standard error of the mean (SEM) and p value < 0.05 was considered statistically significant. Approved and carried out in accordance with the Ethics Committee of the Federal University of Lavras/Brazil and Animal Experiments Control Council (CONCEA), according to protocol nº 078/17.

Results: The DHMC treatment reduced fasting blood glucose levels [F (1, 28) = 4,515 p=0,0426] independently of voluntary physical activity. Moreover, physical activity showed anxiolytic effect in the elevated plus maze task [F (1, 16) = 22,76 p=0,0002] and DHMC produced additional anxiolytic behavior, evidenced by reduced activity during the light cycle in the physical activity group [F (1, 286) = 9,71 p=0,0020], without changing the same parameters in the dark period. Although we did not find any differences in hypothalamic or hippocampal adult neurogenesis, DHMC increased gene expression of VEGF [t=3,094, df=6; p=0,0213], which was correlated to the reduced fasting glucose levels [F= 6,802; DFn, DFd= 1,14; R= 0.32; p= 0,0207].

Conclusions and Support: In conclusion, our data emphasize the potential of physical activity in reduce development of neuropsychiatric conditions, such as anxiety, and highlights DHMC as an attractive compound to be investigated in future studies addressing neuropsychiatric disorders associated to metabolic conditions. Support: São Paulo Research Foundation; CAPES; FAPESP; CNPq; UFLA and UNICAMP.

ID: 3736

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR OUTCOMES RELATED TO EXCESSIVE ALCOHOL USE BY VULNERABLE HOMELESS POPULATION IN DOWNTOWN SÃO PAULO

Introduction: Introduction: Cardiovascular diseases (CVD) emerge first among the causes of death in Brazil, representing 30% of the cases reported in the country in 2019. The WHO in the recent survey conducted in 2015 about 17.7 million people died representing 31% of the global population. In the case of people in a situation of street vulnerability, a greater problem in this context of risk factors (RF) for cardiovascular diseases is observed. Among them, excessive alcohol use is an important RF for cardiovascular involvement in adding the curve for coronary heart disease, heart failure, transient ischemic attack, and peripheral arterial disease including cardiac arrest.

Objective: To relate alcohol consumption and its cardiovascular effects in the vulnerable homeless population in downtown São Paulo

Methods: We used the quantitative method, being an exploratory and cross-sectional field research, approved by the Institutional Ethics Committee under protocol 036417,CAAE:21519413.40000.5511. Conducted in downtown São Paulo, the survey included 200 volunteers in vulnerable homeless situations between November 2019 and March 2020, between 18 and 60 years old, submitted to a questionnaire previously selected for convenience. We applied an instrument with socio-demographic characterization, indexing THE, for cardiovascular diseases, with measurement of blood pressure and heart rate and anthropometric data.

Results: After data analysis and statistical treatment, we observed that the population studied has gender characteristics: 64% male, 7% female 3% Transsexuals from 100% of the interviewees 74% reported using alcoholic beverages, those who claim not to use alcoholic beverages stands out 18% of the population studied, 84% of the interviewees in general did not know how to characterize alcohol consumption as

an RF. Against hand to another identified result regarding the use of health services, as a form of self-care and control, we observed as a response, a low demand for them associated with broad disinformation

Conclusions and Support: : We conclude that alcohol use is related to frequent lifestyle and substitute for other fluids such as water, and for psychoemotional and active purposes, of the population studied. It is possible to observe that it contains several reasons for alcohol consumption, misinformation observed in the population, the lack of demand for health units for treatment is a great challenge for the SUS, educating and raising awareness of the population and the health team about the harms of alcohol abuse. Nursing plays a fundamental role in promoting lifestyle changes based on public health practices, interventional proposals and reducing the incidence of alcoholism, in order to improve quality of life. Keywords: Heart disease; Risk Factors; Alcoholism; Cardiovascular diseases, Nursing interventions.

ID: 3481

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: RELATIONSHIP BETWEEN RATE OF PERCEIVED EXERTION, STRENGTH PRODUCTION, AND CHANGE OF DIRECTION PERFORMANCE IN FUTSAL

Introduction: Strength level, power and speed are determinants of futsal performance. It is unclear how these performance markers relate with internal training loads estimated by rate of perceived exertion (RPE). It is difficult to establish an objective criteria based on RPE to classify athletes considering the neuromuscular performance, but wins and defeats in team sports significantly depend on physiological aspects such as strength production, power and agility. The relationship of RPE with performance requiring speed and agility remains unclear. In futsal, change of direction (COD) involves speed and agility and is considered a fundamental ability for a successful performance. COD requires ability to decelerate, reverse or change movement direction, and accelerate again, requiring flexor and extensor strength both in the moment of acceleration and deceleration. Therefore, neuromuscular capacity to produce strength is a mandatory demand for futsal athletes, but little is know about its relationship with internal training load and consequences in functional tasks.

Objective: Here we set out to verify the relationship of internal load estimated by RPE with the strength capacity, and the performance in speed tasks involving linear and change of direction movements in futsal athletes. We hypothesize that high levels of internal load can impair to the ability to produce strength and this relationship negatively affect performance in change of direction and linear acceleration.

Methods: We evaluated athletes from a professional male futsal team (n = 14, mean age 24 years) to determine the relationship of internal loads with strength capacity and performance in linear acceleration and change of direction tasks. We quantified weekly internal load (RPE Borg scale), knee extensor and flexor strength (isokinetic concentric and eccentric torques), knee strength balance (hamstring to quadriceps ratio, H:Q ratio) linear speed (20-m run), power (timed 6-m single hop test), and change of direction speed (COD zigzag speed test). The significance level adopted was 0.05 for all procedures.

Results: Internal load was inversely related with COD speed ($r = -0.59$, $p = 0.02$), concentric (right: $r = -0.54$, $p = 0.02$; left: $r = -0.56$, $p = 0.04$) and eccentric knee flexor strength (right: $r = -0.62$, $p = 0.02$). COD deficit was directly related to internal load ($r = 0.54$, $p = 0.04$), inversely correlated with concentric (right: $\rho = -0.602$, $p = 0.02$), and directly correlated with eccentric H:Q ratio (right: $r = 0.58$, $p = 0.03$).

Conclusions and Support: The inverse relationship of internal load with strength and speed capacity suggests that knee flexor weakness influences internal loads. Muscle weakness and imbalances may also explain the relationship between COD deficits and internal load. A more precise quantification of internal loads should consider the speed performance and knee flexor strength. Training load in high-performance futsal athletes is related to the ability to produce strength in the lower limbs and higher training loads combined with muscle weakness affects negatively the ability to change direction in the presence of high training loads. We recommend coaches to consider strength tests especially for the knee flexors and monitor the H:Q ratio as a complementary tool for monitoring training loads and its effects on performance.

ID: 3737

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: CARDIOVASCULAR COMPLICATIONS IN A HOMELESS POPULATION FACING THE DIFFICULTY IN MAINTAINING EFFECTIVE SLEEP

Introduction: Cardiovascular health needs the interaction of all systems to keep it effective. Sleep is one of those factors essencial in life, it is characterized as a set of behavioral and physiological changes. Reversible to stimuli, it permeates between phases such as non-REM and REM1 sleep. According to the Brazilian Society of Cardiology (SBC), a deficient sleep rotine can affect changes in the Autonomic Nervous System (ANS), causing problems for cardiovascular diseases (CVDs). Restless night sleep can cause cardiorespiratory fluctuations, loss of temperature control, sensitivity to $CO_2$, changes in blood pressure (BP) and respiratory rate (RF), decreased peripheral vascular resistance,

alveolar ventilation and reduced airway muscle tone higher. Such hemodynamic changes are associated with mortality during the early morning hours, especially in patients with cardiopulmonary diseases. In 2017, in Brazil, 383,961 deaths were recorded on average, due to the complications of CVDs. A deficient sleep rotine can impair daily activities, affecting mental and emotional skills, causing anxiety, mood swings, difficulty in making decisions, compromising the ability of the power of choice. In homeless people, such symptoms are aggravated due to lifestyle and lack of basic human conditions.

Objective: To relate sleep interferences with CVDs in the homeless people of downtown São Paulo.

Methods: Exploratory, transversal and quantitative field research, carried out in the Central Region of São Paulo between November 2019 to March 2020. A previously structured questionnaire was applied, approved by the institutional Ethics Committee, protocol: 036417, CAAE: 21519413.4.0000.5511, a 173 volunteers selected by convenience, respecting the age group 18-60 years, collected information related to cardiovascular health, such as cervical and abdominal circumferences, measurement of SBP and heart rate (HR), in addition to questions about sleep quality and socio-demographic data.

Results: When asked about the sleep period, 81% reported sleeping better at night, and 19% during the day. As for the rest time, 8% reported that they sleep less than 2 hours a day, of these the BP measurement, was 142x91 mmHg, 90bpm on average, 35% between 2 to 5 h, 137x91mmHg, HR of 86 bpm; 42% between 5 to 8 h, 133x86 mmHg, HR of 85 bpm on average; 15% more than 8 h 130x84 mmHg, HR 92 bpm. This population showed an average blood pressure of 134x87mmHg, HR 87 bpm, high blood pressure levels compared to that recommended by the 7th Brazilian Hypertension Directive.

Conclusions and Support: It was evidenced that among the population that reported fragmented sleep in daily portions of 2 hours, they may have difficulties in entering the REM phase. It is also concluded that violence, stress and lack of comfort are issues that hinder the initiation and maintenance of peaceful and restful sleep for this population. Other issues such as lifestyle, homelessness, irregular schedules, use of drugs, inadequate nutrition, absence of social interaction surrounded by negative emotions affect the well-being of this population, significantly relates to the quality of sleep, which can cause depression, reduced response to the immune system, eating disorders, among others, showing risk for CVDs.

ID: 3482

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF ROSE OXIDE ON THE CARDIOVASCULAR AND AUTONOMIC SYSTEM OF WISTAR AND SPONTANEOUSLY HYPERTENSIVE RATS (SHR).

Introduction: Arterial hypertension (AH) in the spontaneously hypertensive rat (SHR) model or humans is a multifactorial condition that includes in its etiology an abnormality in the autonomic modulation of arterial blood pressure characterized by an increase in the sympathetic activity and a reduction in the vagal tone. Besides that, the number of reports which demonstrate the role of inflammation in the development and maintenance of hypertension is increasing. The monoterpene rose oxide (RO) was recently documented as a natural compound with anti-inflammatory activity, and even though inflammation contributes to the pathogenesis of AH, there are no reports on the effect of this substance on the disease.

Objective: This study is aimed at evaluating the acute effects of RO on systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and heart rate (HR) of Wistar rats and SHR, as well as investigating whether RO acts upon activation of the autonomic nervous system (ANS).

Methods: The research was approved by CEUA/UFPI (registration No. 563/2019). Wistar and SHR animals at the age of 12 weeks were anesthetized (ketamine - 80mg / kg and xylazine - 20mg / kg) and underwent cannulation of the femoral artery and vein for recording pulsatile arterial pressure and for intravenous drug administration, respectively. The experimental protocol was performed 24 hours after cannulation. After 60 minutes of acclimatization, the Wistar and SHR animals received Saline (0.3 ml; i.v) or RO (1.25; 2.5 or 5.0 mg/kg; i.v) and had their hemodynamic parameters monitored for another 60 minutes. Next, to investigate the participation of ANS receptors in the mechanism of action of RO, SHR animals received the autonomic blockers atropine (2 mg/kg) or propranolol (4 mg/kg) 15 minutes before OR administration (2.5 mg/kg). Alternatively, a control group of SHR received only the autonomic blockers and no RO doses.

Results: The results indicate that none of the RO doses were able to alter SBP ($\Delta$ = -3 ± 3 vs -3 ± 1, mmHg), DBP ($\Delta$ = 0 ± 2 vs 0 ± 2, mmHg), MAP ($\Delta$ = -1 ± 3 vs -2 ± 2, mmHg) and HR ($\Delta$ = -1 ± 16 vs -2 ± 2, bpm) in Wistar rats when compared to Wistar saline group. On the other hand, in SHR animals the three doses tested promoted a significant reduction in SBP ($\Delta$ = -31 ± 3 vs -1 ± 2), DBP ($\Delta$ = -22 ± 3 vs 2 ± 2), MAP ($\Delta$ = -25 ± 3 vs 1 ± 3) and HR ($\Delta$ = -41 ± 8 vs 0 ± 5) when compared to SHR saline group. Pretreatment with atropine did not affect the reductions promoted by RO in MAP ($\Delta$ = -25 ± 2 vs -7 ± 3, mmHg), but was able to attenuate the bradycardic effect ($\Delta$ = 15 ± 11 vs 6 ± 12, mmHg) when compared to atropine group. Pretreatment with propranolol was also not able to attenuate in MAP ($\Delta$ = -29 ± 6 vs -8 ± 4) and bradycardia ($\Delta$ = -29 ± 13 vs -52 ± 15) induced by RO when compared to propranolol group.

Conclusions and Support: Thus, we can infer that RO showed antihypertensive activity only in SHR animals, and this effect does not involve muscarinic and beta-adrenergic autonomic receptors. On the other hand, the bradycardic response induced by RO in SHR animals seems to be dependent on the activation of muscarinic receptors. Support: Universal/CNPq-409109/2018-5; Capes.

ID: 3484

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF PHOTOBIOMODULATION THERAPY ON INSULIN-RESISTANT C2C12 MYOTUBES

Introduction: The global obesity epidemic is a growing problem and several diseases are associated with it, such as type 2 diabetes mellitus (DM2). DM2 is characterized by insulin resistance (IR) in tissues sensitive to the action of this hormone, such as adipose tissue and skeletal muscle. Although effective, traditional strategies for treating IR and preventing or mitigating DM2, such as physical exercises, medications and diets, have low adherence by the population and, therefore, new interventions should be investigated. In this sense, our group was a pioneer in evaluating the effects of photobiomodulation therapy (PBMT) on the intracellular signaling pathway of insulin related to glucose metabolism. In a previous study, we showed that PBMT with infrared laser improved glucose tolerance and signaling of the insulin pathway in epididymal adipose tissue. In a recent publication we showed that PBMT with red light-emitting diode (LED) caused similar effects to infrared laser on adipose tissue, in addition to improving the phosphorylation of protein kinase B (PKB / Akt) serine 473 (ser473) and reversing the changes caused by the high fat diet (HFD) in β-oxidation proteins and mitochondrial dynamics in skeletal muscle tissue (quadriceps) and also to reverse RI and improve glucose tolerance systemically in mice with HFD-induced obesity.

Objective: Despite the results already observed, it is still necessary to better understand what are the effects exerted by PBMT on skeletal muscle cells, which doses and wavelengths are more efficient in treating IR and what are the adjacent mechanisms.

Methods: Mouse myoblasts (C2C12), after differentiation, were cultured in high glucose medium only, control (CTRL), or containing palmitic acid, sodium oleate and L-carnitine to induce IR. Then they received Sham treatment (off) or PBMT (LED, 630 nm, 28 mW/cm2, 4.23 J/cm2), applied once, for 150 seconds per well. Results: PBMT did not interfere in cell viability and promoted an increase in Akt (ser473) phosphorylation in insulin-resistant myotubes.

Results: PBMT did not interfere in cell viability and promoted an increase trend in Akt (ser473) phosphorylation in insulin-resistant myotubes.

Conclusions and Support: It is concluded that the PBMT protocol used is safe for myotubes, does not impair viability, and has the potential to treat IR in skeletal muscle cells. As a perspective, we intend to investigate the effects of the combination of red and infrared wavelengths, in different doses (2, 4 or 8 J/cm²), on the IR in C2C12 myotubes and adjacent mechanisms, such as redox imbalance, mitochondrial dysfunction and inflammation. Support: CAPES (PROAP and PNPD-2455/2011), CNPq (447007 / 2014-9 and 407975 / 2018-7), FAPEMIG (APQ-01915-13 and APQ-03058-16 - Gabriela Silva receives scholarship from FAPEMIG).

ID: 3741

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: DISTINTIC NEURONAL EXCITABILITY IN THE PARAVENTRICULAR NUCLEUS OF HYPOTHALAMUS AFTER BAROREFLEX CHALLENGE IN SALT-LOADED RATS

Introduction: High salt intake is a determinant factor for hypertension in humans and animals' models. Many studies indicate that the paraventricular hypothalamus (PVH) contributes to the regulation of body fluids homeostasis and neural control of circulation in salt-induced hypertension, with the involvement of the baroreflex function, as part of a hypothalamic-brainstem circuitry.

Objective: Here, our aim was to evaluate the neuronal activity of PVH in the modulation of the baroreflex response and autonomic balance in animals subjected to high salt intake.

Methods: Ethical protocols were approved by the Institutional Animal Care and Use Committee (n.127/2017) of the ICB/USP. Male Wistar rats (300-400 g) received a solution of NaCl 2% in replacement of the tap water (SALT; N=6) for 7 days, while the control (CT, N=6, each protocol) received only tap water. On the sixth day, rats had femoral artery catheterized for monitoring of the MAP and HR, and the femoral vein to infusion of drugs. The next day, baroreflex function was evaluated by bolus injections [phenylephrine (PHE; 0.1-12,8 µg/Kg) and sodium nitroprusside (0.2-25.6 µg/Kg)]. Sigmoidal logistic equation was used to analysis baroreflex function. The cardiac autonomic balance was evaluated with injection of muscarinic receptor antagonist (ATROP; methylatropine bromide; 2 mg/Kg) and 15 min later with beta-1-adrenergic receptor antagonist atenolol (ATN; 4 mg/Kg). The neuronal activity in the PVH was evaluated by the FOS expression during baroreflex function challenge [a ramp infusion PHE (18-22 µg/Kg/min)]. After 90 min the animals were euthanized, and brain tissue fixed and immunoperoxidase procedures, and subsequent cells counting analysis. Data were expressed as mean±SEM, analyzed by Student's t-test or ANOVA two way (*P<0.05).

Results: Salt-loading elicited an increase in the MAP (SALT: 115±3 vs. CT: 109±3* mmHg) and HR (SALT: 406±10 vs. CT: 318±9* b/min) followed by an attenuation on the range of the baroreflex function (SALT: 169±14 vs. CT: 233±22* b/min/mmHg). As for the autonomic balance salt-loaded rats have shown an increase in the TS (SALT: 104±11 vs. CT: 59±7* Δb/min), but no change in the PT (SALT: -68±13 vs. CT: 59±10 Δb/min). The activation of the arterial baroreflex resulted in an increase in the number FOS neurons in the PVH in SALT

group (SALT-PHE: 1,012±96 vs. SALT-NOT-PHE: 141±66* vs. CT-PHE: 345±57* vs. CT-NOT-PHE: 53±1* unity; *P<0,05 vs. SALT-PHE), but no change within CT-PHE vs. CT-NOT-PHE either SALT-NOT-PHE. The large number of FOS-positive neurons in the SALT group occurred in medial level of the PVH, specifically in the neuron clusters of the lateral magnocellular (90%), dorsal cap (83%), medial parvicellular (71%) and ventral part (66%) when compared to other groups.

Conclusions and Support: Taken together, these results show that 7 days of high salt intake elicits hypertension, impairment of baroreflex function and increase in the sympathetic tone to the heart with activation of distinct neuronal populations in the PVN. The precise neuronal mechanisms involved in these responses are still under investigation. Grants: CAPES (001), FAPESP (2016/21991-3, 2019/19894-8) and CNPq (141749/2019-9).

ID: 3487

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECT OF TESTOSTERONE UNDECANOATE TREATMENT AND MATE TEA ON THE SALIVA'S BIOCHEMICAL PARAMETERS OF THE ORCHIECTOMIZED WISTAR RATS

Introduction: Several factors affect the oral health of men, such as androgenic hormones. Hypogonadism can cause indisposition, low bone mineral density, reduced muscle strength, favor the onset of periodontal diseases and also induce oxidative stress. Hormone replacement therapy (HRT) appears as option to reestablish hormone levels. Already, the herbal treatment with mate tea (MT, Ilex paraguariensis) is an alternative to reduce oxidative damage. However, few studies have investigated the influence of HRT in association with natural products as a possible treatment to restore normal saliva physiology to oral health

Objective: To evaluate the effects of treatments with testosterone undecanoate (TU) and MT on the salivary biochemical parameters of orchiectomized (ORX) wistar rats

Methods: 60 male wistar rats (3 months old) were either castrated bilaterally or underwent fictitious surgery (SHAM) and were divided into 5 groups: SHAM, ORX, TU (100 mg/kg B.W., via intramuscular, monthly), MT (20 mg/kg B.W., via intragastric gavage, daily) and TU+MT, for 4 weeks, beginning 4 weeks following ORX. Water and food were given ad libitum throughout the experiment. The treatment started 1 month after ORX. The protocol was approved by local institutional animal ethics committee (Process FOA N. 00455-2019). At the end of the treatment, saliva secretion was stimulated by pilocarpine (5 mg/kg BW, intraperitoneal). The salivary flow rate (SFR), salivary buffering capacity (SBC) was determined, in addition to being also analyzed by spectrophotometric methods to determine of total protein content (TP), salivary amylase activity (AMY), oxidative damage to lipids (TBARS) and proteins (PC), total non-enzymatic antioxidant capacity (TAC), content of calcium (Ca) and salivary inorganic phosphate (Pi). Data were expressed as mean ± standard deviation and submitted to ANOVA statistical analysis, followed by the Tukey test. For all tests, the level of rejection of the null hypothesis was set at 5%

Results: The SFR was accentuated in groups ORX and MT over SHAM. The SBC increased in the groups ORX and TU compared to SHAM, whereas the MT group decreased compared to the ORX. T deficiency caused a lower concentration of PT in the ORX and MT groups compared to the SHAM and TU+MT. AMY activity was reduced in the ORX group compared to all others. Regarding the content of TBARS, the ORX group showed a higher concentration in relation to the SHAM, MT and TU + MT, whereas the TU group also presented superior results vs. TU+MT. The PC content was higher in the ORX vs. SHAM, TU and TU+MT, being also high in the MT vs. TU+MT. TAC showed superior results in both ORX and MT groups compared to the SHAM and TU+MT, and the ORX group also showed better results than the TU. The concentration of salivary Ca was reduced in the TU and TU+MT vs. the SHAM and ORX. TU+MT animals also had lower Ca content compared to those treated with MT. Salivary Pi was higher in ORX vs. SHAM, TU and TU+MT, whereas the MT group had its salivary Pi content increasing in relation to the SHAM and TU+MT

Conclusions and Support: The results presented show that T deficiency can negatively impact the biochemical parameters of saliva. However, HRT and MT administered alone obtained partial positive results, while the joint administration of both therapies resulted in better results. The authors thank the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES) for master schorlarship

ID: 3488

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: DEVELOPMENTAL CHANGES OF DORSAL COCHLEAR NUCLEUS FUSIFORM NEURONS

Introduction: The dorsal cochlear nucleus (DCN) in the auditory brainstem integrates auditory and somatosensory information. The fusiform neuron is the principal neuron in the DCN responsible for the integration of somatosensory and auditory information. Mature fusiform neurons express two qualitative intrinsic states in equal proportions, referred to as quiet, with no spontaneous regular action potential firing, or active, with regular spontaneous action potential firing.

Objective: Here we aimed to investigate the development of these intrinsic firing states before and after hearing onset at P12.

Methods: For this, we performed slice whole-cell patch-clamp studies in DCN fusiform neurons from Swiss mice from P4 to P19.

Results: We found that before hearing onset (P4-P11) there are no active fusiform neurons, which gradually appeared after P12. Quiet fusiform neurons from mice ages P4 to P11 and P12 to P17 had similar resting membrane potentials, but neurons from P4-P11 animals presented bigger input resistances ($p<0.01$, $n=28$). They also have bigger membrane sag depolarizations ($p<0.0001$, $n=31$). Voltage-clamp experiments of subthreshold currents showed a bigger membrane slope conductance in quiet neurons from P12-P19 (post-hearing; $p<0.001$) animals, and a bigger tail current which reflects the expression of h current ($p<0.001$). We compared the I-V profile from quiet and active neurons from P12 to P19, and they had similar slope conductances as previously described.

Conclusions and Support: We conclude that before hearing, all neurons are quiet and there are developmental changes after hearing onset in intrinsic subthreshold currents in DCN fusiform neurons. We are current investigating the development of conductances leading to quiet and active states. This work was supported by CNPq (164610/2018-9) and FAPESP (2016/01607-4).

ID: 3491

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: MiR-29a-c Regulate PGC-1α, PEPCK and G6Pase Expression in Liver of Weaning Rats Exposed to Dexamethasone in utero

Introduction: Fetal excess of glucocorticoids is one of the main insults that lead to metabolic impairment in the liver, generated in cases of malnutrition or stress during pregnancy. In the present study, we used an experimental model to induce metabolic reprogramming: maternal treatment with dexamethasone (DEX) during the third period of pregnancy. A master regulator of mitochondrial biogenesis and a primary regulator of liver gluconeogenesis is the peroxisome proliferator-activated receptor gamma coactivator 1 alpha (PGC-1α). PGC-1α plays a pivotal role in the transcription of genes that encodes gluconeogenesis-limiting enzymes, and is modulated by epigenetic mechanisms such as cytosine methylation and miRNAs.

Objective: This study aimed to evaluate whether hepatic changes in PGC-1α expression and epigenetic mechanisms occur to explain the glucose intolerance and persistent upregulation of gluconeogenesis enzymes of weaning rats exposed to dexamethasone (DEX) in utero.

Methods: All experimental procedures were approved by the Committee for Ethics in Animal Experimentation at the Institute of Biomedical Sciences, University of Sao Paulo, Brazil (protocol No. 5367250619). Male Wistar rats born to mothers treated or not treated with dexamethasone during the last week of pregnancy (respectively DEX and CTL) were used in the experiments. After birth, the offspring were euthanized on the first day of lactation (L1), eighth day of lactation (L8) and at weaning (21st day of lactation; L21) for sample collection and analysis.

Results: On the 21st day of life, rats exposed in utero to DEX displayed glucose intolerance (71% higher than CTL; $P = 0.002$) and increased conversion of pyruvate into glucose (53% higher than CTL; $P = 0.02$). In the liver, either Pck1 mRNA expression, PEPCK protein content and PEPCK activity were upregulated (respectively 106%, 21% and 16% higher than CTL; $P = 0.0006$, $P = 0.008$ and $P = 0.02$) along with enhanced G6pc mRNA expression, G6Pase protein content and G6Pase activity (respectively 270%, 32% and 89% higher than CTL; $P = 0.0008$, $P = 0.019$ and $P = 0.001$). Rats born to DEX-treated mothers exhibited increased hepatic PGC-1α protein content at L21 (43% higher than CTL; $P = 0.006$). Conversely, there was a progressive decrease in Ppargc1a mRNA expression throughout early postnatal life, reaching the lowest value at L21 (6.7-fold lower than L1 and 6.1-fold lower than L8; $P<0.0001$ and $P = 0.0019$, respectively) and an increase in the Ppargc1a promoter cytosine methylation at L21 (90% higher than CTL; $P = 0.01$). Such rise in PGC1α protein content, instead, was paralleled by decreased miR-29a-c expression (2.5-fold lower than CTL; $P = 0.01$). Of note, miR-29a-c are validated negative regulators of Ppargc1a gene translation. In addition, rats born to DEX-treated mothers presented impaired lipid metabolism, which was associated with reduced PPARα protein content (37% lower than CTL; $P < 0.0001$), altered expression of putative PPARα target genes and increased lipid density in hepatocytes (65-fold higher than CTL; $P = 0.0003$).

Conclusions and Support: Our data suggest that a reduction in miR-29a-c expression prevail over an increase in promoter methylation, resulting in greater hepatic PGC1α content. Such results reveal a novel mechanism to explain the upregulation of key enzymes of gluconeogenesis and demonstrate the genesis of fat accumulation in hepatocytes of rats subjected to metabolic programming. Financial Support: FAPESP (grants 2013-05/2024 and 2019/03196-0; CNPq; CAPES)

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Área: FISIOLOGIA DO EXERCÍCIO

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Title: EXERCISE TRAINING ON METABOLIC, HEMODYNAMIC AND AUTONOMIC PARAMETERS IN AN EXPERIMENTAL MODEL OF MENOPAUSE AND OBESITY: EFFECTS OF DIFFERENT VOLUMES AND INTENSITIES

Introduction: Exercise training (ET) is an important non-pharmacological approach in the cardiovascular risk factors management. Understanding how the variables of exercise training (such as intensity, and volume) can influence its effects can contribute to greater effectiveness of this approach.

Objective: To compare different volumes and intensities of exercise training on metabolic, hemodynamic and autonomic parameters in an experimental model of menopause and obesity.

Methods: (Approval protocol 037/2019, Ethics Committee for the Use of Animals in Research of São Judas Tadeu University). Thirty-two ovariectomized C57BL/6J high-fat-fed mice were divided into 4 groups (n=8 each group): sedentary (S), moderate-intensity continuous ET (MICT), or high-intensity interval ET with similar volume to the moderate-intensity ET (HIIT-hv), or high-intensity interval exercise training with reduced volume by 50% of moderate-intensity (HIIT-lv). The high-fat diet lasted 9 weeks. Ovariectomy was performed at the end of the 4th week. Fasting glucose and oral glucose tolerance (OGTT) were assessed before ovariectomy and at the end of the study. The exercise training lasted 4 weeks, with intensity 50-60% for the MICT group and 25-90% for the HIIT-hv and HIIT-lv groups. At the end of the study, the animals were cannulated for direct arterial pressure (AP) recording, baroreflex sensitivity and cardiovascular autonomic modulation analysis.

Results: The prescription of high-intensity and high-volume exercise training (HIIT-hv) can benefit glucose metabolism more than MICT and HIIT-lv (Glycemia - S: 146±5; MICT: 143±5; HIIT-hv: 115±7; HIIT-lv: 143±7 mg/dL; AUC in OGTT - S: 21894±645; MICT: 21599±545; HIIT-hv: 18464±792; HIIT-lv: 22658±849 AUC of glycemia). Regarding cardiovascular parameters, the prescription of exercise training at moderate intensity (MICT) and the prescription of high-intensity with low-volume (HIIT-lv) were more effective than HIIT-hv in hemodynamic values (mean AP - S: 118±6; MICT: 95±6; HIIT-hv: 117±1; HIIT-lv: 115±1 mmHg; Heart rate - S: 680±15; MICT: 561±41; HIIT-hv: 557±39; HIIT-lv: 575±23 bpm) and in autonomic values (VAR-PI - S: 17±3; MICT: 28±11; HIIT-hv: 14±3; HIIT-lv: 59±11 ms2; LF/HF - S: 2.1±0.5; MICT: 0.6±0.2; HIIT-hv: 0.8±0.1; HIIT-lv: 1.0±0.1; VAR-SAP - S: 35±7; MICT: 12±2; HIIT-hv: 20±2; HIIT-lv: 16±2 mmHg2; LF-SAP - S: 5.3±1.3; MICT: 1.5±0.8; HIIT-hv: 5.7±0.9; HIIT-lv: 1.6±0.2 mmHg2).

Conclusions and Support: The results showed that the manipulation of variables in the prescription of exercise training can imply greater effects on metabolic or cardiovascular parameters. The animals submitted to moderate-intensity continuous exercise training (MICT) and submitted to high-intensity interval exercise training and low volume (HIIT-lv; 50% of the volume used in MICT) presented greater cardiovascular benefits, such as better autonomic control of heart rate, reduced sympathovagal balance, and reduced sympathetic vascular modulation. While animals trained in high-intensity and high volume showed only benefits in glucose metabolism. These results reinforce the importance of individualized prescription to achieve the specific objectives of each patient. Support: This study was financed in part by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES), CNPq Universal 435123/20181.

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Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: REDUCTION OF SYNAPTOPHYSIN EXPRESSION IN THE PREFRONTAL CORTEX IS ASSOCIATED WITH THE PRESENTATION OF AUTISM-LIKE SYMPTOMS

Introduction: Inflammation during pregnancy in models of maternal immune activation (MIA) has been shown to affect several vulnerable aspects of brain development in the fetus, which contributes to the various manifestations of neuronal and behavioral dysfunctions that can manifest throughout life as an autistic spectrum disorder, schizophrenia, depression, anxiety, among others.

Objective: The aim of this study was to evaluate behavioral changes in the offspring of females submitted to MIA induced with LPS during the 16th day of gestation, in addition to quantify the proteins synaptophysin and oxytocin receptor (OTR).

Methods: Female Wistar rats were treated with saline (control,1 ml/kg i.p.) or LPS (500 μg/kg i.p.) at 16th day of gestation. In order to evaluate sickness behavior, locomotion in the open field was recorded and analyzed 2 hours (hrs) after LPS administration, as well as food intake and weight gain at 24 hrs. In the offspring, ultrasonic vocalizations (USV's) were assessed at postnatal day 13 (PND13); at PND29

animals were submitted to the novel object recognition test (NOR); at PND30 to play behavior test; and finally, at PND34 to the Barnes Maze. Then, prefrontal cortex and hypothalamus were collected for western blot analysis. All experimental procedures followed the Ethical Principles in Animal Research adopted by the Ethics Committee on the Use of Animals of the Federal University of Alfenas (protocol 17/2019).

Results: In the pregnant females, LPS decreased the distance traveled (1526±90.48 to 862±88.52 cm; $p<0.0001$) and increased immobility time in the open field (97.63±6.66 to 173.5±12.94 seg.; $p<0.001$), decreased food intake (26.2±1.69 to 5.515±2.22 gr; $p<0.0001$) and weight gain (11.83±0.98 to -10.29±3.46 gr; $p<0.001$). In the offspring LPS did not alter the number of USV's in the groups nor the performance in the Barnes maze. In the NOR test there were no differences except for the male recognition index in the 2-hour test (0.79±0.039 to 0.65±0.030; $p<0.01$). LPS decreased time of social behaviors in the male offspring (41.03±3.60 to 29.77±2.94seg.; $p<0.05$) and frequency of social behaviors both in male and female offspring (males: 31.80±3.14 to 22.20±2.28; $p<0.05$, and females: 24.0±2.69 to 12.75±1.88; $p<0.05$) compared to the control group. About OTR, in the males of LPS group, was observed greater expression in the prefrontal cortex (88.35±10.1 to 159.7±21.17; $p<0.01$) and in the hypothalamus (60.47±9.6 to 109.8±12.85; $p<0.05$) compared to control group. Synaptophysin, a protein involved in the regulation of synaptic transmission, was decreased in the LPS group males in the prefrontal cortex (99.11±4.81 to 79.25±4.94; $p<0.05$) compared to control group.

Conclusions and Support: The administration of LPS during 16th day of gestation was able to modify the behavior of the offspring, mostly social behavior. Also, male offspring of LPS-treated females showed increased expression of OTR in the prefrontal cortex and hypothalamus, and decreased expression of synaptophysin in the prefrontal cortex. Support: CAPES. FAPEMIG, CNPq.

ID: 3496

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: MEIOTIC AND DEVELOPMENTAL COMPETENCE OF ZEBU CATTLE OOCYTES RECOVERED FROM DISTINCT FOLLICLE SIZES

Introduction: The acquisition of oocyte competence is a gradual process that occurs in parallel with the growth and differentiation of the ovarian follicle and depends on the close relationship between the oocyte and the adjacent follicular somatic cells. As it grows and differentiates, the oocyte acquires both the meiotic competence (ability to resume and complete nuclear maturation) and the developmental competence (ability to undergo successful fertilization and reach the blastocyst stage). It is known that the competence of the oocyte is related to the degree of chromatin compaction enclosed within the nucleus.

Objective: The aim of this study was to evaluate the chromatin configuration and developmental competence of bovine oocytes retrieved from follicles of different diameters.

Methods: Cumulus-oocyte complexes (COC) were obtained from Nellore cattle (B. taurus indicus) ovaries collected at a local abattoir by puncturing follicles measuring 2 to 6 mm (Medium - M group; n=473) and larger than 6 mm in diameter (Large - L group; n=408). Follicles were punctured with the aid of a 10 mL syringe coupled to an 18-G needle, as is traditionally done in the routine of laboratories that use the IVP biotechnology (in vitro production of embryos) for research purposes. Follicles smaller than 2 mm (Small - S group; n=310) were isolated by dissection and oocytes were obtained by rupturing their wall. Next, selected COCs were in vitro-matured (IVM) for 22h in IVM medium (TCM-199 with bicarbonate, 0.5 mg/mL FSH, 100 IU/mL hCG, 10% FCS and hormones) and then fertilized in vitro (IVF). Presumptive zygotes were cultured until day 7 to evaluate the embryonic development to the blastocyst stage. Oocytes were stained with Hoechst 33342 immediately after follicle removal to assess the chromatin remodeling [% germinal vesicle (GV) stage in immature oocytes, graded from GV0 (fully incompetent) to GV3 (fully competent)], and after IVM to assess the meiosis progression (% metaphase II - MII). Data were analyzed by ANOVA, followed by Tukey's test ($P<0.05$).

Results: The mean follicular diameter of S, M and L groups were 1.37±0.26 mm, 3.51±0.04 mm and 9.77±0.14 mm, respectively. Regarding chromatin configuration in immature oocytes, the S group had higher ($P<0.05$) GV0 rates (82.0%±5.5) when comparing to M (9.9%±3.5) and L (12.8±2.8) groups; however, there were no differences ($P>0.05$) between groups in the GV1 (15.1%±2.6 to 30.6±13.5), GV2 (2.9%±2.9 to 56.9%±5.0) and GV3 rates (0.0% to 9.1±9.1). The highest MII rates were reached by L group (87.3%±4.2), which differed ($P<0.05$) from M group (57.9%±4.0). No oocyte from S group reached MII, differing ($P<0.05$) from the others groups. Blastocyst yelds were similar ($P>0.05$) for M (34.7%±4.8) and L groups (46.7%±5,7), and no blastocyst was developed in S group.

Conclusions and Support: The results demonstrate that zebu cattle oocytes retrieved from small follicles (smaller than 2 mm in diameter) have no meiotic or developmental competence, probably because of the higher GV0 rates found in such oocytes. In conclusion, the follicle diameter is direct related to the oocyte meiotic and developmental competence. Financial support: CNPq (#307416/2015-1), PIBIC, FAPESP (#2015/06733-5 and #2019/11174-6).

ID: 3497

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: PROTEIN RESTRICTION DURING ADOLESCENCE AND THE IMPLICATION OF AUTONOMIC NERVOUS SYSTEM IN ADULT RATS HYPERTENSION

Introduction: Exposure to low protein diet in perinatal life induces hypertension related to cardiovascular autonomic dysfunction in adulthood. However, it is not known if this insult during adolescence affect the cardiovascular system.

Objective: This study aims to evaluate whether low protein diet during adolescence induces hypertension related to autonomic dysfunction in adult male rats.

Methods: The research ethics committee approved the study under CEUA nº 4833210519. Thirty-day-old Wistar rats were fed a low protein diet (4% protein as casein) for 30 days and subsequently fed a 20.5% normal protein diet for a 60-day recovery period (LP). Control animals (NP) were fed a 20.5% protein diet throughout life. At 120 days of age, direct measurements of arterial pressure were recorded from conscious animals. Statistically significant differences were evaluated by T-Student test.

Results: LP rats were hypophagic (-13%; p<0,021) until 60 days. LP animals has smaller body weight (-10%; p<0,0003) and body length (-4%; p<0,015), hyperphagia (+21%; p<0,001), hyperglycemia (+13%; p<0,0081) but the lipid profile and visceral fat deposits were similar to NP. Systolic (SBP), diastolic arterial pressure and mean arterial pressures (MBP) were increased in LP (+19%, 23% and 20%, respectively; p <0.0003, p <0.005 and p < 0.002) but heart rate was unchanged. In the spectral analysis, the LP rats showed a greater amplitude in the low frequency zone (LF) of MBP (+41%; p<0,035). In the pulse interval, the LP group showed an increase in LF, LF/HF ratio and total variability (+73%, 45% and 37%, respectively; p<0,014, p<0,048 and p<0,011) but the high frequency zone (HF) was similar to NP. After intravenous injections of atenolol (4mg/kg) and methylatropine (3mg/kg), the bradycardia and tachycardia responses and the intrinsic heart rate were similar to NP. The MBP response to phenylephrine (8 µg/kg, iv) was increased in LP (+26%; p<0,049) but the baroreflex sensitivity (ΔHR/ΔMAP) in response to phenylephrine (8 µg/kg, iv) and sodium nitroprusside (50 µg/kg, iv) was similar between groups. The LF-MBP decrease and depressor response to the ganglionic blocker, hexamethonium (30 mg/kg, iv), was greater in the LP group (57% and 36%; p<0,032 and p <0.006, respectively).

Conclusions and Support: Low protein diet during adolescence leads to hypertension later in life, sustained by a greater sympathetic activity. CNPQ and Capes

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Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: IN VITRO EVALUATION OF THE EFFECTS OF DIFFERENT POLYSACARIDE CONCENTRATIONS FROM Euterpe oleracea Mart. (AÇAÍ), ABOUT THE VIABILITY OF THE MURINO B16F10 MELANOMA LINE

Introduction: Melanoma is considered the most serious type of skin cancer, presenting the highest incidence among malignant tumors recorded in Brazil. Giving the high cost of treating the disease, the development of new drugs based on abundant matrices of lower cost and with low side effects, has been considered of great importance. Brazil has a high biodiversity of plants with natural compounds presenting biotechnological potential for the pharmaceutical industry. Studies show that polysaccharides from natural sources, such as fruits, can play an important role in the prevention and treatment of diseases such as cancers.

Objective: Therefore, this research aimed to evaluate in vitro the effects of different concentrations of a mixture of polysaccharides obtained from the peel and pulp of Euterpe oleracea Mart. (AÇAÍ), on the viability of B16F10 murine melanoma cells.

Methods: The evaluation of polysaccharides cytotoxicity was performed in a model with normal murine fibroblast 3T3 cells. The cells lines (tumoral and normal) were grown in RPMI culture medium, supplemented with 10% SFB and antibiotics, and then incubated for 24h at 5% CO2, under controlled temperature and humidity. After incubation, the cells were treated with different concentrations (0, 5 and 10 µg/ml) of the polysaccharide mixture. Seventy-two hours after treatment, the cells were submitted to the analysis of Neutral Red (NR) and Diphenyltetrazolium Bromide Reduction (MTT). The results data were compared through one-way ANOVA and the Tukey test (P<0.05).

Results: In both MTT and NR analysis, B16F10 melanoma cells treated with the concentrations of 5 and 10 µg/ml of the E. oleracea polysaccharides presented significantly reduced cell viability in comparison to the control group (0 µg/ml). No significant difference was observed between the concentrations of 5 and 10 µg/ml in neither tests. Regarding the toxicity analysis of the polysaccharide on normal 3T3 cells, it was verified that groups treated with 5 µg/ml of the polysaccharides presented a significant reduction in viability compared to the control group in the MTT assay, with no statistical difference being observed between the concentrations os 5 and 10 µg / ml. The NR assay did not point significant differences in the viability of 3T3 cells among the tested concentrations.

Conclusions and Support: Thus, we can evaluate that the use of polysaccharides from the peel and pulp of E. oleracea, is a potential tool in the treatment of tumors, since its use in the concentrations used in this study, results in reducing the viability of tumor cells, with low toxicity for normal cells. Support: Fundação Aracária, CAPES.

ID: 3502

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: MELANOPSIN EXPRESSION IN THE RETINAS OF OWLS WITH DIFFERENT DAILY ACTIVITY PATTERNS

Introduction: Melanopsins are photopigments responsible for several physiological responses to light, such as pupillary light reflex, melatonin suppression, and regulation of circadian rhythms. The group of birds, with its astonishing diversity, represents a remarkable system to investigate the evolution and characteristics of the sensory systems. In this study, we took advantage of the daily activity variability patterns in different owls to investigate melanopsin gene expression, in diurnal, nocturnal, and crepuscular species.

Objective: To characterize the melanopsin encoding genes and compare their expression patterns in retinas of owls with nocturnal (Megascops choliba, Asio clamator, Tyto furcata), diurnal (Glaucidium brasilianum), and cathemeral (Athene cunicularia) habits.

Methods: Owls were euthanized with an intraperitoneal injection of Zoletil (non-lethal doses) at 12 p.m., followed by decapitation (Psychology Institute Animal Ethics Committee 5691140818). Eyes were enucleated and preserved in RNAlater for genetic analysis or fixed in 4% paraformaldehyde for morphology. RNA was extracted and purified using Trizol method from homogenized retinas and transcribed to cDNA. PCRs and Sanger sequencing were performed to amplify the melanopsin transcripts, Opn4x and Opn4m. Sequences were analyzed with BioEdit v7.2.5, and phylogenetic reconstruction was performed by Maximum Likelihood, with GARLI v.0.96. Statistical support was obtained by non-parametric bootstrap. Quantitative PCR (qPCR) was used to detect the level of expression of both melanopsin genes. Data were compared by one-way analysis of variance (ANOVA) followed by Tukey test. For morphological analysis, eyecups were cryosectioned and slices were incubated with antibodies against mouse OPN4m and chicken OPN4x.

Results: Partial sequences of Opn4x and Opn4m expressed in retinas of A. clamator, M. choliba, and G. brasilianum were amplified, with size ranging from 426 to 940 bp. For both paralogs, phylogenetic reconstruction recovered the monophyly of Strigidae subfamilies: Striginae (A. clamator and M. choliba), and Selvagemiinae (A. cunicularia and G. brasilianum). Expression levels of Opn4x were higher in the diurnal G. brasilianum compared to the cathemeral A. cunicularia and nocturnal A. clamator and M. choliba ($p<0.01$). Conversely, the Opn4m expression of the nocturnal A. clamator was higher compared to other species. Additionally, Opn4m expression levels of nocturnal M. choliba were different from A. cunicularia ($p<0.02$), but not when compared to G. brasilianum. Morphological analysis showed that both melanopsins are expressed in the photoreceptor layer, the ganglion cell layer, and in the optic nerve of A. cunicularia, G. brasilianum, and T. furcata. However, only OPN4x was found in the inner nuclear layer of A. cunicularia and T. furcata.

Conclusions and Support: Our results revealed that Opn4x and Opn4m are expressed in the retinas of owls. Phylogenetic reconstruction indicated that both paralogs are conserved and evolved accordingly to the species phylogeny. Morphological analysis indicates that both melanopsins, OPN4m and OPN4x, are co-expressed in different retinal layers, and might be co-expressed with other visual opsins in the photoreceptor layer. Levels of melanopsin expression varied between diurnal, cathemeral, and nocturnal owls, indicating that differential melanopsin expression may be associated with activity patterns. Support: FAPESP, CNPq and CAPES.

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Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF REGULAR SWIMMING PHYSICAL EXERCISE ON THE EXPRESSION OF MYELIN-ASSOCIATED GENES IN HIPPOCAMPUS OF WISTAR RATS TREATED WITH CUPRIZONE

Introduction: Some patients with multiple sclerosis (MS) present extensive demyelination in hippocampus which has been associated with cognitive impairment. Although physical exercise is a promising intervention that may lessen cognitive symptoms in MS patients, its underlying mechanisms are still not clear. Feeding experimental animals with cuprizone (CPZ) has been used as highly reproducible model that produces very consistent demyelinating lesions in several central nervous system areas allowing the investigation of the associated mechanisms.

Objective: The aim of the present study was to investigate of the effects of swimming exercise on hippocampus myelin-associated genes as well as on spatial recognition task in female Wistar rats treated with CPZ by oral gavage.

Methods: After the ethics approval by the Animal Use Ethics Committee of University Center of the Hermínio Ometto Foundation-FHO (051/2019), 57 Wistar female rats were randomly divided into four groups: untrained animals that received vehicle (n = 15); swimming trained animals that received vehicle (n = 13); untrained animals that received CPZ (n = 15) and; swimming trained animals that received CPZ (n = 14). The animals in the exercised groups performed a moderate-intensity regular swimming exercise for eight weeks. For purposes of determining the physical fitness of the animals, a swimming workload test was performed at the beginning and at the end of swimming training. Besides, liver was collected and analyzed by glycogen content. At the end of the fifth week of oral gavage, the animals from the four groups were investigated by the spatial recognition task. At the end of the sixth week of oral gavage, the animals from the four groups were sacrificed and the hippocampus were collected for gene expression analysis by TaqMan real-time reverse transcription (RT)-PCR assays. Investigated genes were of myelin proteins (MBP, PLP and MOG), neurotrophic factors (GDNF and VEGF) and inflammatory factors (TNF and IL6).

Results: The higher physical fitness of the exercised animals was observed by the higher values swimming workload test ($P<0.05$) and liver glycogen content ($P<0.05$) of the swimming trained animals that received vehicle in comparison to the other groups. Therefore, CPZ treatment impaired the trained animals' physical fitness. A similar result was observed for the spatial recognition task in which swimming exercised animals performed better results than the other groups. CPZ treated animals showed reduced genetic transcripts of MBP and PLP compared the respective vehicle groups ($P<0.05$) and the swimming exercise was not able to reverse this change. However, the gene transcription of MOG was only reduced for untrained animals that received CPZ compared to the untrained animals that received vehicle ($P<0.05$), suggesting a slight attenuation by swimming exercise on the demyelination profile.

Conclusions and Support: The demyelinating protocol used in this study caused molecular changes, reducing the parameters of gene transcription of myelin proteins in the hippocampus. The neuroprotective effects of physical exercise on the myelin gene transcripts only slightly observed. Support. Graduate Program of Biomedical Sciences, University Center of the Hermínio Ometto Foundation-FHO. São Paulo Research Foundation (FAPESP).

ID: 3504

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: LOWER LEVELS OF HEPATIC MIR-122 CORRELATE WITH INCREASED VLDL SECRETION RATES IN DIET-INDUCED NAFLD MICE

Introduction: miRs are small molecules of non-coding RNAs that are capable of silencing a target mRNA. miR-122 is known for its role in hepatic lipid metabolism, in addition to be the most abundant and exclusively miR in the liver, representing approximately 70% of total miRs in this tissue. This miR seems to be downregulated in the liver and upregulated in the circulation, maybe because a migration from the liver to the blood to cell communication, in models of obesity and non-alcoholic fatty liver disease (NAFLD). NAFLD pathogenesis is characterized by altered liver metabolism that leads to increased triglycerides (TG) input within this organ by diet excess nutrients (mostly fat), accumulation of fatty acids originated from the adipose tissue lipolysis and increased TG synthesis in this organ. The output of hepatic TG is dependent of Very Low-Density Lipoprotein (VLDL), which is produced by the liver to transport mostly TG through the blood to extrahepatic tissues, but some articles show a divergence about its secretion rate in NAFLD development.

Objective: To evaluate the levels of miR-122 in liver and their association with TG output in mice with obesity induced by high-fat diet.

Methods: Swiss male mice were maintained on a normal chow diet or 45% high-fat diet for 8 weeks. For VLDL rate secretion, animals were treated with tyloxapol, which blocks plasma lipolytic activity, and therefore the breakdown of triglyceride-rich lipoproteins. TG content was also analyzed after euthanasia and miR expression was determined by qPCR. Experiments were approved by Ethics Committee on the Use of Animals of the State University of Campinas (CEUA / UNICAMP) with protocol number 4349-1 / 2016.

Results: Mice fed a HFD had increased body weight, greater weight gain, adiposity and glycemia compared to mice fed a control diet, which were expected to induce obesity and NAFLD. Hepatic TG content was elevated in obese mice. The levels of miR-122 were reduced in liver of obese mice and VLDL rate secretion were higher in this group. These two variables had a strong and significant negative correlation.

Conclusions and Support: High-fat diet was able to cause changes in the liver including downregulation of miR-122, which was associated with higher levels of TG secretion to circulation, through VLDL and possibly miR-122 could be exported by this lipoprotein to the circulation to reach target tissues. This study was financed by CAPES and FAPESP.

ID: 3507

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: DOSE-RESPONSE EFFECTS OF HYPOXIA ON HEMODYNAMIC AND AUTONOMIC CONTROL IN HEALTHY HUMANS

Introduction: Hypoxia has captured the attention of many physiologists around the world due to its relevance in the environmental physiology and for the understanding of several diseases. Classically, acute hypoxia increases heart rate (HR) by autonomic changes leading sympathetic predominance. However, the influence of inspired oxygen fraction (FiO2) and blood oxygen saturation (SpO2) on autonomic and hemodynamic responses are unknown.

Objective: To evaluate hemodynamic and autonomic responses during stepwise hypoxia.

Methods: Before participating, the volunteer's written consent term (CEP:1.252.971/2015). Eleven participants (26 ± 4 yrs; 72 ± 10 kg; 1.71 ± 0.08 m) breathing spontaneously were exposed to stepwise hypoxia (FiO2: 21; 17.5; 14.5; 11.5; 10.0%) lasting 10 min each stage. Cardiac output (CO), stroke volume (SV), R–R intervals, blood pressure (BP), total vascular resistance (TPVR) and SpO2 were continuously recorded. Spectral analysis of the R–R intervals and systolic BP oscillations, and all other variables were analyzed in a timeframe of 300 heartbeats to each hypoxic dose. Baroreflex sensitivity was estimated by α–LF index. Pearson's correlation was applied to autonomic markers and SpO2 changes. One-way ANOVA for repeated measures was carried out to compare all stages.

Results: SpO2 was lower under all hypoxic stages [SpO2(17.5%): 93 ± 2; SpO2(14.5%): 90 ± 2; SpO2(11.5%): 80 ± 5; SpO2(10.0%): 75 ± 7] than normoxia [SpO2(21%): 96 ± 1 %; $p<0.05$]. HR was higher in all hypoxic levels [HR(17.5%): 75 ± 7; HR(14.5%): 77 ± 7; HR(11.5%): 83 ± 9; HR(10.0%): 86 ± 11] than normoxia [HR(21%): 74 ± 7 bpm; $p<0.05$]. CO was increased by hypoxia only in higher hypoxic levels [CO(11.5%): 6.18 ± 1.38; CO(10.0%): 6.28 ± 1.39] than normoxia [CO(21%): 5.66 ± 1.14 L.min–1; $p<0.05$]. BP was unchanged, but TPVR was decreased by hypoxia only in higher hypoxic levels [TPVR(11.5%): 14.3 ± 3.5; TPVR(10.0%): 13.9 ± 3.9] than normoxia [TPVR(21%): 15.8 ± 3.6 mmHg.L.min–1; $p<0.05$]. LnHF and α–LF were decreased under severe hypoxic levels [LnHF(11.5%): 5.75 ± 1.09; LnHF(10.0%): 5.71 ± 1.16] than normoxia [LnHF(21%): 6.41 ± 0.71 ms2; $p<0.05$]; [α–LF(11.5%): 6.72 ± 2.12; α–LF(10.0%): 6.74 ± 2.54] than normoxia [α–LF(21%): 9.18 ± 3.46 ms.mmHg2; $p<0.05$]. Vagal withdrawal and the baroreflex sensivity reductions were correlated to oxygen desaturation: ΔLnHF and ΔSpO2: $r = 0.65$; $p<0.0001$; Δα–LF and ΔSpO2: $r = 0.43$; $p<0.004$.

Conclusions and Support: Conclusions: The chronotropic effect of hypoxia starts earlier than consistent autonomic changes, but under severe hypoxia, it is stepped up by vagal withdrawal and the reduction on baroreflex sensitivity, which elicits increases in cardiac output. Blood pressure did not change, but the vascular resistance was decreased in severe hypoxia. Support: CAPES, CNPq and FAPERJ. Keywords: autonomic regulation, hypoxia, peripheral chemoreflex, baroreflex.

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Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: IN VITRO EVALUATION OF THE EFFECTS OF DIFFERENT POLYSACARIDE CONCENTRATIONS FROM Passiflora edulis f. flavicarpa (PASSION FRUIT), ABOUT THE VIABILITY OF THE MURINO B16F10 MELANOMA LINE

Introduction: Brazil has a high biodiversity of plants presenting natural bioactive compounds with high biotechnological potential for the pharmaceutical industry, from which a wide variety of polysaccharides can be mentioned. The Passiflora edulis f. flavicarpa, also known as passion fruit is a very important fruit economically for the country. Although the effects of several plant extracts are already known (anxiolytic, anti-inflammatory and antioxidant activity), few studies focus on the antitumor potential of the polysaccharides presente in these extracts.

Objective: Thus, this research aimed to evaluate in vitro the effect of different concentrations of a mixture of polysaccharides obtained from the peel and pulp of Passiflora edulis f. flavicarpa on the viability of the B16F10 murine melanoma cell.

Methods: The evaluation of cytotoxicity of polysaccharides was performed in a model with normal murine fibroblast 3T3 cells. The cells lines (tumoral and normal) were grown in RPMI culture medium, supplemented with 10% SFB and antibiotics, and then incubated for 24h at 5% CO2, under controlled temperature and humidity. After incubation, the cells were treated with different concentrations (0, 5 and 100 µg/ml) of the polysaccharide mixture. Seventy-two hours after treatment, the cells were submitted to the analysis of Neutral Red (NR) and Diphenyltetrazolium Bromide Reduction (MTT). The results data were compared through one-way ANOVA and the Tukey test ($P<0.05$).

Results: In both MTT and NR analysis, B16F10 melanoma cells treated with the concentrations of 5 µg/ml of the P. edulis f. flavicarpa polysaccharides presented significantly reduced cell viability in comparison to the control group (0 µg/ml). Interestingly, in both tests, the group treated with 5 µg/ml showed less cell viability compared to the group treated with 100 µg / ml of the polysaccharides. For the analysis of cytotoxicity in normal 3T3 cells, both MTT and NR assays demonstrated results similar to those observed for B16F10 cells.

Conclusions and Support: These data demonstrate that, although the use of the polysaccharide under study in low concentrations reduces the viability of tumor cells, it can also present high cytotoxicity for normal cells. However, further studies are needed to prove this dose-dependent effect. Support: Fundação Araucária, CAPES.

ID: 3511

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: ESTRADIOL IMPAIRS HYPOPHAGIA AND HYPERGLYCEMIA INDUCED BY PITUITARY ADENYLATE CYCLASE-ACTIVATING POLYPEPTIDE (PACAP) IN FEMALE RATS

Introduction: The anorexigenic neuropeptide PACAP (pituitary adenylate cyclase-activating polypeptide) acts in hypothalamic pathways participating in the neural control of food intake. In females, estrogens play an important role in energy balance and food intake. Removal of ovaries eliminates estrogenic actions and this effect is reversed with estradiol treatment.

Objective: The present study evaluated the role of estrogens in the effects of PACAP on food intake and plasma parameters in female rats.

Methods: Adult Wistar rats (body weight=250-270 g), under anesthesia, were submitted both to stereotaxic surgery to implant a guide cannula in the lateral ventricle (ICV; AP=0.8 mm; L=1.5 mm; H=3.6 mm; Atlas of Paxinos and Watson, 1983), and to bilateral ovariectomy (OVX). Afterwards, the rats were separated into two groups and received, subcutaneously, oil (OVX-O) or estradiol (OVX-E); they were kept in collective cages in controlled light (12 h light/dark) and temperature (22 ± 2 °C) and with free water and food. On the 7th post operative day, at 4 pm, food was removed and at 6 pm the rats received ICV microinjections of PACAP (Sigma Co., CA; 4.0 ng/g b.w. in 6 µL) or saline (SAL, 6 µL NaCl 0.9%); after microinjection they were placed in metabolic cages and after 15 min submitted to one of the following protocols: 1) Refeeding and food intake determination after 2 hours; or 2) Euthanasia by decapitation for blood collection and plasma assays. The normal distribution and homogeneity of the data were tested and then analyzed by two-way Analysis of Variance (ANOVA) (significance $p<0.05$). This protocol was approved by Ethics Commission on the Use of Animals of UEL (protocol 21997.2017.34).

Results: PACAP significantly reduced the food intake (g/100g body weight) in OVX-O animals (OVX-O/SAL, n=11, 1.60±0.14; OVX-O/PACAP, n=9, 1.14±0.11; $p<0.014$) but not in those animals treated with estradiol (OVX-E/SAL, n=10, 1.12±0.082; OVX-E/PACAP (n=10, 0.96±0.14, $p>0.375$). PACAP also promoted hyperglycemia (mg/dL) in OVX-O/PACAP group (n=8, 94.72±2.07; $p< 0.005$) when compared to the OVX-O/SAL group (n=11, 83.03±2.56), but there was no difference in blood glucose between OVX-E/PACAP (n=12, 82.80±2.86) and OVX-E/SAL (n=12, 86.61±2.27) groups, with glucose plasma levels being higher in OVX-E/PACAP than in OVX-O/PACAP group.. There was no difference in corticosterone plasma concentration (µg.dL-1) between PACAP and saline microinjections, both in OVX-O (PACAP: n=10, 5.15±0.48; saline: n=10, 6.07±0.50)and OVX-E (saline: n=8, 6.66±0.49; PACAP: n=11, 6.07±0.36); however, there was significant difference between oil and estradiol treatments ($p<0.009$), showing increase in corticosterone plasma levels in animals treated with estradiol.

Conclusions and Support: The data show that both hypophagia and hyperglycemia induced by PACAP in OVX-O group was not observed in estradiol-treated animals, and PACAP did not modify corticosterone plasma levels in both groups, but treatment with estradiol was able to promote the increase in corticosterone. In conclusion, these results demonstrate that estradiol reduces the anorexigenic and hyperglycemic effects induced by PACAP, suggesting that the mechanisms underlying hypophagic and hyperglycemic actions of PACAP may be altered by estradiol, however further studies are necessary to confirm this hypothesis. CAPES, CNPq

ID: 3512

Área: FISIOLOGIA GERAL

Sala:

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal da Bahia - IMS-CAT - VITÓRIA DA CONQUISTA - Bahia - Brasil

Title: EFFECTS OF THE KETOGENIC DIET WITH LINSEED OIL ON THE METABOLIC PROFILE AND INSULIN RESISTANCE IN OBESE WISTAR RATS SUBMITTED OR NOT TO EXERCISE

Introduction: Obesity is a chronic and multifactorial disease associated with metabolic complications such as hypertension, dyslipidemia, type 2 diabetes mellitus and insulin resistance. Ketogenic diets low in carbohydrates and rich in vegetable oils, such as linseed oil, associated or not with the practice of physical exercise, seem to have beneficial effects in preventing obesity and, consequently, its metabolic complications.

Objective: To evaluate the effects of the high-fat ketogenic diet with linseed oil on the metabolic profile and insulin resistance in obese rats submitted or not to exercise.

Methods: Male Wistar rats (n=50), weighing between 150 and 200g, were kept in an environment with light and temperature control with free access to water and the normocaloric (n=16) or hypercaloric (n=34) diets for 8 weeks for obesity induction. After this period, six animals from each group were euthanized and the remaining animals were subdivided into 6 groups, with different diets and submitted or not to training for 12 weeks: control and sedentary (CS, n=5); control and trained (CT, n=5); hypercaloric and sedentary (HCS, n=7); hypercaloric and trained (HCT, n=7); high-fat ketogenic with linseed oil and sedentary (HFLS, n=7); high-fat ketogenic with linseed oil and trained (HFLT, n=7). The exercise protocol was based on moderate intensity exercise (55% of VO2 max) at a speed of 10 m/min for 60 minutes on alternate days. The body weight and blood pressure were measured weekly. Glucose tolerance was monitored by the glucose tolerance test, while insulin sensitivity and resistance by the HOMA-β, HOMA-IR and QUICK indexes. At the end of the experiment, the rats were euthanized and the adipose tissue deposits were removed and weighed to measure the total abdominal adipose tissue and the adiposity index. The study was approved by the Ethics Committee on Animal Use (IMS / CAT-UFBA) under number 054/2017. Statistical analyzes were performed using GraphPad Prism, version 5.0, with a significance level of 5%.

Results: After the 12-week experimental period, the animals in the HCS and HFLS groups showed increases in body weight, in the adiposity index and in the total abdominal fat tissue, however, the animals in the HCT and HFLT groups reduced these parameters, evidencing the training effect. Systolic blood pressure was higher in the HCS group compared to the CS group. In addition, the animals in the HCT group showed higher glycemic levels in the 30 and 60 minutes of the glucose tolerance test, when compared to the animals in the CT group. The HFLS group showed higher blood glucose than the CS group, within 30 minutes of the tolerance test. There were no effects of the high-fat ketogenic diet with linseed oil and training on diastolic blood pressure, mean arterial pressure, heart rate, fasting serum glucose and insulin concentrations, as well as on HOMA-β, HOMA-IR and QUICK indexes.

Conclusions and Support: Although the high-fat ketogenic diet with linseed oil and moderate intensity exercise did not alter parameters of insulin resistance and sensitivity, the consumption of this diet promoted increases in weight and body adiposity, which in turn were minimized by training. Support: FAPESB.

ID: 3513

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: UFABC - Santo André - Sao Paulo - Brasil

Title: Blockade of ryanodine receptors promotes chances in electrophysiological parameters during SE.

Introduction: Prolonged seizures are implicated in the development of temporal lobe epilepsy, and both events are related to Ca+2-dependent processes such as pathological synaptic plasticity and neuronal cell loss, as demonstrated by our group. It has been shown that status epilepticus (SE) increases ryanodine receptor (RyR)-dependent intracellular Ca+2 levels in neurons, influencing the epileptogenic process.

Objective: The effects of the RyRs-blocker dantrolene (DAN) on the epileptiform activity were investigated.

Methods: Male Wistar rats (250-300 g) were submitted (CEUA 13/2014) to stereotaxic surgery for implantation of hippocampal cannula and electrodes. For local field potential (LFP) recordings, animals were submitted to 30min of recording of basal activity. Rats were treated with methyl scopolamine (1 mg/kg; sc) followed by pilocarpine (360 mg/kg; ip) or vehicle. After 30 min of SE establishment, animals received intrahippocampal injection of DAN (n=7) or vehicle (n=7) (1 mM; 1 µL), and recordings were acquired for at least 2 h. The basal, methyl, SE, and post-DAN (or post-vehicle) recordings from CA1 left and right electrodes were acquired using open-source electrophysiology system, Open Ephys (www.openephys.org). We computed power spectral densities (PSD) using the pwelch.m function (Signal Processing Toolbox) using 4-s Hamming windows with 50% overlap, using data sampled from epochs of 20 – 30 seconds to represent each period. The frequency ranges analyzed were delta 1.5-4 Hz, theta 4-10 Hz, beta 10-30 Hz, gamma 30-80 Hz, 80-200 Hz fast, and 200-500 Hz ultrafast oscillations.

Results: The preliminary results showed significant changes in Flat periods, isoeletric periods longer than 250 ms, occurred more frequently in the DAN recordings compared with vehicle. Furthermore, the analyses have shown longer duration of flat Periods in the DAN group compared with vehicle, indicating the RyRs influence on the ictal activity.

Conclusions and Support: Therefore, the results revealed the effects of the RyRs-blocker DAN in the epileptiform activity, and presented a fundamental role of intracellular Ca2+ in pilocarpine-induced SE. Financial Support: CAPES, CNPq e FAPESP

ID: 3514

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Instituições: UNESP - BOTUCATU - Sao Paulo - Brasil

Title: IMPLEMENTING THE CULTURE OF WELL-BEING AND MENTAL HEALTH AT THE UNIVERSITY: THE CASE OF "COLETIVA-MENTE" PROGRAM

Introduction: According to data from the National Association of Graduate Studies (ANPG), recent research indicates problems related to the mental health of graduate students, such as conditions of anguish, depression, among other mental disorders. Therefore, actions in the academic environment focused on well-being, self-knowledge and training in crisis management that allow sustainable human development become important.

Objective: Share the experience of a program aimed to promote the discussion, self-knowledge and well-being, through diversified activities that included psychologists and professionals related to the arts.

Methods: This program was contemplated by Unesp-Santander Agreement. Firstly, an organizing committee composed of undergraduate, graduate students and professors was created and the student demands were received as start point for building an program faced to well-being and health mental. o promote an identity and a belong feeling of students to the program a logo and the name "Coletiva-Mente (Collective-Mind)" were teamwork proposed by the students. This program was developed from March to October 2019, and 12 activities were carried out. The activities were held biweekly to monthly and were always managed through a free online registration and certification. Each event was widely publicized through flyers, on the institution's page and on social networks such as facebook (https://www.facebook.com/programacoletividade). After each activity, participants received a form to evaluate the activity, thus actively participating in the construction of the program. The activities carried out were of themes such as purpose, stress and burnout, depression and suicide, time management, women in science, competitiveness, integration between mind and body and stress management.

Results: Approximately 420 students participated in the activities. In all activities, between 80 and 90% of the participants considered that their participation was satisfactory in promoting self-reflection and the main learnings appointed were: 1) Self-knowledge; 2) Focus on the positive; 3) Harmony between mind and body; 4) Live in the present; 5) Troubleshooting; 6) Empathy; 7) purpose 8) Planning; 9) Self-care; 10) Control of anxiety; 11) "Each individual is unique".

Conclusions and Support: A major challenge is the awareness of the academic community in seeking a culture of well-being, promoting mental health as a starting point for academic activities of reflection, knowledge construction and individual transformation. In this sense, the Program found limitations in relation to adherence, mainly by graduate students who report difficulties in reconciling academic activities and demands with actions aimed at self-knowledge and well-being. There are a variety of justifications: 1) personal difficulty in prioritizing time for physical and mental self-care; 2) lack of empathy and institutional recognition for time spent on wellness activities when compared to academic production line; 4) culture of immediacy that prevents a journey of self-reflection and self-knowledge towards sustainable individual and social transformations. Despite the challenges, the pioneering implementation of the Program and its continuity in 2020 represents progress in establishing a culture of well-being at the university. Support: Convênio Unesp-Santander

ID: 3515

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Instituições: FCAV/UNESP - JABOTICABAL - Sao Paulo - Brasil

Title: ROLE OF MEDULARY RAPHE IN THE CONTROL OF TERMOEFFECTORS OF PRECOCIOUS BIRDS

Introduction: In mammals, caudal brain regions, such as raphe nuclei, are involved in the modulation of thermoeffectors for heat loss and heat production, such as peripheral vasodilation/vasoconstriction, nonshivering and shivering thermogenesis. In birds, it is still completely unknown if the same scenario occurs.

Objective: The aim of the present study was to verify the effect of GABAA and GLU inhibition in the medullary raphe on body temperature (Tb), oxygen consumption, ventilation and heat loss index (HLI) of precocious birds under neutral (31ºC) and cold (25ºC), using of one-week-old chicks as animal models.

Methods: The Tb, oxygen consumption (index of thermogenesis), ventilation and heat loss index were measured in chicks implanted with a mini temperature sensor in the coelomatic cavity, before and each 20 min up to 2hs after intra-raphe microinjections of the GABAA receptor antagonist, bicuculline (0.05 mM and 0.5 mM), and the NMDA receptor antagonist, AP5 (0.5mM and 5mM), or vehicle. Protocols were approved by the local Animal Care Committee (CEUA of FCAV/Unesp, nº 013907/17).

Results: Bicuculline (0.5 mM) at 31°C significantly decreased (P<0.05) Tb (vehicle: 41.2±0.1°C; Bicuculline 0.05mM: 40.9±0.1°C; Bicuculline 0.5mM: 40.6±0.2°C) and oxygen consumption (13.9±0.7% decrease) of the animals when compared to the vehicle group. Bicuculline (0.05 mM) at 25°C significantly reduced (P<0.05) Tb (vehicle: 41.4±0.1°C; Bicuculline 0.05mM: 40.6±0.1°C) and oxygen consumption (12.6±1.4% of decrease) of the animals when compared to the vehicle group. AP5 (5 mM) at 31°C significantly decreased (P<0.05) Tb (vehicle: 41.3±0.1°C; AP5 0.5mM: 40.9±0.1°C; AP5 5mM: 40.3±0.2°C) and oxygen consumption (14.7±0.6% decrease) of the animals when compared to the vehicle group. AP5 (0.5 mM) at 25°C significantly reduced (P<0.05) Tb (vehicle: 41.2±0.2°C; AP5 0.5mM: 40.7±0.1°C) and oxygen consumption (17.4±3.1% of decrease) of the animals when compared to the vehicle group. Regarding ventilation, only treatment with AP5 transiently increased breathing frequency during cold exposure (30.6±9.8% increase; P <0.05). At 31ºC, the highest doses of bicuculline and AP5 increased HLI at the beginning of the Tb reduction (P<0.05) and at 25°C there was no difference on HLI. At 31ºC, the highest doses of bicuculline and AP5 increased HLI at the beginning of the Tb reduction (P<0.05) and at 25°C there was no difference on HLI.

Conclusions and Support: Our preliminary results suggest that GABAA and NMDA receptors inhibition in raphe neurons show an inhibitory effect on Tb of chicks affecting thermogenesis under neutral (31ºC) and cold (25ºC) conditions. Support: FAPESP (2017/17278-2)

ID: 3517

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Rio Grande do Sul - Porto Alegre - Rio Grande do Sul - Brasil

Title: PROGRESSION OF EXPERIMENTAL PULMONARY ARTERIAL HYPERTENSION IS CHARACTERIZED BY LUNG NITROSATIVE AND OXIDATIVE STRESS

Introduction: Pulmonary arterial hypertension (PAH) is a fatal disease, which, through a remodeling of the pulmonary vasculature, induces an increase in mean pulmonary arterial pressure (mPAP). These changes promote increased right ventricle (RV) afterload, leading to its hypertrophy – RVH and failure. The role of reactive oxygen and nitrogen species has been linked to these changes. However, little is known about the effects of these species at different stages of the disease.

Objective: To analyze the role of oxidative and nitrosative stress during different stages of experimental PAH.

Methods: This study was approved by the Ethics Committee of the UFRGS (number 32151). Male rats were first divided into two groups: Monocrotaline (MCT) and Control. MCT group received a single injection (60 mg/kg, i.p.) of MCT, while Control received saline. The MCT and control groups were further divided into 3 groups: 1, 2, and 3 weeks. Animals were submitted to hemodynamic (mPAP) analysis. RV weight and right tibia length were used for RVH estimation. Lung was used for histological (pulmonary wall thickness determination, extend of tissue damage, cell quantification, and collagen deposition), biochemical (activity of NADPH oxidase –Nox, catalase –CAT, superoxide dismutase –SOD, glutathione peroxidase –GPx, and nitric oxide synthase –NOS, concentration of sulfhydryl, total reactive oxygen species –ROS and TBARS), molecular (eNOS expression and the ration between endothelin-1 receptors [ETAR and ETBR]), and immunohistochemical (nitrotyrosine labeling) analysis. Results were analyzed by the two-way analysis of variance, complemented by the Student-Newman-Keuls test or by Kruskal-Wallis analysis (P<0.05).

Results: In the lung, MCT promoted increase in Nox and SOD activities, increase in ROS, eNOS expression, and nitrosative damage in the first week. After two weeks, MCT led to increase in NOS and reduction of CAT activities. In the third week, MCT increased SOD and NOS activity, decreased eNOS expression and sulfhydryl content, increased ETAR/ETBR ratio and ROS, and induced oxidative (TBARS) and nitrosative damage (nitrotyrosine). All these alterations in MCT animals were accompanied by morphological changes, including remodeling of pulmonary vessels, extensive damage in the lung parenchyma, with marked inflammation and the presence of neutrophils and lymphocytes over the weeks. Also, collagen deposition was found after 3 weeks of experimental protocol. As a consequence of this pulmonary remodeling, there was an increase in mPAP and RVH after 2 and 3 weeks compared to CTR groups.

Conclusions and Support: The first week was marked by the presence of nitrosative stress. This increase is probably due to the higher formation of peroxynitrite, through the interaction of the superoxide anion (due to the greater activity of Nox, SOD and ROS) with nitric oxide (through the expression of eNOS). These alterations lead to an adaptation of NO production by NO synthase activity after 2 weeks. Oxidative stress was evident in the third week, probably by an imbalance between endothelin-1 receptors, resulting in extracellular matrix remodeling, endothelial dysfunction, and RVH. The relevance of this study is precisely to show these events over time, suggesting the blocking of nitrosative and oxidative stress as therapeutic targets. Support: CNPq, CAPES e FAPERGS.

ID: 3520

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Instituições: Faculdade de Odontologia de Piracicaba - Unicamp - Piracicaba - Sao Paulo - Brasil

Title: EFFECT OF THE ACTIVE TEACHING-LEARNING METHODOLOGY ON KNOWLEDGE ACQUISITION, STRESS AND ANXIETY TEST

Introduction: Academic stress, including test anxiety, can impair the performance of university students in assessments. However, it is not yet known if the use of active teaching-learning methodology (ATLM) could reduce stress and anxiety before assessments and thus improve learning.

Objective: The aim of this study was to evaluate the effect of ATLM on student learning and on levels of stress and anxiety test.

Methods: This study was approved by the institutional ethics committee (CAAE 10859119.0.00005418). Fifty-six of the eighty students enrolled in the second semester of Dentistry course accepted to participate in this study. The ATLM consisted of the following strategies to teach the cardiac cycle: 50 min-lecture, study at home using a textbook, an educational game activity, and three formative assessments on the topic of cardiac cycle. The traditional teaching strategy consisted of 2 lectures of 2 hours of duration on blood pressure control systems, delivered orally. In the second week of the semester (basal) and in the following class after the traditional or active teaching strategies used, the students provided saliva samples, answered an anxiety test, and undertook an assessment about cardiac cycle or blood pressure control systems. The level of stress was assessed using the salivary concentrations of the stress biomarkers cortisol and alpha-amylase. Anxiety was assessed using the State-Trait Anxiety Inventory (STAI) questionnaire. As the topics taught were not the same, in order to identify if any differences in results could be influenced by one topic being more difficult than the other, only the data from students that considered the two topics equally difficult (n = 30) were used in this study. The average concentration of salivary cortisol and α-amylase and STAI scores, obtained at the baseline, before the assessments about cardiac cycle or blood pressure control systems were compared by the one-way ANOVA test for repeated measures and the assessments scores were compared by Student's t-test for paired samples ($p<0.05$).

Results: The students achieved a significantly higher average score in the test concerning the content taught using the ATLM (8.80±1.38), compared to the average score in the test on the content taught using traditional lectures (6.74±2.91). The students presented higher concentrations of salivary cortisol (0.69±0.42) and α-amylase (55.11±37.84), and STAI scores (51.80±11.88) before the assessment on content taught with traditional than ATLM (0.41±0.24; 37.73±26.96; 43.30±7.05), with no difference in cortisol (0.44±0.25), α-amylase (32.93±17.72) and STAI scores (39.33±9.02) between basal values and those obtained before the test in the topic taught with ATLM.

Conclusions and Support: These results demonstrate the positive effects of combining active teaching strategies with formative assessments, leading to reduced levels of stress and anxiety, together with an improvement in performance of university students in assessments. Support: FAPESP, CNPq and CAPES.

ID: 3521

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: HEATED ENVIRONMENT INFLUENCES CARDIAC AUTONOMIC CONTROL AND BAROREFLEX SENSITIVITY DURING ACTIVE STANDING IN HEALTHY INDIVIDUALS

Introduction: The heat stress (HS) induces thermal mechanisms of heat loss (skin perfusion and sweating) which provokes venous pooling, decreases venous return that can be a challenge in blood pressure (BP) control at rest, and is increased by orthostatic stress (ORT). Neural control of circulation represented by baroreflex sensitivity (BRS) and heart rate variability (HRV) have been shown controversial results that seem to be influenced by the exposure time, heating method and autonomic analysis. However, no study evaluated cardiovascular autonomic control to the active postural challenge in a heated environment (warm chamber).

Objective: To investigate the combined and isolated effects of HS and ORT on autonomic responses during rest and active standing test.

Methods: Sixteen healthy individuals (27 ±5 yrs.) performed two active standing test under a hot (HOT; ~ 36°C) and a thermal comfort (TC~ 24°C) environment, randomized at the same day (ethics committee:1.252.971). Blood pressure (BP) was recorded by the infrared photoplethysmography method and heart rate (HR) was acquired by the transthoracic impedance technique through ECG. Skin temperature (Tskin) was real-time monitored by wireless physiological system. All variables were continually recorded in supine (SUP; 30min) and orthostatic (ORT; 6min) positions. Spectral analysis was performed through the autoregressive model to identify low (LF) and high frequency (HF) components of R-R and SBP time series. R-R LF and HF were normalized (LFnu and HFnu) and LF/HF was calculated. Alpha LF was considered as the baroreflex sensitivity index. Non-linear symbolic analysis classified R-R variations into 2 patterns families: no variation (0 V; sympathetic modulation) and 2 variations (2UV or 2LV; vagal modulation). ANOVA two-way with repeated measures in both factors (thermal and body position conditions) and Sidak post-hoc were employed. Paired test-t was used for Tskin comparisons.

Results: Tskin increased in HOT compared than TC ($p=0.01$). HOT provoked an increment in LFn, and a decrement in Alfa LF (baroreflex sensitivity), and HFn compared to TC ($p<0.01$). However, ORT stress had an additive increment (body position and thermal condition interaction; $p<0.01$) in LF/HF and 0V% indexes. Also, 2UV% reduced in both SUP and ORT positions under HOT compared to TC.

Conclusions and Support: Orthostatic stress had an additive increase in cardiac sympathetic modulation under hot environment. Cardiac vagal modulation and baroreflex sensitivity decreased under hot independently of body position. Support: CAPES, FAPERJ, CNPq.

ID: 3523

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Estadual Paulista UNESP - Arararaquara - Sao Paulo - Brasil

Title: EFFECTS OF CASEIN AND WHEY PROTEIN COINGESTION ON AMINOACIDEMIA AND mTOR SIGNALING PATHWAY IN WISTAR RATS

Introduction: during overnight sleep, the longest post-absorptive and inactive phase of the day cause protein catabolism and loss. However, the daytime ingestion of dairy proteins has been shown to stimulate muscle protein synthesis and growth

Objective: this study compared the effects of pre-sleep supplementation of a protein blend (PB) composed of micellar casein (MCa) and whey protein (1:1) versus isolate MCa on the plasma levels of branch chain amino acids (BCAAs) and the activation of the mechanistic target of rapamycin (mTOR) signaling, a critical intracellular pathway involved in the regulation of muscle protein synthesis.

Methods: after 10 h of fasting during the active phase, rats were fed with a single dose of PB or MCa (5.6 g protein/kg of body mass) by gavage, and samples of blood and gastrocnemius muscle were collected at 30, 90 and 450 min. All experiments and protocols were approved by School of Physical Education and Sport of Ribeirão Preto, University of São Paulo - The Ethics Committee on Animal Use (CEUA 2018.5.14.90.3).

Results: PB and MCa supplementations induced an increase (~3-fold, $P < 0.001$) of plasma BCAAs at 30 and 90 min. Most importantly, the stimulatory phosphorylation levels of mTOR and its downstream target ribosomal protein S6 kinase (p70S6K) were similarly higher (~2.5-fold, $P < 0.001$) 30 and 90 min after MCa and PB. Plasma levels of leucine, isoleucine, valine, and overall BCAAs were correlated with activation of mTOR ($P < 0.001$) and p70S6K ($P < 0.001$).

Conclusions and Support: MCa and PB supplementations before the inactive phase of rats resulted in an anabolic milieu in skeletal muscle by inducing a transient increase in plasma BCAAs and a similar activation of the mTOR/p70S6K axis. Support: Fundação de Amparo à Pesquisa do Estado de São Paulo-FAPESP, under Grant 12/18861-0 and 2018/19107-3, and "Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – Brasil (CAPES)" – Finance Code 001

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Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: FASTING-INDUCED CHANGES IN THE mRNA EXPRESSION OF NUCLEAR AND MEMBRANE RECEPTORS OF IN THE SUBFORNICAL ORGAN IN MALE WISTAR RATS

Introduction: The subfornical organ (SFO) is a sensory circumventricular organ (CVO) able to sense changes in plasma levels concentration of peptidergic hormones and relaying its information to hypothalamic nuclei involved in the control energetic, hydromineral, cardiovascular and reproductive homeostasis.

Objective: The present study aimed to evaluate whether food deprivation is can modulate the mRNA expression for nuclear and membrane receptors expressed in the SFO.

Methods: This study was approved by the Ethics Committee on the Use of Animals of the Federal University of São Paulo (7055281119). Male Wistar rats (250-300 g) were divided into three groups: control with free access to food; food deprivation for 24 hours; and food deprivation for 48h ($n = 8/7$ per group). All animals had free access to water throughout the experiment. Gene expression analysis was

performed by qPCR after micropunch of the SFO. The data were analyzed using one way ANOVA, with statistical significance when $p < 0.05$.

Results: The mRNAs expression of Ribossomal Protein L19 (Rpl19) and Glyceraldehyde-3-Phosphate Dehydrogenase (Gapdh) were significantly increased by food deprivation, indicating that those genes are not suitable as housekeeping genes in the SFO during fasting. Thus, we used Actin Beta (Actb) as endogenous control, since its expression was stable between across the groups. Food deprivation increased gene expression of the following mRNAs: Activin A Receptor Type 1 (Acvr1); Gastric Inhibitory Polypetide Receptor (Gipr); Neuriotrophic Receptor Tyrosine Kinase (Ntrk1); Lamim B Receptor (Lbr); Retinoid X Gamma Receptor (Rxrg); Reticulon 4 Receptor Like 1 (Rtn4rl1); and Sphingosine-1-Phosphate Receptor 1 (S1pr1). Food deprivation decreased the mRNAs expression of Melanocortin 4 Receptor (Mc4r) and Cholecystokinin B Receptor (Cckrb). No significant differences were observed in the expression of mRNAs for Retinoid X Receptor Alpha (Rxra) and Neurotrophic Receptor Tyrosine Kinase 2 (Ntrk2).

Conclusions and Support: In conclusion, we showed that 9 out 11 receptors had their expression mRNA regulated in the SFO by food deprivation. Thus, it is possible that these receptors could be implicated in changes on the activity of SFO neurons in negative energy balance conditions, such as food deprivation. Suporte: CAPES, CNPq e FAPESP.

ID: 3526

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: RUNNING EXERCISE HAS POSITIVE EFFECTS ON MEMORY, BUT WHEN COMBINED WITH STRENGTH (CONCURRENT EXERCISE) THESE BENEFITS ARE LOST.

Introduction: Alzheimer's disease is a progressive neurodegenerative disease related to amyloid-β protein accumulation, and that affects cognition. Physical exercise appears to be a potential prevention strategy to maintain neural functions and to reduce oxidative stress.

Objective: To determine the effects of aerobic (running) and anaerobic (strength) exercise, performed alone or associated (concurrent) on memory deficits and hippocampal oxidative stress induced by β-amyloid neurotoxicity.

Methods: All experiments were approved by the Animal Use Ethics Committee (Protocol 031/2018). Male adult Wistar rats were initially divided into 4 groups (n=16-24/group): Control: sedentary animals; Strength: rats submitted to the anaerobic exercise; Running: rats submitted to aerobic exercise; Concurrent: rats submitted to both exercise types on the same day. After 8 weeks of exercise, the animals were submitted to stereotactic surgery to infusion of amyloid-β protein (Aβ) or vehicle. After the surgery, the animals were subdivided into 8 groups (n=8-12/group): Control: sedentary animals; Aβ: sedentary animals that received Aβ infusion; Strength; Strength+Aβ; Running; Running+Aβ; Concurrent; Concurrent+Aβ. The Object Recognition (OR) Long-Term Memory was evaluated. Then, the animals were euthanized and the hippocampi isolated for biochemical analyzes: level of reactive oxygen species (ROS/DCFH), lipid peroxidation (TBARS), and total antioxidant capacity by ferric reducing/antioxidant power (FRAP). For OR analysis, the discrimination index [(T novel–T familiar)/(T novel+T familiar) x 100 (%)]) was calculated. The results were analyzed by two-way ANOVA, followed by Sidak's post hoc.

Results: Differences between groups ($P=0.0178$) and interaction between the analyzed variables ($P=0.0008$) were found in OR memory. The infusion of Aβ protein promoted OR memory deficit ($P=0.0366$ in comparison to the control group). The Running exercise improved memory (Running+Aβ vs. Aβ: $P=0.0115$). On the other hand, Strength and Concurrent exercise were not able to prevent memory deficit induced by Aβ (Strength+Aβ vs. Aβ: $P=0.9989$; Concurrent +Aβ vs. Aβ: $P=0.1703$) Biochemical results also presented differences between groups ($P<0.05$). Aβ infusion increased lipid peroxidation ($P=0.0002$) and decreased antioxidant capacity compared to the control group ($P=0.0003$). The concurrent promoted increased ROS in Aβ rats (Concurrent+Aβ vs. Aβ: $P=0.0390$). All types of exercise promoted a decrease in lipid peroxidation in Aβ rats (Running+Aβ vs. Aβ: $P=0.0111$; Strength+Aβ vs. Aβ: $P=0.0039$; Concurrent+Aβ vs. Aβ: $P=0.0202$). Strength exercise was able to increase antioxidant capacity in Aβ animals (Strength+Aβ vs. Aβ: $P=0.0009$).

Conclusions and Support: Aβ infusion promotes oxidative stress and long-term OR memory deficits. Running exercise alone prevents cognitive deficits and lipid peroxidation of the hippocampus and strength exercise is able to decrease lipid peroxidation and increase antioxidant capacity; on the other hand, exercises performed simultaneously (concurrent exercise) did not promote memory benefices, and seems to prejudice the hippocampal oxidant balance.

ID: 3528

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: ROLE OF THIOREDOXIN-1 IN THE SIGNALING PATHWAYS INVOLVED IN THE PROGRESSION OF EXPERIMENTAL PULMONARY ARTERIAL HYPERTENSION

Introduction: Pulmonary arterial hypertension (PAH) is characterized by pulmonary vascular remodeling, that promotes vessels narrowing, leading to increase in right ventricle (RV) afterload. Over time, these pulmonary changes may induce RV hypertrophy and failure. Reactive oxygen species (ROS) is one of the main activators of the pulmonary remodeling, while thioredoxin-1 (Trx-1) shown a protective effect in controlling these species. However, time-course studies evaluating how these alterations happen in PAH are scarce.

Objective: to evaluate the role of Trx-1 system and different signaling pathways related to pulmonary vascular remodeling in the progression of experimental PAH.

Methods: This study was approved by the Ethics Committee of the UFRGS (number 32151). Male rats were first divided into two groups: Monocrotaline (MCT) and Control. MCT group received a single injection (60 mg/kg, i.p.) of MCT, while Control received saline. The MCT and control groups were further divided into 3 groups: 1, 2, and 3 weeks. Animals were submitted to echocardiographic (myocardial performance index – MPI, fractional shortening – FS, and ratio between acceleration (AT) and ejection time (ET) through the pulmonary artery) analysis. Lung was used for biochemical (activity of thioredoxin reductase activity – TrxR) and molecular analysis (expression of Trx-1 and its regulator VDUP-1- vitamin D(3) upregulated protein 1 –; nuclear factor erythroid 2-related factor 2 – Nrf2; survival [total Akt, pAkt, ERK 1/2] and cell death pathways [caspase-3, HSP70, pJNK, total JNK, p-p38, total p38, pNF-κβ 65, and total NF-κβ 65] . Results were analyzed by Kruskal-Wallis analysis ($P<0.05$).

Results: MCT reduced FS and AT/ET ratio, and increased MPI after three weeks of experimental protocol. In the lung, after one week, MCT increased the activity of TrxR, the expression of Trx-1, VDUP-1, and total ERK 1/2. Reduced expression of Trx-1, Nrf2 and HSP70, as well as increased expression of VDUP-1, caspase 3 and pNF-κβ 65/ NF-κβ 65 ratio were found after 2 weeks of MCT injection. MCT led to increased TrxR activity, reduced expression of Trx-1, Nrf2, and HSP70, associated with increased expression of VDUP-1, ratio between pAkt/Akt, ratio between pNF-κβ 65/ NF-κβ 65 after three weeks. No significant difference was found in the ratio between pJNK/JNK and in the ratio between p-p38/p38.

Conclusions and Support: The reduction in the AT / ET ratio found after three weeks of MCT injection indirectly implies an increase in pulmonary vascular resistance, while the increase in MPI reinforces this change, as it suggests that there is a greater myocardial effort of these animals. Thus, it is believed that these RV changes are a consequence of previous pulmonary vascular changes. Here, we demonstrated these pulmonary changes through an imbalance in the expression of antioxidant defenses, highlighting a reduction in the expression of Trx-1 and an increase in its intrinsic inhibitor, VDUP-1. Thus, it is possible that VDUP-1 bound and inhibited Trx-1 and therefore interfered with its ability to reduce oxidized proteins, resulting in increased susceptibility to apoptosis, as demonstrated by elevated caspase 3 and NF-κβ 65 expression. Hence, a role for Trx-1 and its inhibitor VDUP-1 is evident in the progression of pulmonary remodeling during the time-course of MCT-induced PAH, enabling a new therapeutic target for this severe disease. Support: CNPq, CAPES e FAPERGS.

ID: 3529

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: INFLUENCE OF CHOW SUPPLEMENTATION WITH EXCESSIVE DOSES OF VITAMIN D ON THE MORPHOMETRIC, BIOCHEMICAL AND MOLECULAR PARAMETERS ON THE HEART OF RATS WISTAR MALES AND FEMALES AT DIFFERENT TIMES

Introduction: Vitamin D deficiency (VitD) has been considered a public health problem. Concerns about this deficiency are growing due to new discoveries that associate it with the development of chronic diseases, including cardiovascular diseases, because of this, professionals have encouraged VitD supplementation. However, VitD has a biphasic dose-response curve in cardiovascular pathophysiology, and both deficiencies and excesses can be harmful. A study previously conducted in our laboratory showed that excessive supplementation of VitD, in non-hypercalcemic doses, for 2 months in male Wistar rats led to biochemical and molecular changes that characterize cardiac remodeling process. However, it is still necessary to define which pathways are involved in the process, with the NFkB pathway being one of the main hypotheses, as well as in what moment they occur. Another important question is whether these changes also occur in females, as the metabolism of VitD appears to be different between men and women.

Objective: To assess whether VitD supplementation leads to cardiac changes in male and female rats and if these changes are due to activation of the NFkB pathway at different times.

Methods: The project was approved by the Animal Use Ethics Committee of the School of Medicine of Botucatu (nº 1296/2019). 72 male Wistar rats and 72 female Wistar rats were used. Male and female animals were allocated to receive standard feed without and with VitD supplementation (10,000 IU / kg of feed) and distributed in groups according to the duration of supplementation (20, 40 and 60 days). Therefore, 12 groups were formed (n = 12): C20M, C20F, C40M, C40F, C60M, C60F, VD20M, VD20F, VD40M, VD40F, VD60M and

VD60F (where M = male rats; F = female rats; C = standard feed without vitamin D supplementation; VD = standard chow with vitamin D supplementation; 20, 40 and 60 = duration of supplementation in days). After the experimental period, the animals were euthanized. Heart (dissected and weighed) and serum were collected for biochemical and molecular biology analyzes. The comparison between groups was made by three-way ANOVA taking into account the factors of supplementation, sex and time.

Results: It was observed that values of final body weight and morphometric variables (atria, right ventricle and left ventricle) were influenced by sex and time, but not by VitD supplementation. Biochemical analysis showed interaction between the supplementation and time factors ($p = 0.045$) where animals supplemented for 20 days showed serum calcium values significantly higher than control animals, while for the period of 40 and 60 days the serum calcium values of supplemented animals did not differ from animals that received standard chow. No changes in serum phosphorus were observed between animals with and without supplementation. Molecular biology analyzes showed that VitD supplementation did not increase the total NFkB and phosphorylated NFkB expression.

Conclusions and Support: VitD supplementation significantly altered serum calcium in Wistar rats at different times. There were no changes in the studied variables related to the interaction between the animals' sex and VitD supplementation. Support: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

ID: 3532

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: EXPERIENCE REPORT: THE USE OF MODEL-BASED INSTRUCTION (MBI) IN TEACHING ELECTRICAL AND CHEMICAL SYNAPSES USING THE STOP MOTION TOOLS

Introduction: Learning about the mechanisms of electrical and chemical synapses is the foundation for learning the process of control of physiological systems. It is known that when the learning process involves motor activities as well, it is more effective in terms of understanding the mechanisms. In this regard, the use of model-based instructions (MBI) is rising in undergraduate education. Models enable students to visualize phenomena, question and arrange knowledge, describe and articulate concepts and mechanisms in addition to understanding how they interact in a complex system

Objective: This study had the aim of applying the use of MBI-based modeling, using colored modeling clay associated with the stop motion tool as a strategy for learning electrical and chemical synapses

Methods: The activity was conducted with four classes of approximately 35 students each (2015, 2016, 2017 and 2018) within the subject "Compared Physiology I" of the course of Biological Sciences at UNESP/CLP. The activity was planned in 4 steps: 1) 2-hour class in synapse, 2) Distribution of students in groups and development of a script, 3) Confection of classroom models with the help of the professor and production of a movie using the stop motion tool, and 4) Exhibition of produced videos.

Results: The students produced videos illustrating the two types of synapses where it was possible to observe depolarizations, opening of channels, release of neurotransmitters and their binding to receptors. Although it was not required, some videos were contextualized and the students included scenes showing the regions of the organism where synapses occurred. Some theatre scenes were inserted in the video. During the confection of models, questions related to the mechanisms were fairly detailed once these details were included in the video. We also observed that the students give great importance to the sequence in which the events take place and to the concept of structure and function. This detailing level and extensive synapse reframing related to physiological and behavioral responses were also observed in the written tests given afterwards. In general, students showed to be satisfied with the development of the activity and reported the importance of alternative learning pathways.

Conclusions and Support: The use of models in undergraduate classes has shown to be promising, once it allows the student to have a more active role. As seen from the results, the construction of a stop motion model enabled systemic thinking and long-lasting learning in which we have used different concepts linked to more complex physiological phenomena.

ID: 3534

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: CHRONIC COLD EXPOSURE IN AWAKE PHASE REDUCES SKELETAL MUSCLE MASS AND STRENGTH IN MICE

Introduction: Extreme cold exposure (CE) in Antarctic field mainly occurs during awake phase when expeditioners are out of camp. Chronic CE (CCE) may cause skeletal muscle disorders (e.g., pain) leading to reductions in physical performance and labor activities. In animal models, CE for 24h/day induces a marked muscle atrophy, but these models may also cause sleep deprivation and, consequently, muscle loss

Objective: characterize the alterations in muscle mass and physical performance in a murine model of intermittent CCE (ICCE) during awake phase (i.e., dark light cycle), a condition that mimics an Antarctic camp.

Methods: adult male CD-1 mice were kept in a thermoneutral environment (29 oC; CON, n= 3) or exposed to cold environment (4 oC; ICCE, n=3) from 7 pm to 7 am (i.e., awake phase). After 21 days, aerobic performance and muscle strength were assessed by incremental treadmill and hanging tests, respectively, and animals were euthanized to collect samples of skeletal muscle and brown adipose tissues. All experiments and protocols were approved by Federal University of Minas Gerais (UFMG) - The Ethics Committee on Animal Use (CEUA 84/2020).

Results: ICCE caused a dramatic reduction (70 %) in the latency time to fall in hanging test and tended to reduce ($P = 0.07$) time to exhaustion in treadmill. These deleterious effects of ICCE on physical performance were associated with reduced mass of gastrocnemius (14 %) and plantaris (17 %) muscles and a tendency toward lower mass of tibialis anterior muscle ($P = 0.08$) and increase of heart ($P = 0.07$). As expected, ICCE markedly increased (96 %) the mass of the thermogenic brown adipose tissue (BAT). No change was observed in peak oxygen consumption and body mass.

Conclusions and Support: ICCE during awake phase is sufficient to cause skeletal muscle atrophy and to reduce muscle function in mice. Supported by PRPq-UFMG (27764*27) e CNPq/CAPES/PROANTAR (442645/2018-0)

ID: 3536

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Instituições: Unesp - Faculdade de Ciências e Tecnologia - PRESIDENTE PRUDENTE - Sao Paulo - Brasil

Title: THE EFFECTS OF AEROBIC AND ANAEROBIC PHYSICAL EXERCISE IN LIVER OF WISTAR RATS SUBMITTED TO HIGH-FAT DIET

Introduction: The high consumption of high-fat diet (HFD) causing some diseases as obesity, metabolic disorders, non-alcoholic fatty liver disease (NAFLD), including overweight and other complications. The overweight is a huge problem around the world, and this process is associate with HFD and low physical activity practice, Nonetheless, it is well stablish on the literatura that aerobic physical exercise have most efficacy improving this obesogenic environment and in the health.

Objective: The aim of study have been, verify the effects of HFD related to aerobic and anaerobic physical exercise in Wistar rat-liver.

Methods: 48 Wistar rats were underwent into 6 groups (n=8): CT - the animals receive standard diet and water ad libitum; AE - standard diet, water ad libitum and performed aerobic physical exercise; AN - standard diet, water ad libitum and performed anaerobic physical exercise; OS - the high-fat diet and water ad libitum; OAE - HFD and performed aerobic physical exercise; OAN - HFD and performed anaerobic physical exercise. The high-fat diet was composed by 55% of carbohydrates, 15% of proteins and 30% of lipids from the 60 days of age. The protocol of aerobic physical exercise were performed 5x/week, for 60min in a adapted treadmill until they reach 17,5 m/min. In relation to anaerobic protocol, were performed 3x/week of jump in the water, each season was composed of 4 sequences with 10 repetition each one, 50 -70% of overloads. At 159 days of age, the animals were euthanized, and the liver collected, weighed, and processed. The study was approved by Animal Use Ethics Committee (CEUA) under protocol number 003/2016.

Results: During the protocol, the rats rise the weight gain CT (159,5±19,13), AE (120,1±19,13), AN (124,8±19,96), OS (148,6±18,48), OAE (149,5±19,96) e OAN (161,3±19,13). The trained groups AN (19,51±2,12), OAE (17,72±2,12), mainly AE (29,07±2,29) significantly

increased glycogen in liver compared to CT group (4,9±2,29). On the other hand, the selectively highlight collagen networks, the AE (5,13±1,52), OS (3,40±1,52) and OAN (5,70±1,52) groups decreased collagen compared to CT group (11,29±1,52).

Conclusions and Support: The results showed the groups with physical exercise protocolimprove great effects on the tissue liver, especially physical aerobic exercise when associated with HFD or no, because this one had considerable decrease collagen and increasing glycogen in the liver tissue.

ID: 3537

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: RESPIRATÓRIA

Forma de Apresentação: Ê-POSTER

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Title: ROLE OF SK AND BK CHANNELS IN THE CONTROL OF THE ELECTROPHYSIOLOGICAL PROPERTIES OF PARASYMPATHETIC RESPIRATORY MOTONEURONS IN THE DORSAL MOTOR NUCLEUS OF THE VAGUS FROM RATS.

Introduction: The parasympathetic respiratory motoneurons in Dorsal Motor Nucleus of the Vagus (DMV) project to lower airways to regulate the smooth muscle tone and mucus secretion. The Ca2+-activated K+ channels (KCa2+) regulate the action potential waveform and excitability in a variety of neurons. However, the role of KCa2+ in the control of DMV respiratory motoneurons electrophysiological properties is still unknown.

Objective: To investigate the contribution of small (SK channels) and large (BK channels) conductance KCa2+ in control of electrophysiological properties of DMV respiratory motoneurons from rats.

Methods: Coronal slices of the brainstem from male Wistar-Hannover rats (3 weeks) were obtained for intracellular recordings, using whole cell patch clamp technique, of retrograde labelled parasympathetic respiratory motoneurons in the DMV. Apamin (100 mM) and iberiotoxin (IBTX; 50nM) were used as specific blockers of SK and BK channels, respectively. Data are expressed as mean ± SEM. All procedures were approved by the institutional Ethics Committee on Animal Use (CEUA, 087/2019).

Results: Using voltage clamp, we measured the K+ currents sensitive to apamin (27.93 ± 3.63 pA; n=12) and IBTX (588.6 ± 63.05 pA; n=12) in the DMV respiratory motoneurons. In current clamp mode, blocking SK channels increased the number of action potentials (ramp protocol: 23.32 ± 4.26 vs 27.68 ± 4.46; p=0.04; n=9; square pulse protocol: 29.36 ± 6.46 vs 35.26 ± 6.62; p=0.002; n=9). However, apamin did not affect the action potential half-width (1.80 ± 0.19 vs 1.91 ± 0.19 ms; p=0.24; n=7) and amplitude (58.91 ± 4.11 vs 57.56 ± 3.89 mV; p= 0.32; n=7), as well as the amplitude of afterhyperpolarization potential (24.58 ± 2.05 vs 25.33 ± 4.09 mV; p=0.57; n=7) and depolarizing input resistance (0.033 ± 0.002 vs 0.034 ± 0.002 GΩ; p=0.56; n=9). On the other side, blocking BK channels did not affect the number of action potentials (ramp protocol: 18.26 ± 1.3 vs 17.46 ± 1.31; p= 0.27; n=16; square pulse protocol: 28.04 ± 2.18 vs 27.34 ± 2.12; p=0.9; n=16). However, IBTX significantly increase the action potential half-width (1.78 ± 0.07 vs 1.92 ± 0.09 ms; p=0.022; n=10) without changing the amplitudes of action potential (71.81 ± 3.75 vs 68.21 ± 3.18 mV; p=0.058; n=10) and afterhyperpolarization potential (25.03 ± 2.27 vs 24.66 ± 2.12 mV; p=0.63; n=10), as well as the depolarizing input resistance (0.03 ± 0.002 vs 0.03 ± 0.003 GΩ; p=0.69; n=16).

Conclusions and Support: SK and BK channels play different roles in regulating the electrophysiological properties of the DMV parasympathetic respiratory motoneurons from rats. Funding: CNPq and FAPESP.

ID: 3538

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: α7 NICOTINIC ACETYLCHOLINE RECEPTOR (α7NACHR) DEFICIENCY IN HEPATOCYTE IMPAIRS HEPATIC METABOLISM IN HFD MICE

Introduction: Metabolic inflammation is a leading cause of obesity. The innate immune system is capable of restore the homeostasis and it modulates the activating of the cholinergic anti-inflammatory pathway. This system is dependent of acetylcholine which is released by the vagus nerve stimulated by a central muscarinic receptor signaling. This will inhibit the pro-inflammatory mediators' production through α7 nicotinic acetylcholine receptor (α7nAChR) cascade signaling. It is well known that increased inflammation can affect hepatic metabolic homeostasis, mainly insulin resistance. Previous work from our laboratory shown that KOα7Alb-Cre mice can impair AKT signaling in the liver after high fat diet (HFD) consumption. However few researchers have addressed the metabolic implication in the lack of this receptor in hepatocytes.

Objective: The aim of this study is to determine the metabolic effects of HFD consumption in mice with hepatocyte-specific Chrna7 deficiency.

Methods: Ethics approval was obtained from the State University of Campinas Ethics Committee (Protocol 5375-1/2019). Mice with hepatocyte-specific Chrna7 deficiency were generated using the Cre- loxP system. To obtain KOα7Alb-Cre mice we mated Chrna7flox/flox (B6(Cg)-Chrna7tm1.1Ehs/YakelJ) and Alb-Cre (B6Cg-Speer6-ps1Tg(Alb-cre)21Mgn/J) mice. Both lineages were purchased from the Jackson Laboratory. Chrna7flox/flox animals were used for the control (WT). The male KOα7Alb-Cre and WT mice were fed with a 45% HFD for 8 weeks. Intraperitoneal glucose tolerance test (GTT) and insulin tolerance test (ITT) were performed after 4 and 8 weeks of HFD consumption. Then, mice were anesthetized and euthanized for the tissue extraction.

Results: Firstly we investigated the impact of HFD on body weight gain, adiposity and fasting glycemia. The KOα7Alb-Cre mice were thinner than WT mice after 8 weeks of HFD. However, the KOα7Alb-Cre mice presented higher retroperitoneal fat pad mass. In addition, the fasting glucose levels were increased in both groups after 4 and 8 weeks of HFD consumption. HFD did not alter insulin sensivity in KOα7Alb-Cre mice, although it had glucose intolerance compared to WT mice. The KOα7Alb-Cre mice also presented higher liver somatic index than WT mice. To determine whether hepatic α7nAChR deletion induced liver injury, we measured plasma ALT and AST levels. The KOα7Alb-Cre mice had higher AST levels and lower ALT levels compared to WT mice. The AST/ALT ratio was higher KOα7Alb-Cre mice than WT mice. Then the cytokine levels were analyzed in the liver. KOα7Alb-Cre mice shown lower levels of IL1-β, IL-6 and IL-10 mRNA than WT mice.

Conclusions and Support: Our preliminary findings suggest that HFD can modulate the hepatic metabolism in mice with hepatocyte-specific Chrna7 deficiency. The results obtained so far allow us to conclude that HFD seems to lead to a liver injury in KOα7Alb-Cre mice and modify the metabolism. Support CAPES and FAPESP.

ID: 3540

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: HEAT STRESS BLUNTS BLOOD PRESSURE INCREMENTS DURING ISOMETRIC EXERCISE DUE TOTAL PERIPHERAL RESISTANCE DROP IN WOMEN

Introduction: Blood pressure (BP) and heart rate (HR) increase during isometric handgrip exercise (HG) in thermoneutral condition (TC), but BP and HR responses are blunted when HG is performed under a heated environment (HOT). Heat Stress (HS) may induce thermal mechanisms of heat loss (skin perfusion and sweating), causing venous pooling (venous return and cardiac output [CO] could be reduced), and/or peripheral vasodilation (peripheral resistance could be lower). BP response is mediated by CO and/or peripheral resistance regulations that may be different between males and females. However, most of the studies are not designed to investigate potential sex-differences during HS protocols.

Objective: To investigate sex-differences in hemodynamic responses during isometric exercise in a heated environment. We hypothesized that BP responses to HG under HS are more dependent on peripheral than central mechanisms in women.

Methods: Eight healthy men (29 ± 6 yrs) and eight women (26 ± 4 yrs) participated in this study (CEP: 1.252.971/2015). The experimental protocol was separated into two randomized environmental conditions on the same day: HOT (~ 36° C) and TC (~ 24° C). In both conditions, participants rested for 30 minutes and performed HG for three minutes. BP, RR intervals, stroke volume (SV), and cardiac output (CO) were continuously assessed by non-invasive transthoracic impedance. Total peripheral resistance was calculated (TPR= MBP/CO).

Results: Mean skin temperature increased in both male ($p= 0.001$) and female $p=0.001$) groups. In the female group, SBP ($p=<0.01$), DBP ($p=<0.01$), and MBP ($p=0.01$) were reduced at rest and remained lower during HG under HOT compared to TC. SBP increment was delayed during isometric exercise under HOT in females [i.e. SBP increased at 3min ($p=<0.0001$) of HG under HOT and at 2min ($p=0.02$) under TC]. DBP and MBP had similar increments during HG under HOT and TC. Males showed no effect of HOT in blood pressure responses and a similar increment during HG in both HOT and TC ($p>0.05$). HR increased from baseline to HG in both groups under HOT and values were higher compared to TC ($p=<0.01$). In females, TPR was reduced at rest and remained lower during HG under HOT compared to TC ($p=0.001$). Finally, CO increased during HG under HOT just in males ($p=0.002$), but SV ($p=0.29$) was not influenced by HOT at rest nor during HG for males and females.

Conclusions and Support: HOT has a main effect in BP reduction due TPR drop at rest that persisted during HG in women. Despite of cardiac output increases in men, heart rate rises in both sexes during HG under HOT. FINANCIAL SUPPORT: CAPES, FAPERJ, CNPq.

ID: 3543

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: ACTIVATION OF 5-HT3 RECEPTORS IN THE MEDULLA OBLONGATA PARTICIPATES IN PHASIC CONTROL OF URINARY BLADDER

Introduction: Lower urinary tract disorders represent up to 40% of consultations in nephrology and urology outpatient clinics. The prevalence of those disorders is greater in women. The control of micturition depends on reflex mechanisms, however, it undergoes cortical modulation, as well as regulation from pontine and medullary areas. Different neurotransmitters/neuromodulators are present in the medulla oblongata, among which are L-glutamate, acetylcholine, GABA, norepinephrine and serotonin (5-HT3). It has not been described so far, whether the serotonergic transmission would participate in the neural pathways responsible for regulating the urinary bladder.

Objective: To investigate whether the activation of 5-HT3 receptors in the medulla oblongata influences the regulation of the urinary bladder and cardiovascular parameters in Wistar rats.

Methods: Female Wistar rats (~ 250 g, CEUA protocol # 11/2017, N=7/group) were used. The animals underwent a stereotaxic surgery to implant a guide cannula into the fourth brain ventricle (4th V) under ketamine (50 mg/kg i.p.) and xylazine (10 mg/kg, i.m.) anesthesia. After one week, rats were anesthetized with 2% isoflurane in 100% O2 and submitted to cannulation of femoral artery and vein, cannulation of urinary bladder and placement of a miniaturized Doppler flow probe around the left renal artery for mean arterial pressure (MAP), heart rate (HR), intravesical pressure (IP) and renal conductance (RC) recordings, respectively. All the parameters were recorded in a Power Lab data acquisition system before and after the injection of phenylbiguanide hydrochloride (5 ng/µL, 5-HT3 agonist) or saline (vehicle, 1 µL) or granisetron hydrochloride (7 ug/uL, HT3 receptor antagonist) into the 4th V. The results are expressed as mean ± EP and were submitted to the Student t-test ($p < 0.05$).

Results: The injection of phenylbiguanide (PB) evoked an increase in IP (68.67 ± 0.12%) compared to saline (-4.90±3.53%). The latency for the increase in IP was 5 min and the response persisted for 35 min. A significant decrease in MAP was elicited by PB (-29±6 mmHg) compared to saline into the 4th V (1±3 mmHg). No significant changes were observed in HR and RC after PB injection into the 4th V. Granisetron injection into the 4th V yielded a significant increase in MAP (25±4 mmHg), HR (36±9 bpm) and RC (134.99±64.98%) compared to saline (1±3 mmHg, 7±8 bpm and 11.86±6.91%), but no significant changes were induced in IP (8.34±6.45% vs. 3.82±5.58%, saline). The latency for the responses of granisteron was min ~2 min and long lasted for ~20 min.

Conclusions and Support: The activation of 5HT-3 receptors in medullary areas increases the intravesical pressure and these receptors are involved in the phasic control of urinary bladder. In contrast, 5-HT3 receptors in the medulla oblongata are involved in the pathways of the tonic control of the cardiovascular system. Support: PIBIC-CNPq, FAPESP and NEPAS-FMABC.

ID: 3544

Área: ENSINO E DIVULGAÇÃO CIENTÍFICA

Forma de Apresentação: Ê-POSTER

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Title: HUMANITY IN REMOTE PHYSIOLOGY TEACHING: CREATING A CONNECT AND INTERACTIVITY DURING COVID-19 PANDEMIC

Introduction: Humanity due to COVID-19 is experiencing a complex moment without historical precedents which demands an embracing reflection about teaching and learning process. Human physiology is the science that studies the functioning of the human body; therefore, it is a highly complex discipline, inherent to human existence challenging professor and students in remote learning.

Objective: To share the experience and strategies used to foster the bond and interactivity during remote human physiology discipline offered to undergraduate students in biology, biomedicine, nursing and medical physics at Unesp in Botucatu.

Methods: Since the suspension of presential activities, the professor established communication by email with the classes (133 students) aiming at welcoming and maintaining the institutional bond. The starting point for remote education was to verify: 1) accessibility; 2) interest in remote education; 3) preference for virtual learning environments (VLE) and class format (synchronous or asynchronous). After that, the discipline of human physiology presented the results of this questionnaire to students and organized a proposed schedule of activities that was discussed and reformatted with the active participation of students via synchronous meeting using the Google Meet tool. After the collective construction of the pedagogical contract, Google Classroom was established as VLE and the discipline was offered remotely following the systematic: 1); weekly asynchronous availability of lessons recorded in a reduced format; 2) list of exercises contextualized with motivational cases based on the clinic and everyday physiological situations; 3) suggestion for free accessible reading using Unesp's collection of e-books; 4) synchronous weekly meeting not mandatory for mutual reception, on-call doubts and dynamics of content fixation using "gamification" strategies of learning (Kahoot) and collective construction of knowledge (motivating cases discussed in online groups through document sharing via Google docs).

Results: The initial questionnaire applied to students showed that 83% of students were interested in performing remote activities, signaling a preference for asynchronous classes that respected the diversity of scenarios experienced by students who were now reframing the space from home to dedicate time, physical space and emotional conditions to learn. The remote physiology teaching was first applied to the content previously taught in the presential classroom and served as "tasting" and training. Adjustments were made based on the student's vision for improving the teaching and learning process of the discipline. The results of this experience show that the students classified the progress of the activities as adequate (grade 5, 0 being very slow and 10 being very fast) and high quality (grade 9 / 0-10). The verification

of learning, done through exercises to fix and apply concepts, shows a performance of 78% to 89% by the students. The feedback of the exercises by the teacher attributed a formative character to the activities which had more than 98% adherence by the students.

Conclusions and Support: The remote experience of the discipline of human physiology shows that the diversified pedagogical construction of teaching strategies with the participation of the student humanizes the teaching and learning process, valuing the view of the student who starts to appropriate the process as a co-author. Support: none.

ID: 3546

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal do Rio Grande do Sul - Porto Alegre - Rio Grande do Sul - Brasil

Title: PLASMA DYNAMIC AND NEUROPROTECTIVE ROLE OF LACTATE FOLLOWING NEONATAL HYPOXIA-ISCHEMIA

Introduction: Hypoxia-ischemia (HI) is an important cause of neonatal death and permanent neurological disabilities. Even though lactate (LAC) has shown neuroprotective effects in animal models of cerebral ischemia, understanding of its plasma dynamic is important to allow its use as a cerebral metabolic fuel in neonates that underwent hypoxic-ischemic events.

Objective: To investigate plasma LAC levels after experimental HI and following an intraperitoneal (i.p.) injection of LAC; to analyze if an i.p. administration of LAC affects brain LAC concentrations; to evaluate if LAC administration after HI reduces the volume of brain lesion.

Methods: Seven-day-old (P7) Wistar male and female rats were submitted to a surgery for ligation of the right common carotid artery followed by exposure to a hypoxic atmosphere (8% of oxygen) for 60 min. Blood samples were collected at 5, 20, 30 and 45 minutes after HI (n=8). Sham animals were kept in normoxia and had its blood collected at the same timepoints. Another group of animals (P7) with no previous manipulation received an i.p injection of either LAC or vehicle (phosphate-buffer saline, PBS) and had its blood collected at 5, 30, 45 and 90 minutes after the injection (n=6). Moreover, the hypothalamus of these animals was collected to determine brain lactate concentrations. To evaluate the volume of the brain lesion, additional animals (P7) were assigned to four experimental groups: HI (rats submitted to HI that received PBS), HI+LAC (rats submitted to HI that received LAC), SHAM (underwent a fictitious surgery and received PBS) and SHAM+LAC (SHAM rats that received LAC) (n=8). LAC was administered intraperitoneally following HI. Animals were euthanized in P9 and their brains were sliced (3mm thickness) and stained with TTC (triphenyltetrazolium chloride). The sections were digitalized and the volume of the brain infarct (ipsilateral to carotid occlusion) was expressed as a percentage of lesion relative to the volume of the hemisphere contralateral. Data were analyzed by two-way ANOVA followed by Bonferroni and expressed as mean±SEM. This study was approved by the Institutional Animal Care and Use Committee of the Hospital de Clínicas de Porto Alegre (#2018-0258).

Results: Plasma levels of LAC increased at 5 minutes following HI ($p<0.05$), and returned to baseline values after 30 minutes. Five minutes after an i.p. injection of lactate, plasma levels of lactate increased 4-fold ($p<0.05$) and returned to control levels in 45-90 minutes. Hypothalamic levels of LAC were higher in LAC-injected animals ($p<0.05$). Brain infarct was reduced in both male and female rats from HI+LAC group as compared to HI group ($p<0.05$).

Conclusions and Support: These results suggest LAC administered intraperitoneally reaches the brain and could act as an energy substrate, reducing the brain lesion in neonatal rats submitted to HI. Additional experiments are required in order to understand the mechanism of action by which LAC is protecting the brain. This study was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq), Fundo de Incentivo à Pesquisa e Eventos from Hospital de Clínicas de Porto Alegre (FIPE/HCPA), and Fundação de Amparo à Pesquisa do Estado do Rio Grande do Sul (FAPERGS).

ID: 3547

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: HYPERHOMOCYSTEINEMIA AND PHYSICAL EXERCISE, ISOLATED OR ASSOCIATED, PARTIALLY IMPAIRS THE EPIDIDYMIS IN SWISS MICE

Introduction: Hyperhomocysteinemia is characterized by the elevation of the plasmatic levels of homocysteine due to an unbalance or impairment in its metabolism. This condition is known to impair some of the functions in the male genital system, however, little is known

about its interaction with the epididymis. Physical exercise is also related to oxidative stress, impairing or enhancing the epididymal function.

Objective: On the light of these facts, the aim of this study is to evaluate the effects of hyperhomocysteinemia and physical exercise, associated or isolated, since the pubertal age to adulthood in the epididymis of Swiss mice.

Methods: For that, 48 Swiss mice were randomly divided in 4 experimental groups (C, H, E and H+E) and treated for 52 days. In order to induce hyperhomocysteinemia, animals in H and H+E received, via gavage, 1g/Kg of body weight of dl-homocysteine thiolactone (diluted in water), and the physical exercise was accomplished by animals in groups E and H+E in running wheels. At the end of the experiment, the animals were anaesthetized with isoflurane and euthanized by decapitation. The epididymides were collected, weighted and destined to the analyses of sperm count and histopathology. Sperm cells from the vas deferens were collected and destined to the analysis of sperm motility.

Results: The stereological analysis of the epididymis caput showed a decrease in the percentage of the luminal compartment in groups H, E and H+E compared to the control group. In contrast, there was an increase in the percentage of the epithelial compartment in these same groups. In this region, there was increase in the percentage of stromal compartment only of groups H and H+E compared to the control group. In the epididymal cauda region there was no difference in the percentage of the luminal, stromal and epithelial compartments in between groups. In all groups, the appearance of stroma and epithelium was apparently normal, and the lumen showed only sperm in its content. Hyperhomocysteinemia, physical exercise, or the association of both, did not alter the transit time of spermatozoa through the epididymis in between the experimental groups. There was no significant difference in the number of motile sperm cells in between the experimental groups.

Conclusions and Support: Hyperhomocysteinemia and physical exercise, isolated or associated, did not induce histopathological changes in the epididymis cauda, but induced some changes in the epididymis caput. These partial results show that hyperhomocysteinemia and physical exercise, isolated or in association, impairs partially the epididymis, given that histological remodulation is observed only in the caput region of this organ. The epididymal cauda region was not impaired by the treatment. Therefore, hyperhomocysteinemia and physical exercise, isolated or associated, does not impair the epididymal physiological function. Financial Support: CAPES - PROEX - AUXILIO 690/2018 PATOLOGIA EXPERIMENTAL Keywords: hyperhomocysteinemia, physical exercise, epididymis, sperm cells

ID: 3548

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Instituições: Universidade Federal Rural do Rio de Janeiro - Seropédica - Rio de Janeiro - Brasil

Title: BEHAVIORAL EFFECTS ON OFFSPRING MICE TREATED DURING PERINATAL TIME BY SEROTONIN SELECTIVE REUPTAKE INHIBITOR CITALOPRAM HYDROCHLORIDE

Introduction: Serotonin (5-HT) selective reuptake inhibitors (SSRIs) increase the amount of serotonin in the synaptic cleft as a consequence of the inhibition of serotonin reuptake transporter (SERT). The 5-HT exerts um important role in the embryogenesis of the central nervous system of mammals and therefore, when used during pregnancy SSRIs may affect the ontogeny of several cerebral neurotransmitters systems.

Objective: As suggested by several authors, 5-HT is involved in the pathophysiology of neuropsychiatric diseases, in this study we investigated if perinatal exposure citalopram hydrochloride (CIT) may cause long term neurobehavioral effects which persist through adulthood.

Methods: To reach this aim, two groups of couple swiss mice (n = 4 each, body weight 40 g) were mated. When pregnancy was present, we kept the male and female together up to the delivery time after which male was removed and mother was kept with its offspring up to day 21st. During the perinatal time the male offspring were treated subcutaneously by either NaCl 0.9% (control – CTL) or CIT (1mg/kg) from postnatal day 5th to day 15th. On day 21st offspring were weaned and at day 70th of age (n = 10/group), we performed a sequence of behavioral methods: open field (OF), elevated plus maze (EPM), light-dark box (LDB), social interaction (SI) and tail suspension (TS). Statistical analysis was performed by GraphPad Prism 8.0.2 and the results were expressed as mean ± standard error of mean (s.e.m), when comparing the two experimental groups statistical significance was considered when $p < 0.05$. All the experimental protocols were approved by the local Animal Welfare Committee (CEUA-ICBS-UFRRJ) under the protocol 005/2017.

Results: Our results showed in the OF an increase in the percentage of central square crossings for CIT group when compared to CTL group (CTL - 8.69 ± 1.18 vs. CIT - 13.13 ± 1.09, p = 0.013), increase in the number grooming episodes (CTL - 3.00 ± 0.45 vs. CIT - 6.70 ± 0.87, p = 0.001) and increase in the grooming time (CTL - 7.52 ± 1.58 sec vs. CIT - 15.05 ± 1.23 sec, p = 0.0014) and a decrease in the leaning number (CTL - 25.4 ± 2.71 vs. CIT - 17.40 ± 1.88, p = 0.026). In the EPM, we observed a decrease in the stretch attendance posture (SAP) for CIT group compared to CTL group (CTL - 20.50 ± 1.8 vs. CIT - 15.5 ± 1.41, p = 0.042). In the LDB, we also observed a decrease in the SAP (CTL - 5.10 ± 1.91 vs. CIT - 3.20 ± 0.63, p = 0.043). We did not observe any differences in the other parameters as well as no changes were seen in the SI and TS methods. Therefore, we suggest that perinatal exposure to CIT 1 mg/kg appears to induces either decrease in anxiety-like behaviors or increase in anxiolytic behaviors indicating an anxiolytic effect for CIT that may contribute to program the behavioral profiles of mice in the adulthood.

Conclusions and Support: Our results also revealed no changes in the depression-like parameters as demonstrated by absence of difference in the TS parameters. We believe it is due to modulation of serotonergic function which may happen during early days of life after birth and may be kept along adulthood promoting changes in behavior of offspring adulthood. However, an investigation of molecular mechanisms underlying it must be performed to confirm changes in the protein expression and quantity associated to serotonergic function. Financial support: FAPERJ

ID: 3550

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF THE HYDRALAZINE ON THE CARDIOVASCULAR SYSTEM IN A SEPSIS ANIMAL MODEL

Introduction: Sepsis is characterized by an amplified inflammatory response resulting from an infection by microorganism. This response causes changes in the cardiovascular system and has a mortality rate around of 45.8% in ICU patients. Among sepsis treatments, vasopressors are traditionally used. However, the use of vasodilators in the treatment of sepsis has now been investigated.

Objective: To evaluate the effect of the hydralazine (HDZ), a well-known vasodilator drug, on the cardiovascular system in an animal model of sepsis.

Methods: Male Wistar rats, approved by the Institutional Ethics Committee of the University (protocol #4923121119; ID 000193/2020), were anesthetized and cannulated in the abdominal aorta for hemodynamic records. Sepsis was induced 24 hours later by ligation and cecal puncture (CLP) method. After induction, all animals were randomly distributed into 03 groups (n = 10): Sham; Sepsis; and Sepsis + HDZ. Subsequently, all animals were monitored for 48 h and evaluated for survival rate, clinical sepsis score (CSS), blood lactate, Creatine Kinase (CK), CK-MB, mean arterial pressure (MAP), heart rate (HR), Left Ventricular Developed Pressure (LVDP), electrocardiography (ECG QRS/QT), Myeloperoxidase (MPO), and N-acetyl-β-D-glucosaminidase (NAG) activities at heart. Statistical analysis was performed using the log-rank test (Mantel-Cox) for survival curves, and Student's t test, one- or two- way ANOVA, with Bonferroni post-test for the other parameters ($p < 0.05$).

Results: Sepsis reduces the survival rate (from 100 to 50%), MAP (from 122.78 ± 2.18 mmHg to 105.72 ± 3.66 mmHg) and LVDP (from 46.56 ± 3, 29 mmHg to 19.65 ± 3.89 mmHg) when compared to SHAM. On the other hand, treatment with HDZ improved the survival rate (90%), LVDP (44.14 ± 6.835 mmHg) but further reduced MAP (89.46 ± 2.32 mmHg). In addition, sepsis increased CSS (from 1.50 ± 0.26 to 10.60 ± 0.50 u.a.); lactate (from 14.12 ± 0.86 to 36.28 ± 1.59 mg/dL); CK (from 10.08 ± 1.93 U/L to 43.87 ± 5.98 U/L); CK-MB (from 20.28 ± 1.53 to 40.19 ± 5.25 U/L); MPO (from 0.3 ± 0.08 to 1.6 ± 0.16 U/g); NAG (from 0.7 ± 0.097 to 1.2 ± 0.090 nmol/mg of protein), HR (from 401.39 ± 6.2 to 456.57 ± 12.3 bpm), QRS (from 19.08 ± 1.55 ms for 25.25 ± 1.27 ms) and QT (from 71.32 ± 6.41 ms to 108.3 ± 5.09 ms). However, treatment with HDZ improved CSS (6.50 ± 0.50 u.a.); lactate (18.03 ± 1.19 mg/dL); CK (17.39 ± 2.18 U/L); CK-MB (21.12 ± 2.26 U/L); MPO (0.4 ± 0.09 U/g) and NAG (0.70 ± 0.08 nmol/mg protein), QRS (18.92 ± 1.42 ms) and QT (75, 54 ± 4.76 ms), but increased HR even more (485.6 ± 16.2 bpm).

Conclusions and Support: Treatment with HDZ reduces mortality in animals with sepsis, probably by improving clinical, cardiovascular, biochemical, and inflammatory parameters. In addition, it is possible to infer that HDZ may be improving organ perfusion and cardiac contractile and electrophysiological functions, by reducing myocardial injury induced by sepsis. These findings provides strong evidences that HDZ can be a new therapeutic alternative for treating human sepsis. Support: This work was funded by CNPq (305345/2019-2) and FAPITEC / SE (01844/2011), Brazil.

ID: 3551

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EFFECTS OF CHRONIC SUPPLEMENTATION WITH OMEGA-3 AND OMEGA-6 ON THE LENGTH AND WEIGHT OF THE EXTENSOR DIGITORUM LONGUS, PLANTAR AND SOLEUS MUSCLES OF THE OFFSPRING OF WISTAR RATS

Introduction: The excessive consumption of highly energetic substrates can trigger a metabolic imbalance. Excessive intake of polyunsaturated fatty acids, such as omega-3 (ω-3) and omega-6 (ω-6) by pregnant women, can lead to excessive production of reactive species of oxygen (ROS) and, may result in damage to fetal muscle development, affecting muscle structure and function.

Objective: So, this experiment (CEUA 1303) analyzed the effects of hyper supplementation of Wistar female rats with omega-3 and omega-6 on the length and weight of extensor digitorum longus (EDL), plantar (PLAN) and soleus (SOL) muscles of the offspring.

Methods: So, thirty female rats were divided into three groups: control (CTL), supplemented with omega-3 (SPL3), and with omega-6 ones (SPL6). After twenty days of supplementation, the rats were placed for mating; posteriorly the offspring were separated according to sex for analysis after completing seventy-five days of life; the mothers' supplementation wasn't interrupted until weaning. After the experimental period, the animal's of F1 generation was euthanized and the EDL, PLAN, and SOL muscles were collected to the length and weight analysis.

Results: Evaluating the length of the EDL, PLAN, and SOL muscles, it was observed that, regardless of sex, the CTL has a higher length, followed by SPL3 and SPL6 groups ($P<0,001$). Regarding the weight, the EDL has a higher value on the SPL3 animals, followed by SPL6 and CTL groups; there were no statistical differences between de females. In the PLAN and SOL muscles, it was observed that the male animals of the SPL3 and SPL6 groups showed higher weight than CTL ones; in the female animals, there was no significant difference in weight.

Conclusions and Support: In this way, it can be inferred that the excess supplementation of the mothers affects significantly the muscle development of the offspring, being that this resulted in the shortening of the supplemented group's muscles and increase their weight. This research was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

ID: 3552

Área: FISIOLOGIA GERAL

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Title: EFFECTS OF EXCESSIVE CHRONIC SUPPLEMENTATION OF OMEGA 3 AND OMEGA 6 ON THE WEIGHT OF LIVER, MESENTERIC AND RETROPERITONEAL TISSUES OF WISTAR RATS OFFSPRING

Introduction: Excessive intake of polyunsaturated fatty acids (PUFAs) by pregnant women and breastfeeding women can attribute metabolic and tissue changes to their offspring, especially on the organs responsible for lipidic homeostasis. In view of this, few studies have evaluated the effects of chronic supplementation of PUFAs omega 6 (ω-6), and omega 3 (ω-3) in female rats, on the organs of the metabolism of these acids.

Objective: The aim of this study was to investigate the effects of chronic omega 3 and omega 6 supplementation on the weight of the liver and messenteric and retroperitoneal tissues of Wistar rats offspring after weaning.

Methods: In this study (CEUA 1303), initially 30 female Wistar rats were supplemented with PUFAs rich in ω-6 and ω-3, divided into supplemented groups SPL-3, SPL-6, and groups CTLE (control). Therefore, the offspring derived from the crossbreeding of these rats was selected, and the animals separated by sex, giving rise to SPL-3, SPL-6 male and female groups, as well as CTLE groups of both sexes. After the experimental period of 60 days of life of the offspring, the animals were euthanized, the liver and the mesenteric and retroperitoneal adipose tissues were collected, standardized per 100 g of body weight, and compared with the test two-way ANOVA.

Results: It was found that the male animals of the SPL-3 offspring had a higher total liver weight, whereas the SPL-6 groups had lower values, while the CTLE groups had intermediate weight. It was also observed that the supplemented offspring of males presented a greater weight of mesenteric and retroperitoneal adipose tissues than the female offspring, being noted that the weight of adipose tissue varied differently between genders.

Conclusions and Support: Thus, it was found that the chronic supplementation of PUFAs ω-6 and ω-3, during pregnancy and lactation, resulted in different changes in the weight of the liver and the mesenteric and retroperitoneal adipose tissues, among which, only the offspring. of male animals showed an increase in the weight of these tissues. This research was supported by the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) .

ID: 3553

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: EVALUATION ON THE NEUROPROTECTIVE ROLE OF STYELA PLICATA HEPARIN IN MODELS OF NEURODEGENERATIVE LESIONS CAUSED BY ROTENONE IN A MURINE NEUROBLASTOMA LINEAGE (NEURO2-A)

Introduction: Rotenone is an isoflavonoid used as a pesticide in the agricultural industry capable of causing oxidative stress on its target in neurons since it can cross the blood-brain barrier and block complex I of the mitochondrial respiratory chain. Hereby, the activity of rotenone in neurons simulates what occurred in neurodegenerative diseases, characterized by the loss of vulnerable neurons, due to metabolic processes or external toxicity, such as exposure to rotenone. This condition culminates in oxidative stress, programmed cell death neuroinflammatory conditions, which increase the progression of these diseases. In cell line models, such as that of murine neuroblastoma (Neuro-2A), the effects of rotenone on neurons can be observed, providing study models to better understand how to reduce the effects of exposure to pesticides in neurodegenerative conditions. In this scenario, heparin, a glycosaminoglycan found in several organisms such as ascidians, will be evaluated in vitro as a molecule capable of minimizing the action of inflammatory mediators, since it is rich in anti-inflammatory properties. The heparin obtained from the ascidian Styela plicata has several advantages compared to the pig extraction model, such as reduced anticoagulant activity and intact anti-inflammatory action.

Objective: To evaluate the neuroprotective and anti-inflammatory role of S. plicata heparin in inflammation mediators in the lesion model made by rotenone in the Neuro-2A strain of S. plicata heparin.

Methods: Heparin was extracted from the viscera of S. plicata through proteolytic digestion with papain, purification and precipitation with 92% ethyl alcohol and 2M NaCl respectively. Finally, the molecule was subjected to ion exchange chromatography on a DEAE-cellulose column. MTT was used as a way to obtain the EC50 of rotenone while the Griss method will be used to determine the EC50 of heparin. Finally, cell viability analyzes will be performed using fluorescein diacetate and propidium iodide markers, which quantitatively determine the presence of viable cells and in the process of cell death. The tests that will predict the state of the neuroinflammatory processes in vitro will be carried out by analyzing the activation of the nuclear transcription factor kB and the production of nitric oxide.

Results: For this, heparin was purified from the viscera using DEAE ion exchange chromatography and increasing gradient of NaCl (0-3.0 M). Then, electrophoresis was performed on agarose gel and measurement of uronic acid and protein for quantification and confirmation of heparin purity. To evaluate the possible cytotoxic effect, the MTT assay was used. The results obtained in the evaluation of cytotoxicity to rotenone (0.01 - 0.2 µg / mL) showed EC50 values in Neuro-2A cells at a concentration of 1µg / mL after 48 hours of treatment and did not show cytotoxicity at low concentrations. Low concentration heparin (15 ng) did not have a neurotoxic effect and was able to reverse the neurotoxic effects of rotenone when added to the strain.

Conclusions and Support: By these means, we seek to better understand the anti-inflammatory role of heparin in the face of chemical damage caused by rotenone.

ID: 3555

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: EXPOSURE TO CYANTRANYLIPROLE CAUSES OXIDATIVE STRESS IN THE UTERUS OF FEMALE WISTER RATS

Introduction: Brazil is the country that consumes the most pesticides in the world it is estimated that the volume used in 2019 is equivalent to 07 liters per inhabitant, being 20% of them classified by ANVISA as extremely toxic. Cyantraniliprole is a systemic insecticide with a record of use only in Brazil and China. It acts in the modulation of calcium channels of the type ryanodine receptors (RyRs), promoting the release of calcium (Ca2+). Studies have shown the presence of RyRs in the uterus but have not related this organ to exposure to anthranilic diamides. In the uterus, Ca2+ is involved in muscle contraction, fluidity of cell membranes, establishment and maintenance of pregnancy. Ca2+ imbalance can induce oxidative stress (OS), favoring the loss of uterine function.

Objective: The objective of this work was to evaluate whether the exposure to Cyantraniliprole can alter the activity of cholinesterase enzyme (ChE), glutathione transferase (GST), glutathione peroxidase (GPx), glutathione reductase (GR), superoxide dismutase (SOD) and lipoperoxidation (LPO) in uterus of Wistar females rats.

Methods: After approval by CEUA-UEL 21106.2017.24, adult female Wistar rats (n=24, 60 DPN) were kept in a light/dark cycle of 12 h, 22 °C, water and standard feed ad libitum. The groups (n=08), 10 and 150mg/Kg BW received (intragastric via) the toxic diluted in distilled water or only distilled water (Control group (C)) for 04 weeks. The animals were euthanized in the estrus phase, by anesthetic saturation with isoflurano. The middle portion of the uterine horn was collected and homogenized in phosphate buffer, pH 7.4 for OS assays and ChE activity. The samples were normalized to 1 mg of protein for the tests. Statistical analysis used was Anova one way, $p < 0.05$.

Results: ChE activity differed between the groups, with means of C 4.8 ± 1.2, 10mg 2.6 ± 1.1 and 150mg 2.4 ± 1.3. There was no difference between 10 and 150mg. GST activity was different between the groups, with averages in C 5.9 ± 1.2, 10mg 9.3 ± 2.5 and 150mg 9.7 ± 2.5, it was not difference was observed between group 10 and 150mg. GPX activity was the same between groups, average in C 210.0 ± 15.2, 10mg 220.0 ± 10.2 and 150mg 207.9 ± 20.1. GR activity was not different between groups, with C 21.6 ± 5.6 in 10mg 23.6 ± 8.8 and in 150mg 24.1 ± 4.8. SOD activity was not different between groups, with C 3.0 ± 0.6, 10mg 4.1 ± 0.8 and 150mg 3.4 ± 1.4. The LPO was different between groups. The averages were C 15.3 ± 0.5, 10mg 16.9 ± 0.9 and 150mg 16.3 ± 1.07. There was no difference between the 10mg and 150mg groups.

Conclusions and Support: Exposure to Cyantraniliprole orally can negatively interfere the antioxidant profile of the uterus of adult female Wistar rats, as it induces an increase in GST activity and the occurrence of lipoperoxidation. The GST genes are upregulated in response to OS and represent the first stage of detoxification, while lipoperoxidation can lead to damage to the structure and permeability of membranes,

inducing the loss of selectivity and formation of cytotoxic products. These findings predict a toxic and xenobiotic role of Cyantraniliprole on the uterus. We understand that the use of pesticides is essential for agricultural development, but we believe that studies showing the action of these substances in mammals are important to promote education in use, aiming at less damage to public health. Support: CAPES PROX 690/2018 Patologia Experimental Keywords: Calcium channels, ryanodine receptors, insecticide

ID: 3557

Área: FISIOLOGIA COMPARADA

Forma de Apresentação: Ê-POSTER

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Title: THE INVOLVEMENT OF GLYCOSAMINOGLYCANS IN THE NEURORREGENERATION OF THE ASCIDIAN STYELA PLICATA

Introduction: The neuroregeneration process can be characterized by the production of new functional neurons, after damage. However, the capacity for neurogenesis in mammals is very limited, especially in adult individuals. In this context, ascidians, chordate marine invertebrates, present high neuroregenerative capacity in adults, unlike vertebrates, becoming excellent models for comparative studies of neurorregeneration. Several molecules have a role in this process and recent studies indicate that glycosaminoglycans (GAGs) can modulate neuritogenesis and synaptogenesis according to their sulfation pattern (positive modulation for 6 sulfated (6S) and negative for 4 sulfated (4S) GAGs), from the activity of carbohydrates sulphotransferases (CST). These include: Dermatan 6-O-sulfate (DS-6S), Heparan 6-O-sulfate (HS-6S), Chondroitin 4-O-sulfate (CS-4S).

Objective: Thus, it is aimed to analyze the profile of GAGs in neurorregeneration using a chemical injury model that mimics some pathophysiological conditions of neurodegenerative diseases in Styela plicata ascidian.

Methods: In the present study, the CNS degeneration of the animal was induced through the systemic injection of 65 mg/kg of 3-acetylpyridine (3-AP), a neurotoxin that promotes chemical injury in neurons with high metabolic activity. To do this, after 1 day and 10 days, the CNS was dissected and processed for light microscopy, using staining with Hematoxylin and Eosin; immunofluorescence; for quantification of total GAGs and PCR. For the analysis of neurorregeneration, used immunofluorescence assays with anti-β-III-tubulin (TUJ - identification of neurons), anti-synaptophysin (synaptic tree identification), anti-CS-4S, HS-6S, DS-6S (evaluation of GAG involvement) antibodies.

Results: 1 day after application of the neurotoxin, neuronal disorder and the presence of vacuolations in the cortex were observed, in addition to reduction of the markings for TUJ and synaptophysin in relation to the control, and in 10 days, these parameters resembled the control. In the quantification of GAGs, there was an increase in total GAGs in the ganglion 10 days in relation to the ganglion 1 day. In the immunofluorescences, apparently, more intense CS-4S, HS-6S and DS-6S markings were found in the cortex of the control animals, and there was an apparent increase in that area in the ganglion 1 day. Within 10 days, all parameters resembled the control marking. In the PCR, increased expression, at 1 day, of CST that sulfate GAGs at carbon 6 and carbon 4 of the N-acetylgalactosamine of DS and CS (positive and negative modulation of synapses and neurite, respectively), was observed.

Conclusions and Support: Therefore, we observed a correlation of the studied molecules with the neurorregeneration process in Styela plicata, suposing that DS-6S and HS-6S GAGs contribute to synaptogenesis and neuritogenesis, counterbalancing the inhibitory effect of CS-4S, ensuring safe and effective regeneration.

ID: 3558

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: FUNCTIONAL EVALUATION OF PERIESTROPAUSE WISTAR RATS SUBMITTED TO DIFFERENT METHODS OF PHYSICAL TRAINING.

Introduction: Aging promotes numerous physiological, morphological and behavioral changes, where each individual can respond in an odd way to these changes, with daily life habits being one of the main determining elements of responses and degrees of impairment. Physical exercise is widely described in the literature as an antagonistic agent to several diseases and changes resulting from aging.

Objective: To evaluate changes in gait and the behavior of Wistar rats during the periestropause period (21 months) submitted to different methods of physical training.

Methods: Multiparous rats (17 months), with irregular estrous cycle (periestropause) and adherence to physical exercise (CEUA-Unesp: 00826-2018) were randomly distributed in groups: 1- Control / not submitted to training (NT) ; 2- Aerobic Training (AT); 3- Strength Training (ST); 4- Concurrent Training (CT). Trainings were performed 3 times a week for 120 days. The AT was performed on a treadmill, 40 minutes per day of training with an intensity of 70% Vo2 peak, the ST was performed via climbing on the stairs, 10 climbs per day of training with an interval of 3 minutes between them, with an intensity of 80% of the CCVM and the CT was performed on the stairs, 5 climbs

per training day with an interval of 3 minutes between them (80% of the CCVM) plus running on the treadmill for 20 minutes per training day (70% Vo2 peak), with tests of performances repeated monthly. After 120 days, the animals were subjected to behavioral tests of foot print test (walking), open field (locomotion) and elevated cross maze (anxiety).

Results: Physical training promoted an increase in the stride length of senescent rats, more significantly in the AT and CT groups ($p < 0.005$). Only the ST and CT groups significantly increased the stride width ($p < 0.05$). The groups submitted to physical training had greater locomotion than NT animals and demonstrated a longer time of central locomotion, as well as a higher frequency of passage through the center ($p < 0.05$). The AT showed longer time in the open arm ($p < 0.05$) and in the center ($p < 0.0001$) and shorter time in the closed arm ($p < 0.05$). The ST and CT groups had a lower frequency of passage through the open arm ($p < 0.005$) and a higher frequency of passage through the closed arm ($p < 0.05$).

Conclusions and Support: The different methods of physical exercise provided beneficial changes in the functional and behavioral activity of Wistar rats when performed in the period of periestropause, increasing the stride length, increasing locomotion and reducing anxious behavior, suggesting a better quality of life during aging.

ID: 3563

Área: FISIOLOGIA DO EXERCÍCIO

Forma de Apresentação: Ê-POSTER

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Title: BENEFICIAL EFFECTS OF PHYSICAL TRAINING ON BODY COMPOSITION PARAMETERS, CALORIC INTAKE AND HEART OXIDATIVE STRESS IN AN ANIMAL MODEL OF OBESITY INDUCED BY HYPERCALORIC DIET

Introduction: Sedentary lifestyle and unhealthy eating habits are strongly linked to the onset and progression of cardiometabolic disorders. On the other hand, physical exercise is shown as a non-pharmacological alternative for the prevention and treatment of the effects of the association between obesity and physical inactivity. Given the importance of the topic, the present study is justified by the need to better understand the effects of physical training on redox cardiac changes resulting from the use of hypercaloric diets.

Objective: To evaluate the effects of physical training on parameters of body composition, caloric intake, and cardiac oxidative stress in an animal model of obesity induced by a hypercaloric diet.

Methods: 24 male Wistar rats were randomly divided into four experimental groups: sedentary fed a control diet (CDS / n = 5), sedentary fed a hypercaloric diet (HDS / n = 7), trained fed a control diet (CDT / n = 5) and trained fed a hypercaloric diet (HDT / n = 7). The induction of obesity lasted 8 weeks, and after that period the animals were kept on their respective diets and underwent an moderate intensity aerobic training on treadmill for 12 weeks, on alternate days. This study was approved by the Animal Use Ethics Committee of IMS-UFBA (protocol nº 053/2017). Body weight, energy intake, adiposity index and serum creatine kinase (CKMB) were evaluated. In the cardiac ventricle, the levels of thiobarbituric acid reactive substances (TBARS) and the antioxidant activity of the enzyme catalase were measured. The data were analyzed by the Kolmogorov-Smirnov test and ANOVA two-way using the GraphPad Prism software.

Results: Analyzes between sedentary groups showed that hypercaloric diet caused an increase in body weight (HDS: 627.5 ± 25 vs CDS: 457.4 ± 33.8 (g), P = 0.01), caloric intake (HDS: 111.9 ± 3.8 vs CDS: 69.7 ± 0.7 (Mkcal), P <0.01), adiposity index (HDS: 8.88 ± 0.5 vs CDS: 5.31 ± 0.8, P = 0.001), in addition to increasing TBARS levels in the cardiac ventricle (HDS: 4,807 ± 0.765 vs CDS: 1,334 ± 0.34 (uM / mg protein), P = 0.03) and reduce the activity of the catalase enzyme (HDS: 0.156 ± 0.0102 vs CDS: 0.228 ± 0.023 (U / mg protein), P = 0.04). Among the control diet groups, an increase in caloric intake was observed in response to physical training (CDT: 87.8 ± 1.36 vs CDS: 69.7 ± 0.7 (Mkcal), P = 0.02). The analysis of body weight parameters showed that the trained group submitted to the hypercaloric diet, compared to the sedentary group of the same diet, determined a reduction in body weight (HDT: 499.9 ± 9.4 vs HDS: 627.5 ± 25.3 (g), P = 0.001 ), adiposity index (HDT: 5.18 ± 0. vs HDS: 8.88 ± 0.5 (%), P = 0.05) and reduction in serum CKMB (HDT: 296.2 ± 146.5 vs HDS: 935.6 ± 132.4 (ng / ml) , P = 0.01). Regardless of the diet, physical training was able to reduce TBARS levels (P <0.001) and increase the activity of catalase enzyme in the cardiac ventricle (P <0.001).

Conclusions and Support: Taken together, the data showed that the use of the hypercaloric diet led to unfavorable outcomes on all parameters studied, reinforcing the risks associated with unhealthy lifestyles. In contrast, the performance of physical training contributed actively to mitigate the changes resulting from diet-induced obesity, showing the benefits of regular exercise, especially on the cardiac redox balance. Support: Thanks to FAPESB for the granting of the Master's scholarship

ID: 3566

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: UNIVERSIDADE FEDERAL DA BAHIA-IMS-CAT - VITÓRIA DA CONQUISTA - Bahia - Brasil

Title: IMPACT OF THE KETOGENIC DIET WITH COCONUT OIL AND THE MODERATE INTENSITY EXERCISE ON HEPATIC PARAMETERS IN AN ANIMAL OBESITY MODEL

Introduction: Obesity is associated with the development of a series of metabolic abnormalities and, therefore, new strategies such as changes in dietary patterns and physical exercise have been described as playing a fundamental role in its treatment. Ketogenic diets, low in carbohydrates and rich in vegetable oils, such as coconut oil, despite contributing to weight loss, still have gaps in knowledge about their effects on metabolic and hepatic parameters.

Objective: To evaluate the effects of the high-fat ketogenic diet with coconut oil and moderate intensity exercise on liver parameters in an animal model of obesity.

Methods: Male Wistar rats (n=50), weighing between 150 and 200g, were kept in an environment with light and temperature control with free access to water and the normocaloric (n=16) or hypercaloric (n=34) diets for 8 weeks for obesity induction. After this period, six animals from each group were euthanized and the remaining animals were subdivided into 6 groups, with different diets and submitted or not to training for 12 weeks: control and sedentary (CS, n=5); control and trained (CT, n=5); hypercaloric and sedentary (HCS, n=7); hypercaloric and trained (HCT, n=7); high-fat ketogenic with coconut oil and sedentary (HFCS, n=7); high-fat ketogenic with coconut oil and trained (HFCT, n=7). The exercise protocol was based on moderate intensity exercise (55% of VO2 max) at a speed of 10 m/min for 60 minutes on alternate days. The body weight was assessed weekly. At the end of the experiment, the rats were euthanized by decapitation, the liver was removed, weighed and fixed for histological assessment, lipid peroxidation and antioxidant status. The adipose tissue deposits were also removed and weighed to measure the total abdominal adipose tissue and the adiposity index. The study was approved by the Ethics Committee on Animal Use (IMS / CAT-UFBA) under number 054/2017. Statistical analyzes were performed using GraphPad Prism, version 5.0, with a significance level of 5%.

Results: At the end of the experiment, the animals of the HCS and HFCS groups increased their body weight, the adiposity index and the abdominal adipose tissue, however, the animals of the HCT and HFCT groups reduced these parameters, evidencing the training effect. In addition, the development of microvesicular steatosis and elevated liver concentrations of the enzyme catalase were observed in the HCS and HFCS groups when compared to the CS group. In contrast, only animals in the HFCS group had macrovesicular steatosis and higher concentrations of total nitrites in the liver, effects that were reversed by training, as observed in the HFCT group. Hepatic levels of thiobarbituric acid reactive substances (TBARs) and glutathione peroxidase enzyme were higher in the HCS group compared to the other sedentary groups. The HFCT group had lower levels of TBARs when compared to the HCT group.

Conclusions and Support: The high-fat ketogenic diet with coconut oil increased body weight and adiposity, in addition, promoted hepatic disorders such as steatosis and increased levels of total nitrites and catalase. However, the exercise of moderate intensity determined beneficial effects on most of the analyzed parameters. Support: FAPESB.

ID: 3567

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: Unicamp - Campinas - Sao Paulo - Brasil

Title: FETAL OUTCOME AND MODULATION OF PLACENTAL PROTEOSTASIS IN AN ANIMAL MODEL OF MATERNAL OBESITY

Introduction: Obesity has become a public health problem, with growth mainly in young women of reproductive age. It is known that maternal health can have a significant impact on the intrauterine environment and therefore on fetal development and child health. During pregnancy some maternal adaptations should occur and, among them, the development of specific tissues such as the placenta. Thus, considering that obesity may be an important component of self-perpetuation, studying adaptations during the maternal phase related to the placenta becomes important to understand the processes that operate during this phase of life and its relationship with the fetal outcome in a maternal obesity animal model.

Objective: The objective was to investigate the modulation of placental proteostasis and the relationship between fetal outcome in an animal model of maternal obesity induced by hyperlipidic and hyper caloric diet.

Methods: The experimental procedures were submitted for approval by the Ethics Committee of UNICAMP (CEUA: 5412-1). After four weeks of adaptation, swiss female mice were divided into two groups and fed with standard (CT) or hyperlipidic (HF) diet during another four weeks. After, the mating was performed. Data on intake and feeding efficiency, weight characterization, glycemic and lipid profile were performed in the pre-gestational and gestational phases. After the gestational period, placental tissue was extracted and collected for subsequent analysis by Western blotting.

Results: The higher feed efficiency and higher pre-gestational weight gain of the HF group suggested higher fat tissue accumulation. These nutritional changes culminated in a worsening of glucose tolerance control in this phase. As for the fetal outcome, the lower weight of the HF offspring indicated important changes in development or in pathways that regulate the efficiency and transport of nutrients to the fetus. Although preliminary, we suggest that there may be a disruption in self-regulating processes in autophagy, one of the methods of cell degradation, and a higher expression of LC3 could suggest a greater amount of autophagosomes and, therefore, greater autophagy in the HF group. In addition, an alteration, even if subtle, in this control system, could generate undesirable outcomes. We did not observe a combined regulation between the evaluated proteins, in the sense of synchronization between the processes, as is expected in the regulation of proteostasis.

Conclusions and Support: Conclusions: According to all the results found, we can conclude that the modulation of placental proteostasis occurred in order to alter the expression of LC3, one important protein involved in processes and pathways important for the development of pregnancy. Diet represented an important factor in modifying metabolic and body parameters, affecting both maternal health and the somatic fetal outcome. Financial Support: CNPq, FAPESP, CAPES, FAEPEX.

ID: 3569

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Instituições: INSTITUTO MULTIDISCIPLINAR EM SAÚDE/UNIVERSIDADE FEDERAL DA BAHIA - VITÓRIA DA CONQUISTA - Bahia - Brasil

Title: INFLUENCE OF HIGH-PROTEIN KETOGENIC DIET ON SYSTEMIC INSULINIC RESPONSE AND IN THE SKELETAL MUSCLE IN OBESE WISTAR RATS

Introduction: Obesity and associated metabolic disorders have been focus of studies, especially in the perspective of therapeutic possibilities. Diets restricted in carbohydrates and rich in proteins have gained important visibility due to the allegations of their effects on food intake, body weight and adiposity, muscle metabolism, glycemic and insulinemic profiles. However, the understanding about the mechanisms of systemic and tissue insulin response still has gaps.

Objective: To evaluate the impact of the high-protein ketogenic diet on the systemic insulin response and the insulin signaling pathway in the skeletal muscle of obese male rats.

Methods: Nineteen lean and obese male Wistar rats with eight-week old were divided into three experimental groups for the evaluation of dietary treatments for 12 weeks, namely: Lean Control Diet (LC, n=5); Obese Hypercaloric Diet (OHC, n=7); and Obese High-Protein Ketogenic Diet (OHP, n=7). At the end of 12 weeks, animals were fasted and euthanized. Evaluations of body weight, food and caloric intake and glucose tolerance were performed. Serum levels of insulin, glucose, total cholesterol and triglycerides were determined. Abdominal fat tissues and gastrocnemius muscle were collected, weighed and stored. The Adiposity Index was calculated, as well as the HOMA-IR, HOMA-β and QUICK indexes were determined to estimate systemic insulin response. Western blotting was performed for the expression of insulin receptor (IR), AMP-activated protein kinase (AMPK), protein kinase B (Akt), glycogen synthase kinase-3β (GSK3β) and Glucose transporter type 4 (GLUT4), involved with the insulin signaling cascade in the gastrocnemius muscle. The study was approved by the Ethics Committee on Animal Use (IMS/CAT-UFBA), protocol number 053/2017. Data expressed as mean ± standard error and analyzed by One Way ANOVA, Newman-Keuls posttest, $p<0.05$.

Results: After 12 experimental weeks, the high-protein ketogenic diet promoted reduction in body weight and adiposity in the OHP group, even without determining significant difference in food and caloric intake in relation to the OHC group. Although no differences were observed in glucose and insulin serum levels, the OHP group presented better glucose tolerance than the OHC group, whose area under the curve was moderately correlated with the adiposity index ($r=0.67$, $p<0.05$). HOMA-IR, HOMA-β and QUICK indexes didn't indicate a systemic improvement or worsening or deterioration in insulin sensitivity and alteration of the pancreatic beta cell functionality in the OHP group, compared to the other groups. There wasn't also difference between the groups regarding the levels of triglycerides and total cholesterol. The evaluation of the insulin signaling pathway in the gastrocnemius muscle revealed an increase in the expression of ser256 Akt and ser9 GSK3β proteins and a decrease in the expression of GLUT4 in the OHP group. Both tyr1345 IR and thr172 AMPK showed no significant change in the gastrocnemius muscle after dietary treatment.

Conclusions and Support: The high-protein ketogenic diet was decisive for the reduction of body weight and adiposity, accompanied by an improvement in glucose tolerance. Although no changes were observed in the systemic response to insulin, the increased expression of some signaling proteins and the reduction of GLUT4 in the gastrocnemius muscle suggests a metabolic adaptation to the restricted carbohydrate consumption in an obesity situation. Support: Fundação de Amparo à Pesquisa do Estado da Bahia (FAPESB).

ID: 3571

Área: FISIOLOGIA CELULAR

Forma de Apresentação: Ê-POSTER

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Title: POSSIBLE ROLE OF STIM/ORAI1 IN HYBRIDOMA ANTIBODY EXOCYTOSIS

Introduction: The immune system consists in a collection of cells and structures that protects organisms against harmful external substances. The immune cell repertoire ensures complexity and efficiency in pathogen responses. Among these cells, plasma cells, that are components of the acquired immune system, are responsible for the production and secretion of antibodies, which are glycoproteins capable of neutralize pathogens and regulate other cellular responses, such as the complement system. Despite their importance, little is known about the cell mechanisms related to the exocytosis of these proteins by plasma cells. One of the questions that still needs to be answered relates to the role of calcium channels in the antibody secretion mechanism. Studies on the function of calcium in the exocytosis machinery of other cells of the immune system have already been carried out. However, this knowledge gap on the plasma cell physiology still exists.

Objective: In light of these issues, this work aimed to analyze the influence of calcium on antibody secretion following antigen exposure.

Methods: For this purpose, we used a hybridoma cell line, which is an immortalized monoclonal B cell. All antibody's secretion experiments and western blot experiments were performed in hybridoma 11B11, which specifically receive IL-4 as antigen.

Results: The results demonstrates that due to exposure to antigen over time, cells increase the concentration of secreted antibody in buffers with calcium chloride and cobalt chloride, but with different patterns. Experiments with calcium chloride buffer showed a gradual increase in the antibody secretion, unlike the group with cobalt chloride buffer, which showed a superior increase in the first minutes before reaching a plateau.

Conclusions and Support: Analyzing the two groups it is possible to notice that only the group with cobalt chloride buffer had a plateau, what may be explained by the STIM/ORAI1 mechanism, that function as store-operated calcium channel. Since the group with cobalt chloride buffer didn't have any calcium in the medium, those cells probably couldn't regulate intracellular calcium required for the exocytosis mechanism. Further studies on the subject still needs to be done in order to confirm that hypothesis.

ID: 3572

Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: CARDIOVASCULAR

Forma de Apresentação: Ê-POSTER

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Instituições: Centro Universitário Barão de Mauá - Ribeirão Preto - Sao Paulo - Brasil

Title: EFFECT OF THE DIFFERENT WAVEFORMS APPLICATION ON HEART RATE DURING EXPERIMENTAL VAGUS NERVE ELECTRICAL STIMULATION

Introduction: Electroceutical therapy has been widely explored over time for the treatment of several diseases. Specifically, the vagus nerve stimulation (VNS) has been used as an alternative treatment for clinical and experimental conditions as depression, epilepsy, heart failure, rheumatoid arthritis, cluster headache, traumatic brain injury, Parkinson's disease, and diabetes mellitus. The choice of electrical stimulation parameters such as frequency, pulse width, electric tension and waveform shape is fundamental to the success and efficacy of the therapy. However, this step of the experimental design is not always explored, which can lead to misinterpretation of some findings.

Objective: To evaluate the effect of three different waveform shapes [monopolar pulse (MP), bipolar pulse (BP), and depolarizing prepulse (DPP)] on heart rate (HR) responses during the VNS in anesthetized rats.

Methods: Under ketamine/xylazine mixture anesthesia, male Wistar rats (250 - 300 g) were implanted with an electrode for electrocardiogram (ECG) recording and a bipolar stainless-steel electrode into the cervical portion of the vagus nerve to perform the VNS. Next, still under anesthesia, animals had the ECG recorded and HR calculated on a beat-to-beat basis. After 5 minutes of baseline recording, rats were assigned into three groups considering the shape of the waveform: MP, BP and DPP, and VNS was started. Three sessions of VNS were carried out in order to compare the longevity of the preparation in each electrical stimulation protocol. Each session lasted 30 seconds, with 3 minutes apart between them. Stimulation parameters were the same for all groups (frequency: 5 Hz; pulse width: 100 microseconds; electric tension: 1 V). HR response during VNS was calculated to ensure the reliability of the preparation and was taken as the difference between average HR preceding VNS onset and maximum bradycardic response during the 30 seconds-long session. All procedures were approved by the Committee on Animal Research and Ethics of the Barão de Mauá University Center (protocol #344/18).

Results: In the first VNS session, the DPP group showed a higher bradycardic response ($\Delta 115 \pm 23$ bpm) when compared to MP ($\Delta 37 \pm 9$ bpm) and BP ($\Delta 83 \pm 14$ bpm) groups. In addition, comparing the averaged bradycardic response among the three successive sessions of VNS, it was observed a trend towards higher bradycardic response in DPP group ($\Delta 90 \pm 32$ bpm), compared to MP ($\Delta 56 \pm 24$ bpm) and BP ($\Delta 70 \pm 5$ bpm) groups, as observed in the first stimulus.

Conclusions and Support: Using the same parameter of stimulation, the DPP waveform induced a higher bradycardic response than MP and BP waveforms. Moreover, it seems that the DPP waveform contributes more to the vagus nerve longevity during VNS in anesthetized rats than the other waveforms shape tested, suggesting that its application would be more viable in chronic studies. Barão de Mauá University Center (#344/18) and FAPESP (#2017/05163–6).

ID: 3573

Área: NEUROFISIOLOGIA

Forma de Apresentação: Ê-POSTER

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Title: LUTEIN-LOADED NANOPARTICLES PROTECT AGAINST DEFICITS IN SURVIVAL, DOPAMINERGIC AND EXPLORATORY IN Drosophila melanogaster EXPOSED TO ROTENONE.

Introduction: There is considerable evidence that oxidative stress selectively damage the dopamine system that have various motor, physiological and cognitive functions. In front of this, many studies use rotenone, an insecticide capable of inhibit complex I of the electron transport chain, inducing oxidative stress and the loss of dopaminergic neurons, causing behavioral changes. Thus, such as oxidative damage contributes to the evolution of diseases in the central nervous system, study with lutein has increased exponentially due to its antioxidant action. The lutein has the ability to cross the blood-brain barrier, can perform a neuroprotective effect. It is still the main carotenoid found in the human brain. In addition, it is a potent antioxidant that protects dopaminergic neurons. Bioavailability is other important factor that must be considered. In this sense, polymeric nanoparticles have been widely used to improve the therapeutic action, especially in relation to the controlled liberation of the drug in the target tissue, avoiding toxicity and undesirable collateral effects. Drosophila melanogaster is an excellent organism model used in studies that evaluate neurodegenerative diseases, as it have 75% of the genes homologous to human diseases. This model also presents abnormalities, such as dopaminergic degeneration and locomotor deficit.

Objective: To evaluate the effects of lutein-loaded nanoparticles on survival, dopaminergic, and exploratory deficits in Drosophila melanogaster exposed to rotenone.

Methods: Flies of both sexes were used, aged 1 to 3 days, divided in to 4 groups: control, lutein-loaded nanoparticles (6µM), rotenone (500 µM), rotenone (500 µM) + lutein-loaded nanoparticles (6µM) (coexposure) for 7 days. The survival percentage was checked during 7 days. At the end of the 7th day of exposure, they were anesthetized on ice and euthanized for the dosage of dopamine in head samples, the open-field behavioral test was also performed to evaluate the motor and exploratory activity of D. melanogaster. The data were analyzed by (two-way ANOVA), followed by Bonferroni's post hoc analysis. The GraphPad Prism5 program was used, being considered a significant difference in the control group $p < 0.05$.

Results: It was possible to observe a decrease in the survival rate, deficits in the dopamine levels, in addition to motor and exploratory impairment in the groups exposed to rotenone. The coexposure of lutein-loaded nanoparticles versus rotenone was able to protect against damage to the survival rate ($P < 0.05$) and restored dopamine levels [(two-way ANOVA), $F(1.36) = 8.69$; $P < 0.05$], in addition to protecting against motor and exploratory deficits in the Open-field test [two-way ANOVA, $F(1.20) = 18.28$; $P < 0.05$] in D. melanogaster, the result similar to the control.

Conclusions and Support: In view of this, we observed that lutein-loaded nanoparticles considerably preserved the survival rate, dopamine levels and the motor and exploratory activity of D. melanogaster exposed to rotenone. The protective action of lutein can be due to its antioxidant properties and its nanoencapsulation may represent an increase in its bioavailability. Support: FAPERGS, CAPES, CNPq.

ID: 3574

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: PRE-GESTATIONAL AND GESTATIONAL WEIGHT GAIN AND THE IMPACT ON MATERNAL METABOLISM AND FETAL GROWTH

Introduction: Obesity is a chronic non-communicable disease of large epidemiological importance. The pre-gestational and gestational nutritional status may be one of the factors responsible for the higher prevalence of obesity, since maternal nutrition is one of the predictors of metabolic programming. In addition to increasing the risk of other negative outcomes in fetal development and in the child's health throughout life, obesity is capable of causing damage to maternal health, such as preeclampsia, gestational diabetes and puerperal hemorrhage. Thus the study of obesity and its metabolic impacts during pregnancy is necessary to elucidate mechanisms and key points for preventing this condition.

Objective: The objective of this study was to verify pre-gestational and gestational weight gain through the high-fat diet and its impact on blood glucose.

Methods: The experimental procedures were submitted for approval by the Ethics Committee of UNICAMP (CEUA: 5412-1). After four weeks of adaptation, swiss female mice were submitted to fed with standard (CT) or hyperlipidic (HF) diet during another four weeks. After, the mating was performed. For each group of two females, it was assigned to a male, held together for three days at 12 hours intervals, when they were examined for the presence of signs of mating and detection of the vaginal plug (day E0.5 of pregnancy). Data on weight characterization and glycemic were performed in the pre-gestational and gestational phases. After the gestational period, gonadal fat and retroperitoneal fat were extracted, collected and weighed.

Results: The results showed that the pre-gestational body weight and body weight at the end of pregnancy were higher in the HF group, as well as the feeding efficiency. In addition, the weight of gonadal fat and retroperitoneal fat were higher in the HF group. Such results indicate that the greatest weight gain by the HF group was due to the greater accumulation of adipose tissue. The area of the blood glucose curve did not differ between the groups before and after pregnancy, although the HF group has a tendency towards greater AUC at both times. The correlation between fasting blood glucose and fetus weight showed an inversely proportional trend, indicating that pregnancies with high blood glucose may cause impaired fetal development. In addition, fasting blood glucose has an inverse correlation profile with placental weight. This may justify the smaller weight of the fetuses because smaller placentas may have caused a smaller passage of nutrients and impaired fetal development.

Conclusions and Support: According to all the results found, it is possible to conclude that the pre-gestational and gestational body weight is greater in the HF group as well as the gonadal and retroperitoneal fat mass. The higher glycemia modulated placental and fetal growth in an inverse way, suggesting that weight gain impaired the health outcome for offspring. Support: CNPq, FAPESP, CAPES, FAEPEX.

ID: 3575

Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Instituições: UFScar - São Carlos - Sao Paulo - Brasil

Title: THE INFLUENCE OF OBESITY OVER INTRACRANIAL PRESSURE, BODY COMPOSITION, BLOOD PRESSURE, BRAIN TISSUE AND INFLAMMATION, IN RATS FED A HIGH-FAT DIET

Introduction: Obesity is an inflammatory chronic disease that may lead to hypertension, diabetes, among other pathologies, and to the increase of intracranial pressure (ICP). Intracranial pressure (ICP) is the pressure exerted inside the cranial box, through the internal volume of its three components: brain, cerebrospinal fluid (CSF) and cerebral blood volume (CBV). Therefore, changes in volume can cause Intracranial Hypertension (IIH). In addition to changes in volume, the inflammatory state of obesity may also be related to increases in ICP.

Objective: Thus, the aim of this study was to analyze the influence of obesity over Intracranial Pressure, Body Composition, Blood Pressure, Brain Tissue and inflammation, in rats fed a high fat diet.

Methods: Male Wistar rats (n=63, n=9/group), were fed a chow diet (CD) or high-fat diet (HFD) during 24 weeks. Cross-sections were performed, with evaluations every 8 weeks. BP, HR, ICP, fat percentage (%g), body mass (BM), fat-free mass (FFM), bone mineral content (BMC), glycaemia, lipid profile, inflammatory agents, brain lipids (BL) and finally brain weight (BW) were evaluated. For statistical analysis, the Kolmogorov-Smirnov, One-Way ANOVA, Tukey's post-hoc test, Hedges' g with Cohen's d tests were used.

Results: An increase of 70.42% of % fat, 23.2% in BM and 24,38 % in BMC from W24-HFD vs W24-CD, although without differing in FFM, only in W0-CD. There was no statistical difference in BP, HR and ICP, but probability of increasing ICP and HR in HFD. Glycemia values were elevated (W24-HFD 119,78 ±9,04 mg/dL vs W24-CD = 91,57±8,52 mg/dL), as was Leptin in the HFD group, and probability of BDNF decrease. No difference in BL was found, but there was a decrease in BW in W24-HFD 0,34 ±0,06 g/100g vs W0-CD 0,42±0,05 g/100g and probability of decrease for W24-CD. Obesity did not increase BP, HR and ICP statistically, but there was a strong probability of increasing HR. Being sedentary can increase BP, HR in non-obese rats, explaining the lack of statistical difference in ICP. The increase in glycemia may indicate insulin resistance in HFD. And the increase in leptin concentrations found in rats fed with HFD indicates, in addition to metabolic changes, the increase in cerebrospinal fluid. The decrease in BW in the HFD group may be due to a decrease in neural plasticity caused by BDNF. The absence of a statistical difference in BL indicates that there is no infiltration of fat and other agents in the brain.

Conclusions and Support: There was an influence of obesity on body composition, HR, Leptin and BDNF, and the change presented may reduce the protective activity of BDNF, with loss of brain mass and increased ICP. This work was supported by the Brazilian agency CNPq and by grants from the FAPESP (2017/09602-4).

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Área: FISIOLOGIA DE ÓRGÃOS E SISTEMAS: ENDÓCRINA

Forma de Apresentação: Ê-POSTER

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Title: TREATMENT WITH RITALINA® IN RATS DURING ADOLESCENCE CAN CHANGE METABOLIC PARAMETERS

Introduction: The prevalence of attention deficit hyperactivity disorder (ADHD) has increased in recent years in childhood and adolescence. The etiology of the disease is still unknown; however, studies suggest that catecholaminergic disorders may be responsible for the appearance of symptoms. Thus, the most used treatment is the administration of Methylphenidate, active ingredient of the drug Ritalin®, which inhibits the reception of dopamine and noradrenaline in the prefrontal cortex and striated nucleus.

Objective: The aim of this work is to investigate the effect of treatment with Ritalin® during adolescence on the metabolism of adult rats.

Methods: The research ethics committee approved the study under CEUA nº 5343210520. Thirty-day-old Wistar rats will receive Ritalin® through gavage at a dose of 5 mg / kg of body weight during adolescence (30 to 60 days of life; Rit). Control animals will receive 0.9% Saline in the same volume (Sal). Body weight and food consumption were evaluated throughout the protocol. At 120 days of age biometric, histological analysis and cardiovascular parameters were evaluated. Statistical comparisons were performed by Student´s T test.

Results: The animals Rit did not show any differences regarding food consumption (1924 ± 40.51 vs 1950 ± 31.04; p= 0.6216) or body weight (3995 ± 108.0 vs 4102 ± 98.27; p=0.4686) when compared to Sal group animals. At 120 days of life, the Ritalin® exposure induced an increase mesenteric fat (+ 13%; p <0.002); However, there was no variation in the weight of the other fat stores (retroperitoneal and periepididimal) when comparing the Rit and Sal groups. When evaluating the area under the curve of the results of OGTT we did not observe statistical difference between the groups, however the Rit animals were statistically resistant to insulin in three points of the curve in relation to the Sal group (p <0.0001). In reference to the area under the iTT results curve, there was an increase in the Rit group in relation to the Sal group (+ 10%; p <0.0001).

Conclusions and Support: Exposure to Ritalin® in adolescence programs to dysfunctions in insulin production during adulthood, characterized by insulin resistance. Our study points to the susceptibility of adolescence as a critical window of development, capable of programming for diseases later in life. Funding: CNPQ and Capes.

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Área: FISIOLOGIA GERAL

Forma de Apresentação: Ê-POSTER

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Title: OBESITY BEFORE AND DURING PREGNANCY LEADS TO A CHANGE IN THE PLACENTAL ASSOCIATED GROWTH FACTOR RECEPTOR

Introduction: Maternal obesity has been shown to be a condition capable of negatively interfering with fetal outcomes. Countless evidences have suggested that maternal obesity and the consumption of a diet rich in lipids during pregnancy, increase the risk of complications such as: gestational diabetes, pre-eclampsia, low birth weight and fetal macrosomia. Considering the importance of the placenta in a successful pregnancy, and the high growth of obesity in women of childbearing age, it is necessary to investigate the factors that relate these parameters. Additionally growth factors are fundamental for the proper development of the placenta and consequently for the fetal growth development. It is known that a failure in the action of these placental growth factors can compromise its development and the fetus ones. Maternal obesity can cause several complications, including changes in the action of these factors.

Objective: To Evaluate the levels of some growth factors in the placental tissue of obese mice.

Methods: The experimental procedures were submitted for approval by the Ethics Committee of UNICAMP (CEUA-5401-1). Were used Swiss female mice subjected to the high-fat diet (45%) for four weeks before mating. After 4 weeks of diets, they were submitted to mating, maintaining the same diet, with changes only in protein content (growth diet). On day 19.5, the pregnancy was interrupted, in order to collect samples for later analysis. Intake parameters and body weight were evaluated and the placental tissues were processed and the mRNA levels of PGF, EGFR and PDGFRA were assessed by PCR analysis. The data were analyzed using Student's t-test and differences were considered significant for p <0.05.

Results: The initial weight showed that there was no difference between the groups before the high fat diet. After the administration of the diet, the hyperlipidic group showed greater weight gain, due to the greater feeding efficiency presented by this group in relation to the control. However, the groups showed no difference regarding gestational weight gain, showing that at this stage weight may be more associated with the number of fetuses than with diet. Although no difference in placental weight has been reported and in the levels of mRNA of PGF and PDGFRA between groups, the level of mRNA of EGFR was lower in the hyperlipidic group compared as a control. Studies show that the deficiency of this receptor generates babies and small placentas at birth, possibly due to the spongiotrophoblast cell layer reduction and a flaw in the development of decidua.

Conclusions and Support: Conclusion: Obesity can harm the placenta development and function by decreasing its growth factors. Support: CAPES, CNPq, FAPESP, FAEPEX.

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Forma de Apresentação: Ê-POSTER

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Title: MORPHOMETRIC ANALYSIS OF VISCERAL DEPOTS OF OBESE RATS AFTER DIETARY AND EXERCISE INTERVENTION

Introduction: : Obesity is a characterized by an excessive accumulation of adipose tissue. Its progression is linked to the development of hypertension, type 2 diabetes mellitus and metabolic syndrome. This process is intensified by visceral adipose tissue (VAT), which has greater lipolytic activity, is more resistant to the action of insulin and secretes more inflammatory cytokines compared to subcutaneous adipose tissue. The compartments of VAT include: mesenteric (mWAT), retroperitoneal (rWAT) and epididymal (eWAT) depots. The heterogeneity among visceral depots has a strong impact on mitochondrial and lipid metabolism. Thus, physical training and caloric restriction have been proposed as non-pharmacological strategies for controlling the expansion of VAT. Physical training and diet composition can effectively regulate body mass, decrease abdominal fat and reduce visceral adipose tissue in obese animals.

Objective: : To characterize the morphometric changes in the visceral depots of obese rats, in face of a protocol of aerobic training of moderate intensity and caloric restriction.

Methods: : For that, 14 male Wistar rats were induced to obesity for 8 weeks on a palatable high-fat diet (20% fat). After this, the animals were divided into two groups (n = 7): HFD-Ex: animals fed a high-fat diet that were submitted to the treadmill protocol (3x/week, 60 min, 50-80% Vmax, 8 weeks); and the CD-Ex group: who started consuming a standard diet (4.8% fat) and were submitted to the same exercise protocol (CEUA nº 7631210617). After euthanasia, body mass (BM) and fat mass (FM) were evaluated. The eWAT, rWAT, mWAT depots were dissected and weighed. To analyze histopathology, cuts of 4-5 µm were stained for 2 minutes in Harris' hematoxylin. For morphometric analysis, 20 images each sample were collected with a 20x magnification for quantification. The files were analyzed for the adipocyte area and diameter by the Adiposoft plugin (v. 1.15) from ImageJ Fiji (v 2.0.0). All statistical analyses were performed using Graph-Pad Prism Version 8.0 and R. To verify if the data followed a normal distribution, the Kolmogorov–Smirnov test was performed. Comparisons between groups were performed using a two-tailed Student's t-test. Statistical significance was $p < 0.05$ (two-tailed).

Results: A significant reduction in BM, FM, eWAT, rWAT and mWAT in CD-Ex animals was observed. Furthermore, the morphometric evaluation showed that the diameter and area of the eWAT, rWAT and mWAT depots was high in the HFD-Ex group, when compared to the CD-Ex animals. In HFD-Ex animals, the mass and diameter of the eWAT adipocytes recorded the highest values when compared to rWAT and mWAT. In the CD-Ex group, the eWAT mass was greater, however the rWAT diameter was greater than the other depots. The area of rWAT adipocytes was greater in both groups. The mass, diameter and area of the mWAT adipocytes registered the lowest values in both groups.

Conclusions and Support: Visceral depots have a similar behavior towards obesity. However, it has been confirmed, that in rodents eWAT tissue is the depot that contains larger adipocytes and where fat is preferably stored. Besides may be more involved in the metabolic changes resulting from obesity. This work was supported by the Brazilian agency CAPES and by grants from the FAPESP (2017/09602-4).

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Title: NON-STEROID ANTI-INFLAMMATORY DURING PREGNANCEY REDUCES AUTISTIC-LIKE SYMPTOMS IN OFFSPRING RATS TREATED WITH LIPOPOLISACCHARIDES

Introduction: Autism spectrum disorder (ASD) is a neurodevelopmental disorder of idiopathic origin and characterized by impairments in social interaction, language and communication. Risk factors such as maternal infections and dysregulation of the immune system have been attributed to the increase in clinical cases of ASD

Objective: The present study aimed to investigate the effects of immunomaternal activation with lipopolysaccharide (LPS) and to correlate with behavioral changes in the offspring as a translational model of ASD. In addition, we assessed whether pretreatment with nimesulide (NIM) is able to prevent the effects caused by LPS.

Methods: On the 16th day of pregnancy the pregnant rats (n = 6-8 per group) received pretreatment with an injection (ip) of NIM (5mg/kg) or saline 0.9% (SAL 1ml/kg) 15 min before of treatment with LPS (500µg / kg) or SAL. 2h later the dams were evaluated in the open field test (OFT) to observe the travelled distance. In other group of dams were evaluated food intake and weight gain 24 hours later of treatments. After birth, the litters were weighed, culled in 8 pups (4 males and 4 females) and the maternal behavior was evaluated on post-natal day (PND2-5). The male offspring were submitted to quantification analysis of ultrasonic vocalizations (USV) on the 5th pos natal day (PND5), homing (preference for the nest) in PND13, hole-board (HB) in PND26, elevated plus maze (EPM) in PND28, play behavior (PB) in the PND33 and OFT in the PND34. All procedures were in accordance with the CEUA protocol 66/2017.

Results: The LPS administration decreased the travelled distance in the OFT (1576.1±124.2 to 824.3±247 cm, $p<0.05$), the food intake (28.9±0.8 g to 12.2±2.1 g, $p<0.05$ ) and weight gain (1.8±2.1 g, to -2.9±2.4 g, $p<0.05$) in dams when compared to saline group. Pretreatment with NIM prevented these effects, that is, there was an increase of the travelled distance in the OFT (1455.5 ±202.4 cm, $p<0.05$), and weight gain (4.7±2.6 g, $p<0.05$) in dams when compared to LPS group. Dams treated with LPS expressed increased maternal care (75.2±7.5 to 87.8±2.3 % of observation, $p<0.05$), when compared to saline group, this effect reversed by the NIM (80.1±2.8 %), as for the offspring behavior, we observed that in the HB test there was a reduction in the number of head-dippings by offspring from NIM when compared to LPS group (22.3±2.2 to 12.9±1.7, $p<0.05$), in the PB test there was a reduction in the following parameter the of offspring LPS when compared to saline group (1.7±0.2 to 3.8±0.6, $p<0.05$)

Conclusions and Support: Administration of NIM prevented the symptoms caused by immunomalternal activation with LPS. Thus, immunomalternal activation seems to be one of the causes that lead to ASD. SUPPORT: CAPES, FAPEMIG, CNPq