2nd INTERNATIONAL MEETING OF THE

PORTUGUESE SOCIETY OF PHYSIOLOGY

Sociedade Portuguesa de Fisiologia
portuguese physiological society

11th and 12th | November 2022

Escola Superior de Tecnologia da Saúde do Politécnico de Coimbra

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2ND INTERNATIONAL MEETING OF THE PORTUGUESE PHYSIOLOGICAL SOCIETY

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Welcome to the 2nd International Meeting of the Portuguese Physiological Society

The 2nd international meeting of the Portuguese Physiological Society was hold in Coimbra 11 and 12th November 2022.

After the pandemic period this was the first opportunity to get together the Portuguese "Physiology Community" involving the main Academies and Laboratories in the country, from medicine to biochemistry and biology, to pharmacy and biomedical engineering areas, and professionals - MDs, health technicians from clinical areas to sport.

The meeting had the high sponsorship of FEPS (The European federation of physiological societies) and IUPS (the international union of physiological societies) represented by its Chairwoman Professor Susan Wray. The Physiological Society (UK) The American Physiological Society (USA) The Physiology Majors Interest Group (PMIG, USA) and the Spanish Society of Physiological Sciences were also associated to this initiative.

A great opportunity to share and exchange experiences and expertise, promoting networking, cooperation and knowledge transfer.

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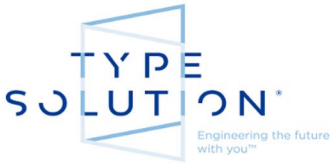

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of BBR are focused on environmental, social, behavioural, technological and political perspectives to promote human health and prevent disease in the individual and their communities. BBR was recently distinguished with the High Sponsorship of CPLP (Community of Portuguese Speaking Countries).

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www.mdpi.com/journal/Symmetry

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www.mdpi.com/journal/physiologia

The Journal of Physiology

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www.physoc.onlinelibrary.wiley.com/journal/

Program

Friday November 11th

08:45 — **Welcome, Registration**

09:45-12:30 — **Workshop 1 ''Exploring biosignals using BITalino" (pre registering required) by PLUX**

11:00-12:30 — **Workshop 2 "new tools to explore hypoxia" (pre registering required) by TypeSolution**

14:00-14:30 — **Opening session with the presence and interventions of:**

H.Ex. The President of the Institute Politécnico de Coimbra and the Director of the Escola Superior de Tecnologia da Saúde

H.Ex. The Minister of Ciência, Tecnologia e Ensino Superior (represented)

H.Ex. Susan Wray, Int Union Physiological Societies and Federation of European Physiological Societies (FEPS) President

L. Monteiro Rodrigues, Chairman of SPFIS

14:30-15:30 — **Invited Lectures**

"Physiology in EUROPE" - Susan Wray (UK) FEPS and IUPS President

"New strategic direction in the US to improve physiology teaching and learning" - Erica Werhwein (USA) PMIG Director

Break - visit to exhibitors and posters

16:30-18:00 — **Seminar I Teaching Physiology**

Moderators: Vicente Martinez Perea -The Spanish Physiological Society and Carlos Nunes Filipe - Nova Medícai School

"Human Physiology in the Portuguese higher education system - a current view" L. Monteiro Rodrigues et al., CBIOS Lisboa, U. Lusofona "Clinical Physiology in Portugal - a recent history" Telmo Pereira, ESTeSC, I.P.Coimbra

"Novel pedagogical tools in the teaching of medical physiology - is new always better?" Diogo Santos Ferreira, Dep. Surgery and Surgery & UnIC@RISE, Fac. Medicine, - U.Porto - NOT SUBMITTED

"Human vs. machine learning: enhancing student metacognition via the active learning of physiology" Jorge Ascenção Oliveira, Dep Pharmacology, Fac. Pharmacy-U.Porto

"Implementation of physiology and pathophysiology teaching in a novel Portuguese undergraduate medical curriculum" André Leite- Moreira, U.Aveiro Dep Medical Sciences

Round table and open discussion

18:00 **Closure**

20:00 **Society Meeting Dinner (business dress)**

Saturday November 12th

09:00-11:00 **Seminar II *Who What Where* - Show room of Physiological research in Portugal Short presentations from representative national labs: BiolSI FCUL ; CBIOS ULusofona; CIAFEL | FADEUP ; CIDESD | UTAD; DCF FMUP; IBEB FCUL; ICBAS MedInUP; iCBR FMUC; IF CCUL FMUL; IF FMUC; NOVA FCMUNL; IT-IST UL; LABINSAUDE IPC**

Break - visit to exhibitors and posters

12:00-12:30 **Wrap-up**

Moderator: Adelino Leite-Moreira, DCF Fac. Medicine U.Porto

12:30 **Lunch break**

13:00 ***SPF General Assembly***

Election of the new board 2022-2025

14:30-16:30 **Podium Session - Selected podium presentations**

Moderators: Ana Sofia Fernandes, CBIOS ULusofona and Telmo Pereira, ESTeSC IPC

Neurophisiology

CL (21493) - VPAC1 and VPAC2 receptors are opposingly altered in the Li2+-pilocarpine model of temporal lobe epilepsy. - Marta Bento et.al

1 - Departmento de Quimica e Bioquímīca, and 2-Bīosystems & Integrative Sciences Institute (BiolSI), Facutdade de Caências da Universidade de Lisboa, Lisboa, Portugal.

CL (21505) - ß-adrenoceptor antagonists affect the establishment of traumatic memories and anxiety-like behaviour in a post-traumatic stress disorder mice model — Rafaela Seįxas et.al

1 - Department of Immuno-Physīotogy and Pharmacology, Laboratory of General Physiology, School of Medicine and Biomedical Sciences (ICBAS), University of Porto (UP); 2 - Center for Drug Discovery and Innovative Medicines, University of Porto (MedInUP); 3 - Department of Biomedicine, Faculty of Medicine, University of Porto (FMUP)

CL (21507) - Contextual fear memory impairment in adrenaline-deficient mice may be related to downregulation of the M4 muscarinic receptor subtype in the hippocampus- Ana Oliveira et.al

1 - Department of Immuno-Physiology and Pharmacology, Laboratory of General Physiology, School of Medicine and Biomedical Sciences (ICBAS), University of Porto (UP); 2 - Center for Drug Discovery and Innovative Medicines, University of Porto (MedInUP),; 3 - Institute for Molecular and Cell Biology (IBMC), Institute for Research & Innovation in Health (I3S), University of Porto

Integrated - Metabolism

CL (21433) - WWOX inhibition by Zfra1-31 ameliorates brain mitochondrial dysfunction and oxidative stress in a mouse model of type 2 diabetes— Cristina Carvalho et.al

1 - Center for Neuroscience and Cell Biology (CNC), University of Coimbra, Portugal; 2 - Institute for Interdisciplinary Research (III), University of Coimbra; 3 - Center for Innovation in Biomedicine and Biotechnology (CIBB); 4 - PhD Program in Experimental Biology and Biomedicine (PDBEB), University of Coimbra, 3030-789 Coimbra, Portugal; 5 - Institute of Physiology, Faculty of Medicine, University of Coimbra, Coimbra, Portugal

CL (21595) - Methyl glyoxal and high fat diet negatively impact perivascular adipose tissue contributing to vascular dysfunction in rat models of metabolic syndrome - Adriana Malheíro et.al

1 - Institute of Physiology, iCBR, Faculty of Medicine, University of Coimbra, Portugal

CL (21495) - Physiology of body composition - how do vegetarians and omnivores differ? - Cíntia Ferreira-Pêgo et.al

1 - CBIOS - Universidade Lusófona's Research Center for Biosciences & Health Technologies

CL (21500) - Long-term management of metabolic diseases after bariatric surgery - Claudia Amaro Dos Santos et.al
1 - CBIOS

Integrated - Cardiovascular

CI (21631) - Ketones impact on cardiac outcomes in a rat model of HFpEF - Alexandre Gonçalves et.al

1 - Faculdade de Medicīna da Universidade do Porto (FMUP); 2 - Instituto de Ciências Nucleares Aptīcadas a Saúde; 3 - Instituto de Investigação Clinįca e Biomédica de Coimbra (iCBR); 4 - University Hospital Würzburg

CI (21437) - Therapeutic implications of urocortin-2 in Heart Failure with preserved Ejection Fraction - Inês Vasconcelos et.al

1 - Faculty of Medicine University of Porto, UnIC-RISE, Department of Surgery and Physiology, Porto, Portugal; 2 - Faculty of Nutrition and Food Sciences, University of Porto, Porto, Portugal

CI (21503) - Cardiac stretch-induced compliance is impaired in a rat model of heart failure with preserved election fraction - André Leite Moreira et.al

1 - Faculdade de Medicina da Universidade do Porto; 2 - UnIC @ RISE;

3 - Centro Hospitalar Universitário sao João

CI (21644) - Muscle reoxygenation kinetics during six different variations of push-up exercise - Andreia Teixeira et.al

1 - University of Frás-os-Montes e Alto Douro, Vila Real, Portugal; 2 - Department of Sports Science, Exercise and Health; 3 - Research Center in Sports Sciences, Health Sciences and Human Development (CIDESD), Vila Real, Portugal

CI (21659) - SALUS - an loT wearable device for the assessment of cardiovascular health-João Brito et.al

1 - Instituto de Biofísica e Engenharia Biomédica, Faculdade de Ciências da Universidade de Lisboa; 2 - Unidade de Sincope, Cardiologia, Hospital de Santa Marta, Centro Hospitalar e Universitário de Lisboa Central; 3 - Medicina 2.4 Núcleo de tnvestigaçSo Arterial, Centro Hospitaler e Universitário de Lisboa Central, NOVA Medical School
Discussion

17:15 **Break - visit to exhibitors and posters Awards and Distinctions**

13:00 **Wrap-up and Closing Remarks. Closing Champagne toast**

Invited Lectures

Physiology in EUROPE – Susan Wray (President of FEPS)

It is not difficult to make the case that Europe has the longest history of studying and writing about physiology. The Ancient Greeks and Romans were clearly curious about, how the body works, which is surely the definition of physiology.

From 1600 onwards the accrual of physiological knowledge that we would recognize today began around the 17th Century. William Harvey's simple, elegant but revolutionary studies, revealing our circulatory system, showed the power of experimental approaches and the application of scientific logic. Marello Malpighi and Antoni van Leeuwenhoek have their place in scientific history for beautifully putting anatomic structure and function together, to increase knowledge of physiology.

Today as physiologists in Europe and beyond we combine disciplines and techniques unheard of then, and even at the start of this century, to continue discovering functions and physiological mechanisms. Working in multidisciplinary teams and with labs across Europe, physiologists give meaning to so many studies, and provide the direct links to translation, and the improving of human and animal health. As physiologists we are trained to think holistically, even when working at the cell or molecular level, and I don't think that is ever going to go out of fashion, even if the departments we work in change names.

I am proud to lead FEPS, the umbrella organization of 35 national societies of physiology in Europe, founded in 1991. The goals of FEPS are to help these national societies, to promote physiology and physiologists, support early career researchers, stimulate scientific research and aid communication and interactions between national societies.

That physiology throughout Europe is vibrant can be seen from the FEPS Newsletter and website. Last month we partnered with three national societies to hold Europhysiology2022 in Denmark. This was a wonderful meeting, not

least because we could come together internationally for the first time in two years and enjoy living and breathing physiology for three days. Perhaps not surprisingly, the meeting attracted well over 1000 participants.

Another indication of the strength of European physiology is, that our newest FEPS member, is holding its 2nd International meeting – the Portuguese Society of Physiology. Congratulations to all involved and wishing you a highly successful meeting, focused on "*Physiology for a Healthier, Longer Life*"

New strategic directions in the USA to improve physiology teaching and learning – Erica Wehrwein – PMIG Director

Physiology is the foundation of medicine.

It is an essential topic for undergraduate, graduate, medical, and other allied health students to master. Bachelor's degree programs in physiology are very popular in the USA with numbers of students enrolled and total number of programs increasing.

The Physiology Majors Interest Group (P-MIG) has recently published a collection of 17 manuscripts on the state of undergraduate physiology in the US and Canada. Medical Schools are increasing in number and size. This creates a challenge to finding enough qualified faculty. Also, there has been a trend for integration of medical curricula, and it is an urgent need to have physiology advocated in the curriculum. Recently, the American Physiological Scoiety (APS) launched a new Center for Physiology Education. This is a public resource that serves all levels of higher education in physiology. Some content is for members only and that includes modules on teaching integrative physiology.

There are 3 keys trends for physiology education to be considered:

1. APS and PMIG have endorsed teaching from the core concepts, 2. physiology education research is a growing trend to improve the scholarly approach to teaching in our field, and 3. A new focus is encouraged that includes explicit coverage and attention to professional and employable skills in physiology courses and programs.

There is a growing awareness about the importance of cultivating excellence in physiology teaching and learning at all levels in the US and we hope to expand the dialogue to our international colleagues facing similar challenges.

Keynote Lectures

SEMINAR I – Teaching Physiology

OC - (21651) - Implementation of physiology and pathophysiology teaching in a novel Portuguese undergraduate medical curriculum

Andre Leite-Moreira*

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**aleitemoreira@gmail.com*

PRESENTING AUTHOR PROFILE

André Leite Moreira currently works at the Cardiovascular R&D Unit, University of Porto and the Department of Anaesthesiology of São João Hospital. His fields of interest include diastolic dysfunction, heart failure and cardiovascular anesthesia. He has expertise in functional and molecular laboratory techniques, as well as in clinical research.

ABSTRACT

The University of Aveiro is submitting a proposal for a new 12 semester undergraduate medical course. This represents an opportunity to implement a modern program featuring vertical and horizontal course-wide curricular integration of basic and clinical sciences and course-long research teaching and tutoring. The areas of physiology and pathophysiology are a central component of the curriculum, most prominent during the first 6 semesters.

After a short introduction to cellular and molecular structure and function, the first 4 semesters focus on the normal and abnormal structure and function of organ systems (sequentially: musculoskeletal, nervous, endocrine, cardiovascular, blood and immunology, respiratory, urinary, digestive and final integration) and the next 2 shift to the basics of pathology, diagnosis and therapy. The syllabus is connected to a parallel teaching vector focusing on clinical communication and procedures and including weekly contact

with real patients in a community or hospital based setting. Physiology and pathophysiology will be taught simultaneously with systems morphology and embryology.

Classes of the former two are divided into seminars (punctuated by questions every few minutes); case-based learning sessions; problem-based theoretical-practical lessons and laboratory classes (including simulation and performance of clinical procedures e.g. echocardiography, respiratory function tests). Assessment methods include: execution of techniques and interpretation of cases with structured objectives; multiple-choice question midterm test; online self-monitoring questions on a gamified system and a final exam structured around problem solving and interpretation of clinical vignettes.

The teaching body firmly believes this model is of great educational value and highly motivational to students and hopes to impart in them a solid foundation of physiology and pathophysiology together with key interconnecting basic and clinical knowledge and skills.

Keywords: undergraduate teaching, physiology, pathophysiology, integrated teaching

OC - (21622) - Human vs. Machine learning: Enhancing student metacognition via the active learning of physiology

Jorge Oliveira*

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Jorge Ascenção Oliveira (PharmD, PhD) coordinates Physiology and Neuroscience units at the Faculty of Pharmacy, University of Porto, where he Presides the Pedagogical Council. He leads the Mitochondria and Neurobiology Lab at UCIBIO - Applied Molecular Biosciences Unit. Jorge is an European Certified Pharmacologist and a trained Data Scientist. He was distinguished with several Pedagogical Awards from the U.Porto (Excellence in e-learning, Pedagogical Excellence, and Pedagogical Innovation).

ABSTRACT

While machines outperform human associative memory, education should emphasise metacognition – including emotional intelligence. Physiology learning provides ample opportunity for cognitive development. Indeed, an updated mechanistic understanding of human body function and its dynamic regulation requires metacognition (awareness and understanding of thought processes, to self-assess, monitor and improve by self-regulation). This study implemented an assessment-based strategy to foster metacognition while students learn Physiology. Pharmaceutical Sciences students self-assessed their interest in Physiology and study strategies (Survey-1); monitored their skills in weekly formative tests (ForTes - including a self-prediction of score and percentile); and received counselling on active study techniques. Students reported their study adaptations in Survey-2; and were rewarded for accurate predictions of performance in Exams. Anonymised data from ForTes and surveys were analysed with R language to compute statistics and perform machine learning (ML). Unsupervised ML of Survey-1 identified 3 student clusters with different levels of motivation and study, which associated with different Exam scores. A supervised ML model trained with ForTes predicted

Exam failures with over 90% accuracy, and the actual Exam scores (0-20) with error under 2 points. Analysis of ForTes over time evidenced significant improvements in students' metacognitive ability to accurately self-assess, despite being challenged with different questions about different Physiological systems over time. Moreover, the frequent report of study adaptations in Survey-2 supports widespread metacognitive regulation. This study provides evidence-based support for enhanced student metacognition and suggests that ML models can accurately predict student failure, enabling early counselling towards success. This study also emphasises the need for authentic assessment to promote Physiological skills.

Keywords: metacognition, active learning, machine learning, human physiology

OC - (21496) - Human physiology in the Portuguese higher education system – A current view

Luis M Rodrigues*, Iris Guerreiro, Joao Gregorio, Vera Isca

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ABSTRACT

The Higher Education System (HES) in Portugal changed in the last forty years, with the Bolonha Declaration being easily recognised as the most important landmark. Signed in 1999 by 30 countries (today almost 50), it created a harmonised European system based on mobility and citizenship. The European Credit Transfer and Accumulation System (ECTS) is a critical instrument of this new reality. More than 15 years have passed, and huge differences are already recognised regarding (a) the mutual recognition of academic degrees and competences (b) the exponential growth of students´ mobility and (c) the access and growth of the HES where the student populations have more than doubled.

Bolonha did not change the core structure organisation of our HES-oriented to main profession-narrow band courses / syllabus, away from the American –system. Widely recognised as a central discipline in medical education, a progressive valorisation of Physiology in the Portuguese HES for health sciences was noted in the late 1970s. Physiology began to be included as part of the syllabus from Pharmaceutical Sciences, to Sport and Physical Education, later to all other areas from Health Technologies to Nutrition Sciences. During the same time in UK countries, an apparent loss of importance of physiology

was indicated as a serious issue, with examples where practical physiology training had reportedly nearly disappeared. Since then, many concerns have been raised worldwide about this reduction of visibility of human physiology in current biomedical curricula as new cycles of development are being designed for the EU HES (the European Universities).

The present approach updates the current status of physiology teaching and learning in our country, through the database available at the regulatory authority (DGES). This exploratory data aims to identify critical characteristics that might help to better prepare the Portuguese physiology teaching and research for the future.

Keywords: Physiology teaching, Higher Education System, Portugal, current views

OC - (21556) - Clinical physiology in Portugal – A recent history

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ABSTRACT

Clinical Physiology is envisioned as an applied branch of physiology, particularly focused in the implementation of sophisticated methods for studying human physiology, in settings including clinical, research and educational contexts. Being a well established field in the north of Europe, Clinical Physiology was only recently established in Portugal and is under a maturing process. This new model was implemented in 2014 as a fusion of two previous programmes, Cardiopneumology and Neurophysiology, with a long tradition of mainly clinical activity in several medical specialties, including Cardiology, Pneumology, Heart Surgery, Vascular Surgery, Sleep Medicine and Neurology. The evolution to Clinical Physiology takes advantage of the similarities between these two components (Cardiopneumology and Neurophysiology), and provides a coherent integration of knowledge, competences and skills that are intertwined to the broad study of human physiology. This evolution offers the possibility to establish a purely physiological professional/researcher that will be able to provide a bridge between basic physiology and many clinical specialties. A comprehensive discussion about the clinical physiology model will be decisive to tailor its evolution envisioning the future challenges and needs of modern Physiology.

Keywords: Clinical Pysiology, Physiology, Education

Seminar II - Who, What, Where

OC - (21411) - The Portuguese physiology road-map from molecules to the individual – perspectives from CBIOS

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ABSTRACT

Physiological research has always been a relevant component of CBIOS activity from its very beginning which can be tracked back to the late nineties as one of the first labs in the country dedicated to human skin functions and mechanisms. Currently CBIOS research is dedicated to principal health issues, all related with major disease burdens (metabolic, cancer, infection, inflammation) under an integrative view and particularly attentive to the Portuguese speaking communities realities and needs. Nevertheless physiological research is always present from cell proliferation and migration mechanisms to development of in vivo models to study function or disease mechanisms, or to explore new technologies and endpoints with clinical interest. These research activities are group in "modulators" and "modelling"

scopes in their areas of expertise and interest. Interdisciplinary collaborative work then results in customisation as assessment / intervention proposals involving new bioactives / ingredients, materials or strategies to tackle problems previously screened from basics.

Keywords: The Portuguese Physiology Road-map

PO - (21429) - Cell migration in health and disease: Research @CBIOS

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ABSTRACT

Cell migration is essential for physiological processes as diverse as morphogenesis, proper immune defence, wound repair, and tissue homeostasis. Aberrant cell migration is found in various pathologies and it is a hallmark of cancer malignancy. Cell motility can occur by different types of cell migration. Cells can move either collectively or individually, in a directed or random way, and involving different mechanobiology processes. At CBIOS, we have established a plethora of techniques, especially in vitro, to experimentally assess different types of cell migration and related mechanisms. These include techniques to evaluate collective migration (e.g., wound-healing and zone exclusion assays), single cell migration (e.g., single cell tracking, chemotaxis), or cell invasion (e.g., transwell invasion, 3D spheroid invasion, gelatine degradation). To explore the mechanobiology processes involved in cell migration, our mechanistic approach includes the analysis of cell adhesion, morphometry, and cytoskeleton characteristics. We have applied these techniques to explore how Ca^{2+} and ROS homeostasis impact cell motility, and to study the effects of xenobiotics (e.g., drugs, food bioactives) at this level, especially in the contexts of cancer progression and skin repair.

Keywords: Cell migration, in vitro, mechanobiology, cytoskeleton

OC - (21432) - Human-centred healthcare innovations of practical utility at it PIA-Lx

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ABSTRACT

Instituto de Telecomunicações (IT) is a private non-profit organisation of public interest, recognized by the Portuguese Foundation for Science and Technology (FCT) with the statute of Associated Laboratory. IT was established with the mission of creating and disseminating scientific knowledge in the field of telecommunications and related areas, and to carry out knowledge transfer to society. Across its main sites and branches, IT gathers 600+ researchers in different stages of their career, organized in groups, and framed under five thematic lines: Wireless Technologies; Optics and Photonics; Information and Data Science (IDS); Networks and Services; and Basic Sciences and Enabling Technologies.

The Pattern and Image Analysis group (PIA-Lx [1], part of the IDS thematic line), located in Instituto Superior Técnico, develops research on several biomedical-related topics: biosignal acquisition and processing; machine learning (ML) and artificial intelligence (AI) for biosignals and medical image analysis (MRI, CT, ultrasound, microscopy); wearable and invisible devices for health and wellbeing monitoring. Highlights of our research include a patented technology for "invisible" electrocardiography (ECG) and biometric

recognition [2] that resulted in a spin-off company, a low-cost research-grade physiological data acquisition system licensed to industry and currently with a global community of 10k+ users [3], or the recent advances in ML and AI in radiomics and radiogenomics [4]. To date, the work developed in our group has resulted in 600+ publications (peer-reviewed journal articles, papers in conferences with scientific refereeing, book chapters, and books), participation in 30+ projects (sponsored by the European Commission, FCT and industry), 12+ patents, and 4 spin-off entrepreneurial initiatives.

Keywords: Biosignal Acquisition, Wearables, Invisibles, Machine Learning, Artificial Intelligence, Radiomics, Radiogenomics, Biomedical Instrumentation

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OC - (21492) - Retinal degenerative diseases: What can we learn from in vitro and animal models?

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António Francisco Ambrósio is Coordinator Investigator at the Coimbra Institute for Clinical and Biomedical Research (iCBR), Faculty of Medicine, University of Coimbra. He is leading the Retinal Dysfunction and Neuroinflammation Lab since 2002. His main research interests are focused on retinal degenerative diseases (diabetic retinopathy, glaucoma and age-related macular degeneration), and particularly on neuroinflammation mediated by microglial cells and on cell-cell crosstalk.

ABSTRACT

The retina is a sensory thin structure that lies at the back of the eye and plays a key role in vision. Retinal degenerative diseases, such as diabetic retinopathy, glaucoma and age-related macular degeneration, affect more than 300 million people worldwide. These diseases have no cure, the treatments available are scarce and mainly targeted for the later stages. Treatments can be also invasive, with adverse effects, and ineffective in a high percentage of patients. At Retinal Dysfunction and Neuroinflammation Lab we have been interested in dissecting disease mechanisms, with the aim of identifying new therapeutic targets and developing novel therapeutic strategies. Two major interests are neuroinflammation mediated by microglial cells, the immune cells of the central nervous system, and the cell-cell crosstalk. We have been using in vitro models, including primary mixed retinal cultures and purified primary cell cultures (retinal ganglion cells, microglial cells, Müller cells, endothelial cells, retinal pigment epithelial cells) from rodents, bovine and porcine, as well as retinal organotypic cultures from rodents and humans, and cell lines. We also use several animal models of retinal degenerative diseases and retinal ischemia-reperfusion. To address our goals, in addition to cell and molecular biology techniques and bioimaging, we use several in

vivo techniques to assess retinal structure (optical coherence tomography) and function (electrophysiology), and visual acuity (optomotor test).

Keywords: Retina, Retinal degenerative diseases, Electrophysiology

OC - (21497) - Exploring the role of metaplasticity in synaptic function under physiological conditions and in animal models of aging and epilepsy using integrative approaches

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ABSTRACT

Metaplasticity is a key regulatory mechanism of synaptic plasticity phenomena, that in turn are essential to every aspect of hippocampal-dependent learning and memory, including those involved in selective memory storage, forgetting and memory reformulation. Maladaptive metaplasticity is also often associated with natural aging or disease processes like epilepsy. The Epilepsy and Aging Lab at DQB and BioISI, FCUL is dedicated to characterizing the synaptic structure and plasticity alterations associated with post-weaning development, aging and epileptogenesis and its potential reversal/therapy by: 1) cognitive training using novelty stimuli; 2) ligands of endogenous neuropeptide receptors (particularly VIP receptors) and 3) the ketogenic diet. To pursue these objectives, we use mostly the rat animal model. *In vivo* approaches include the Li^{2+}-pilocarpine model of epilepsy and accelerated aging induced by D-Gal exposure. Behavioral characterization of altered cognition, locomotion and anxiety levels involve the radial-arm maze, open field, elevated plus maze, novel object recognition and mismatch novelty tasks.

Cognitive training using novelty stimuli is performed using repeated exposure to the mismatch novelty task in the holeboard. *In vitro* models of epileptogenesis in hippocampal slices comprise seizure induction by exposure to chemical agents like bicuculine and altered ionic media composition (absence of Mg^{2+}; elevated K^{+}) as well as hypoxic and ischemic conditions. Alterations in synaptic plasticity (LTP, LTD and depotentiation) are estimated using both electrophysiological methods and molecular biology techniques. Changes in VIP receptors, structural and signaling proteins relevant for modulation of synaptic plasticity use similar experimental approaches as well as IHC techniques. Our Lab is currently developing cell culture models of seizures for following alterations in lipid membrane properties in epileptogenesis using live imaging with fluorescent probes.

Keywords: Neuroscience, Epilespy models, Aging, Postweaning development, VIP, hippocampus, cognition

OC - (21510) - Labinsaúde - A multidisciplinary approach to applied research in health sciences

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ABSTRACT

The LabinSaúde is a research unit that promote a multidisciplinary approach to applied research in health sciences. The research unit's main mission is to promote fundamental and applied scientific activity, aiming to establish a strong link between theory and practice, as well as the transfer of knowledge to society.

LabinSaúde research priority areas are aging and health, promotion of health and welfare and disease prevention (food, tourism, human mobility, prevention), diagnosis and therapy, advanced biotechnologies applied to health (teaching-simulation, early diagnosis), and public, occupational and environmental health.

The LabinSaude have been developed several projects namely in active aging and health promotion and disease prevention. The AGA4life project, implemented an AGA model, based on an individual, holistic and multidisciplinary assessment protocol, with intervention programmes tailored and implemented on an individual basis, in articulation with conventional health care system, aiming preventing frailty and functional, cognitive and social

decline of the elderly, thus promoting autonomy, wellbeing and social inclusion. Another ongoing project focuses on the salt replacement with halophytic plants (Salicornia), in order to reduce cardiovascular disease, the SaliSalt project.

Keywords: LabinSaúde, health sciences, applied research

OC - (21592) - Neurometab.Lab: Exploring new avenues for the treatment of metabolic diseases

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Silvia V. Conde is a Professor of Pharmacology and Neuroscience at NOVA Medical School (NMS) and Principal Investigator at 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. After her PhD, she has been dedicated to understanding the pathophysiological alterations in the CB and autonomic nervous system that are in the genesis of cardio-metabolic and respiratory Human diseases.

ABSTRACT

Metabolic diseases as obesity and type 2 diabetes (T2D) are major public health problems, defined by WHO as worldwide epidemics. The therapeutic strategies are scarce. Our group is focused on exploring the pathophysiological mechanisms behind the development of metabolic diseases and on the identification of prevention strategies and treatment interventions to help stem these epidemics. Our primary focus is the carotid body (CB), a peripheral chemoreceptor, classically defined as a hypoxia sensor. Our group has provided major findings supporting the role of CB as a metabolic sensor whose dysfunction is involved in dysmetabolic states. We found that metabolic diseases are associated with increased CB chemosensitivity in animals and humans and that carotid sinus nerve (CSN) resection, the CB sensitive nerve, prevents and reverses dysmetabolic states induced by hypercaloric diets. More recently, we demonstrated for the 1st time the beneficial effects

of the electrical modulation of the CSN to treat metabolic diseases, as this technology was able to restore insulin sensitivity and glucose tolerance in T2D rats. Aiming to facilitate the emergence of this therapeutic for T2D, we are now mapping CB neural pathways, characterizing the CSN nerve fibers and disclosing the molecular mechanisms involved in the aetiology of insulin resistance and obesity. Additionally, we have a 2nd line of research that aims to investigate if the modulation of adenosine signaling/metabolism in insulin-sensitive tissues ameliorates dysmetabolism.

We use a translational and multidisciplinary scientific approach, going from the study in cells, to animals and humans. As such, we use traditional and cutting edge methodologies from biochemistry, to cell and tissue biology and imaging, to electrophysiology and in vivo studies. We are also focused on the development of mathematical and computational tools to analyze data and to promote the wellbeing of metabolic disease patients.

Keywords: metabolic diseases, carotid body, adenosine, neuromodulation

OC - (21602) - Obesity, diabetes and related complications

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ABSTRACT

The last decades have been marked by an increased prevalence in non-communicable diseases such as obesity and type 2 diabetes mellitus (T2DM). In obesity a major excessive accumulation of fat occurs leading to the release of many adipokines and pro-inflammatory cytokines, which increase the risk of a myriad of chronic diseases including T2DM, hypertension, hyperlipidemia, cardiovascular disease, stroke, dementia, and cancer. Likewise, T2DM confers an elevated risk of developing serious complications, including macrovascular (e.g. cardiovascular disease, stroke) and microvascular (e.g. retinopathy, neuropathy and nephropathy) diseases. Macro and microvascular complications are major comorbidities that need to be tackled to improve and extend the quality of life of patients. At the Institute of Physiology of the Faculty of Medicine, we perform mainly basic research aimed to 1) explore the mechanisms underlying obesity, T2DM, its complications and related disorders and 2) test the therapeutic efficacy of some pharmacological agents. Our studies are performed in cellular and rodent models of disease as well as in human tissue samples, under a translational perspective.

Keywords: Obesity, Type 2 diabetes, Complications

OC - (21629) - Acute and chronic effects of physical exercise on cardiorespiratory and haemodynamic responses

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ABSTRACT

Within the scope of the GERON community of the CIDESD, one of the research areas of Exercise Physiology is related to optimize the physical fitness and health in both clinical and no-clinical settings. Specifically, it is intended to study the effect of different physical exercise scenarios on cardiovascular, hemodynamic and respiratory adaptations in human beings.

The research to pursued this approach, is built-in two paths: one dedicated to studying the acute physiological effects of physical exercise (during and post-exercise), under a precise exercise dose. Understanding how a specific dose of exercise impacts on different body systems, whether it is beneficial or not, and how well it is received and tolerated by different populations. The dose of exercise can be tailored for a specific purpose, such as hypertensive and peripheral arterial disease populations, or promoting a unique stimulus to the cardiovascular system, or even improving the role of specific muscles.

The exercise dose constraints used are the exercise intensity as well the exercise mode (treadmill, cycle, elliptical and row) and the muscle contraction pattern; the other path, is devoted to chronic physiological adaptations to exercise-based interventions, designed specifically to the needs of the Portuguese population physical fitness and health requirements. The effects of long-term multicomponent training programs, in physical fitness components (e.g. cardiorespiratory fitness), blood pressure, markers of arterial stiffness and cardiovascular risk factors, are also an important target of study.

In addition, the interface with other areas of science such as technology, with the use of instruments of reduced dimension and wearables, is also explored for a better representation and knowledge of the physical exercise.

Keywords: Exercise Physiology, Acute responses, Chronic responses, blood pressure, Exercise Dose Monitoring

OC - (21635) - Cardiovascular physiology: From bench to bedside and back

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ABSTRACT

The Cardiovascular R&D Center (UnIC) was created in 1994 to fill the gap in translational research of cardiovascular disease (CVD). CVD is a highly relevant medical and socio-economic research topic since it is the first cause of death globally and one of the leading causes of impaired quality of life, particularly amongst the elderly. Since its creation, UnIC has been devoted to advancing cardiovascular physiology's scientific research and technological development. UnIC includes researchers from several Departments of the Faculty of Medicine of the University of Porto and Centro Hospitalar Universitário de São João and combines basic and clinical sciences to achieve a solid translational and integrative perspective in a bench-to-bedside and back-to-bench approach.

Thus, UnIC relies on the strong collaboration between researchers from multiple medical and non-medical specialities related to cardiovascular medicine,

such as cardiology, cardiothoracic surgery, internal medicine, anaesthesiology, biologists, biochemists, engineers, statisticians and other professionals fully committed to CVD research.

The current research topics at UnIC are focused on: i) Heart Failure (HF); ii) Pulmonary Hypertension (PH) and Right Ventricle (RV); iii) Myocardial remodeling and valvular Heart disease; iv) Ischaemic coronary heart disease and atherosclerosis; and v) Technological and applied cardiovascular research. UniC relies on a dynamic research structure that fosters national and international collaborations, either with academia or with industry, enabling a self-sustainable strategy.

Keywords: Physiology, cardiovascular research, heart failure

OC - (21657) - Physiology in a biomedical engineering context: Challenges and solutions

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ABSTRACT

In this session I will present the Instituto de Biofísica e Engenharia Biomédica at the Faculdade de Ciências da Universidade de Lisboa, as well as the work we have been developing more recently at my research group EDGE, covering longevity, neuromodulation, brain and lung imaging, cancer therapeutics, wearables, physiological computing, and digital health. I will also address the technologies, techniques and methods we use, including artificial intelligence, brain-computer interfaces, virtual and augmented realities, 3D printing, 5G, and blockchain, to address both clinical and non-clinical challenges, including sports, and marketing.

Keywords: Physiology, Biomedical Engineering, Physiological Computing, Wearables, Brain-computer interfaces, Neurophysiology, Neuromodulation, Biomechanics, Sports, Cardiovascular and Lung applications, Cancer

Podium Presentations

Theme: Heart, Circulation and Respiration

OC - (21437) - Therapeutic implications of Urocortin-2 in heart failure with preserved ejection fraction

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INTRODUCTION

Heart failure with preserved ejection fraction (HFpEF) prevalence has increased and accounts for as much as 50% of heart failure cases. Due to limited treatment options, novel therapies evaluation in experimental models is vital. Urocortin-2 (UCN2) has been found to have significant beneficial hemodynamic, hormonal and renoprotective effects in both animal models and humans with heart failure. In this work, we studied the role of the UCN2/CRHR2 system in the pathophysiology of HFpEF and evaluated the efficacy of UCN2 as a novel therapeutic strategy.

METHODS

18-week-old male ZSF1-Lean (n=26) and ZSF1-Obese (n=28) rats randomly received either UCN2 (15µg/kg/day, subcutaneously) or vehicle (0.9% NaCl), for 12 weeks. During the treatment period, evolution of cardiac (dys)function was assessed by echocardiography and exercise tolerance test. After treatment, invasive hemodynamic analysis was performed, with subsequent sample collection.

RESULTS

mRNA expression of UCN2 and CRHR2, as well as protein levels of CRHR2, were decreased in the LV of ZSF1-Obese rats compared to ZSF1-Lean and correlated with LV structure and diastolic function. Obese rats showed systemic hypertension, decreased endurance capacity and impaired LV relaxation. Chronic UCN2 treatment attenuated hypertension and modestly enhanced effort tolerance. In both morphometric and echocardiographic analysis, we found that Obese rats presented significantly higher cardiac and LV weight, compared to Lean counterparts. Cardiomyocyte cross-sectional area and fibrosis were found to be increased in Obese rats, corroborating morphometric and echocardiographic measurements. Chronic UCN2 treatment attenuated both cardiac hypertrophy and fibrosis.

CONCLUSION

This work suggests that UCN2/CRHR2 system is altered in experimental HFpEF and that chronic administration of UCN2 attenuates LV dysfunction and remodeling, in particular the hypertrophic changes of the cardiac muscle.

Keywords: Heart Failure, Animal models

OC - (21503) - Cardiac stretch-induced compliance is impaired in a rat model of heart failure with preserved ejection fraction

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PURPOSE

We recently described stretch-induced compliance (SIC), a decrease in cardiac stiffness in response to increased end-diastolic volume (EDV) partly mediated by titin phosphorylation by protein kinase G (PKG). Titin hypophosphorylation due to low PKG activity is a hallmark of the increased diastolic stiffness observed in heart failure with preserved ejection fraction (HFpEF). Increased EDV is a well-known factor of decompensation in HFpEF, which has been mainly attributed to vascular and systolic stiffening but other mechanisms may at play. We therefore sought to test whether SIC is impaired in an animal model of HFpEF.

METHODS

The hearts of 25 weeks old ZSF1 obese (Ob- HFpEF model), ZSF1 lean (Ln- hypertensive control) and Wistar Kyoto (WKY- wild-type control) rats (n=5 each) were quickly excised and mounted on an isolated ejecting

heart preparation with pressure-volume recording where, after a period of stabilization, the left ventricle (LV) was either stretched by abrupt increase EDV or underwent no change for 15 minutes. Passive tension (PT) was measured in skinned cardiomyocytes extracted from non-stretched and stretched LV (n=5 myocytes per sample) before and after incubation with PKG or serine-threonine protein phosphatases (PP).

RESULTS

After 15 minutes of stretching, end-diastolic pressure significantly decreased in the Ln and WKY groups but not the Ob group. Skinned cardiomyocytes from stretched LV in the former groups exhibited decreased PT compared to non-stretched hearts but this finding was blunted in the Ob group. Incubation with PKG decreased PT in myocytes from non-stretched Ln and WKY groups but not in previously stretched LV. All myocytes from Ob hearts showed significant PT reduction with PKG incubation. PP incubation only increased PT significantly in myocytes from WKY hearts and stretched Ln hearts.

CONCLUSION

SIC seems to be impaired in a rat model of HFpEF, which may be promising as a diagnostic or prognostic marker in this disease.

Keywords: heart failure, diastolic function, titin, protein kinase G, HFpEF

OC - (21631) - Ketones impact on cardiac outcomes in a rat model of HFpEF

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Alexandre Gonçalves is a PhD student at the Faculty of Medicine, University of Porto, holding a BSc in Biochemistry and a MSc in Biomedical Research. He has co-authored 5 original paper, delivered 3 oral presentations and was awarded 9 prizes. He (co)supervises 2 MSc students. He has acquired laboratorial experience in cardiomyocytes function assessment techniques, echocardiographic evaluation, molecular biology methodologies, animal handling, and a strong background in cardiovascular research.

ABSTRACT

Cardiovascular disease remains a major public health concern and the primary cause of death worldwide. A subtype of heart failure (HF), HF with Preserved Ejection Fraction (HFpEF) affects 1.1-5.5% of the general population whilst being associated to poor prognosis and hospitalization. This is particularly concerning given that pharmacological options remain limited. While the specific mechanisms through which these drugs, SGLT2 inhibitors, reduce all-cause mortality remains unknown, data from the recent EMPEROR-Preserved trial shown associations with changes in ketone levels.

In this study, we use a well characterized HFpEF animal model, the ZSF1 Obese rat, to explore the therapeutic potential of increasing ketones in the context

of HFpEF and its cardiovascular and metabolic outcomes. To this end, at 16 weeks of age, when signs of HFpEF are already present, animals (Obese and Lean controls) were randomly allocated to remain on control diet, change to a ketogenic diet (KD) or keep the regular chow but have ketone salts (KS) delivered through drinking water. Several functional and metabolic studies were conducted throughout the protocol, culminating at 23-30 weeks of age.

Hyperglycemia present on ZSF1 Obese rats was reduced by 48% with both treatments, while only KD improved glycemic tolerance and produced sustained high plasma ketone levels. Both KS and KS were shown to significantly reduce HFpEF-associated cardiac fibrosis and hypertrophy. Functional evaluation was performed in isolated cardiomyocytes, exhibiting improvements in Ca^{2+} handling and contractile function with KS. Lastly, these changes seemed to be accompanied by a significant reduction in cardiac complex II mitochondrial respiration with KS, which might constitute a defense mechanism to oxidative stress.

Together, our data seem to suggest that ketones treatment to rise ketonemia might warrant further consideration for future guidelines as coadjutant therapy and pharmacological development.

Keywords: HFpEF

OC - (21659) - SALUS - An IOT wearable device for the assessment of cardiovascular health

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João Brito is preparing to defend his master's thesis in Biophysical and Biomedical Engineering at the Faculty of Science of the University of Lisbon. Throughout his academic career, he developed a keen interest in the interaction between wearable devices and individuals/medical staff, especially its impact on global medical advances. As a result, his master's thesis project was developing an IoT wearable device to assess cardiovascular function.

ABSTRACT

This work describes the designing, prototyping and real-life testing of an Internet of Things (IoT) wearable device, the SALUS device. The solution consists of a purpose-built device, carefully designed for hospital use, that measures Heart Rate (HR), Blood Oxygen Saturation (SpO2), several Heart Rate Variability (HRV) parameters, Breathing Rate (BR) and Peripheral Vascular Resistance (PVR), and, therefore, acquiring most of the data needed for a cardiovascular patient evaluation.

One of the critical challenges was the calculation of a novel way of assessing PVR using PPG. To do so, a regression analysis was performed between the Full Width at Half Maximum (FWHM) of the PPG peak and the value of PVR measured by the Task Force Monitor (TFM).

SALUS was tested in Hospital de Santa Marta following the 2008 front-loaded glyceryl trinitrate head-up tilt protocol used for the tilt test implemented in the Syncope Unit of the Hospital de Santa Marta and the results compared

with the gold standard devices TFM and uMEC10, a cardiovascular monitor. There were limitations to this study since the number of patients tested was small (11) and the sample was clinically heterogeneous. However, the main goal of this pilot study was to show that the SALUS device could be used in a clinical context.

Despite the limitations, the results obtained were favourable for the values of BPM (R^2=0.99), SpO2 (R^2=0.83), and LF/HF (R^2=0.77).

The wearable device here developed holds promise to be a valuable and dependable diagnostic tool, as shown by the values when compared to the gold standard. Further testing and confirmation of other parameters are needed to assess the improvement of this acquisition for rapid screening of cardiac dysautonomia and Cardiovascular Disease (CVD).

Keywords: cardiovascular health, peripheral vascular resistance, heart rate variability, photoplethysmography, wearable, Internet of Things, task force monitor

Theme: Integrative physiology

OC - (21595) - Methylglyoxal and high fat diet negatively impact perivascular adipose tissue contributing to vascular dysfunction in rat models of metabolic syndrome

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ABSTRACT

Obesity and diabetes mellitus promote vascular dysfunction. Perivascular adipose tissue (PVAT) locally influences the functioning of blood vessels. The aim of this work was to characterize PVAT in animal models of metabolic dysfunction and evaluate vascular function and related changes in the vascular wall. An animal model of type 2 diabetes [induced with high fat diet (HFD) and low doses of streptozotocin (STZ)] and an animal model of metabolic syndrome (induced with HFD and methylglyoxal (MG, to promote glycation) will be used.

Wistar rats were divided in four groups: 1) control group; 2) group fed HFD for 4 months; 3) group fed with HFD for 4 months and injected with low-dose STZ (HFDS); 4) group fed with HFD and MG (HFDMG; 75mg/Kg/rat). Several in vivo parameters such as adiposity index, lipid profile, fasting glucose levels, glucose and insulin tolerance tests were determined. At the vascular level, endothelial dependent and independent relaxation and contraction studies were performed in aortic rings in the absence (PVAT–) or in the presence (PVAT+) of PVAT. We also evaluated vascular oxidative stress and determined the inflammatory status of PVAT.

All groups fed with HFD (HFD, HFDS and HFDMG) exhibited insulin resistance, endothelial and PVAT dysfunction. In addition, HFDS rats displayed hyperglycemia, dyslipidemia, high atherogenic index, vascular oxidative stress and dysfunction. PVAT phenotype was pro-inflammatory and pro-contractile. In HFDMG we observed an atherogenic profile, vascular oxidative stress and dysfunction. PVAT phenotype was also changed due to glycation.

The models studied exhibited some similarities such as insulin resistance, vascular dysfunction accompanied by PVAT dysfunction. These models highlight the impact of western type diets (high-fat diet and fat diet with methylglyoxal) in our metabolic and vascular health.

Keywords: Vascular dysfunction, Perivascular adipose tissue, Oxidative stress, Glycation

Theme: Locomotion/Exercise/Muscle / Active Living

OC - (21500) - Long-term management of metabolic diseases after bariatric surgery

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My name is Claudia, I'm a PhD Student, MSc in Exercise and Wellness and Specialist Nurse. My entire professional life has been dedicated to the follow-up of patients with severe obesity, proposed for surgical treatment. The long-term maintenance of the results of the surgery became a challenge and the search for the best results and the best care centered on each patient is my main focus.

INTRODUCTION

Obesity is a chronic disease characterized by excessive accumulation of fat that represents a health risk. In addition to long-term weight loss, surgery results in a further reduction in overall long-term mortality and the incidence of diseases such as diabetes type II (DMII), Hypertension (HTA), obstructive sleep apnea syndrome (SAOS), and others.

OBJECTIVE

The aim of this study is to characterize the effect of bariatric surgery on the control of comorbidity and to evaluate the association between the control of comorbidities and weight regain 5 years after surgery.

METHOD

A retrospective cross-sectional study was performed. The population of interest were patients who underwent bariatric surgery in a reference hospital. Data were collected in the clinical processes in to two time points: before surgery (baseline), and five years after surgery. The variables of interest were the control of the disease (DMII, HTA Dyslipidemia and SAOS) at 5 years after bariatric surgery, weight regain and physical activity level. Statistical analysis was performed in jamovi version 2.2.5. and a 5% significance level adopted.

RESULTS

We evaluated 84 subjects with more than 5 years of bariatric surgery. The prevalence of HTA, DMII, Dyslipidemia and SAOS before the surgery was 38.3%, 24,7%, 37% e 9.9% respectively. Five years after surgery 23.5% HTA, 18.5% DMII, 18.5% Dyslipidemia and 7.4% SAOS patients showed improvement in the control of the disease, with only 3 participants presenting a worsening of their comorbidities. No significant association between disease control with weight regain was found, even patients that had weight regain were able to maintain the improvement of comorbidities.

CONCLUSION

Metabolic disease control has a positive response to bariatric surgery with long-term maintenance. This control is independent of weight regain. This result highlights the possibility of using bariatric surgery as a therapeutic measure to other comorbidities.

Keywords: bariatric surgery, chronic diseases, obesity, weight regain

OC - (21644) - Muscle reoxygenation kinetics during six different variations of push-up exercise

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ABSTRACT

Muscle oxygen saturation (SmO_2) assessment has become increasingly popular as a physiological local stress parameter mainly due to its easy implementation in sports settings. This study compared SmO_2 reoxygenation kinetics, as a recovery parameter during six push-ups variations: diamond, declined, inclined, one-foot knuckles, spartans, and unstable terra-core platform.

After a familiarisation session, ten healthy males (age=25.2$\pm$3.2yr, BMI=24.6$\pm$3.0 kg/m^2, skinfold TRI= 10.3$\pm$3.2 mm and DEL=10.6$\pm$3.0 mm) performed in a random order six different push-ups over 60 sec with 5-min rest (cadence 30-40 bpm). Maximum SmO_2 recovery (SmO_2rec), reoxygenation rate (Δreoxy), and reoxygenation$_{slope}$ were assessed in *triceps* (TRI) and *deltoideus* (DEL) muscles using two MOXY monitors (Fortiori Design, Hutchinson, USA). Results were analysed using a parametric or non-parametric repeated measures comparison (ANOVA or Friedman).

In the six conditions, maximum SmO_2rec reached or overcame baseline values (SmO_2 after 10-min rest period prior warm-up). In TRI and DEL muscles, the values of maximum SmO_2rec, were higher in diamond (88.3%) and declined (82.3%), however no differences were found between variations. The Δreoxy was higher in TRI [0.22%/s (0.13-0.26)] in inclined and in DEL [0.120%/s (0.09-0.24)] in diamond, with no differences (χ^2=4.8, p=ns in TRI and χ^2=3.9, p=ns in DEL). The $reoxygenation_{slope}$ was higher in TRI (0.25±0.22% s^{-1}) and DEL (0.18±0.15% s^{-1}) after the declined push-up variation, showing a slower recovery of SmO_2, nevertheless with no differences between conditions.

The current study provided two important insights: (i) the velocity of SmO_2rec in TRI and DEL is similar in the push-ups variations, regardless of the hand position, body position and levels of stability effect on muscle strain; (ii) SmO2 seems to be a candidate physiological parameter to identify the state of muscle recovery and to adjust, in real time, the recovery time between exercises.

Keywords: Muscle recovery, push-ups exercise, SmO_2, physiological responses

Theme: Neurophysiology

OC - (21493) - $VPAC_1$ and $VPAC_2$ receptors are oppositely altered in the Li^{2+}-pilocarpine model of temporal lobe epilepsy.

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ABSTRACT

VIP binding sites are upregulated in mesial temporal lobe epilepsy (MTLE) patients[1], that also suffer severe cognitive deficits. In rodent models of epilepsy, although changes in VIP and VIP receptor levels were described the specific VIP receptor subtype(s) were never identified[2]. Here we investigated $VPAC_1$ and $VPAC_2$ receptor levels in the Li^{2+}-pilocarpine MTLE rat model. Cognitive performance and synaptic plasticity, as estimated from phosphorylation of AMPA GluA1 subunits on Ser_{831} and Ser_{845} and AMPA GluA1/GluA2 ratio, was also probed.

Wistar rats (12-week-old) were pre-treated with LiCl (300mg/kg, i.p.) and injected with pilocarpine (10mg/Kg) 24h later. Methyl-scopolamine (1mg/

kg, i.p.) was administered 15min earlier to block the peripheral cholinergic effects of pilocarpine. Animals showing spontaneous recurrent seizures (SRSs) for at least 4 weeks showed impaired learning in the radial arm maze (RAM) and decreased $VPAC_1$ and increased $VPAC_2$ receptor levels. In addition, SRSs rats showed increased AMPA GluA1 phosphorylation in Ser831 and Ser845, marked decrease in GluA1 levels and a milder decrease in GluA2 levels. Consequently, the GluA1/GluA2 ratio was also decreased in SRSs rats.

Altered VIP receptor levels may differentially prevent or contribute to MTLE pathology, since $VPAC_1$ receptors promote the endogenous control of LTP, mediate endogenous VIP neuroprotection against altered synaptic plasticity following seizures, and promote anti-inflammatory actions in microglia. $VPAC_2$ receptors instead mediate VIP endogenous neuroprotection against excitotoxicity while preventing reactive astrogliosis. This suggests that the approach to consider VIP receptors as therapeutic targets in MTLE should contemplate a differential targeting of the cellular events contributing to epileptogenesis.

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Keywords: epilepsy, VIP, VPAC1 R, VPAC2 R, cognition, synaptic plasticity

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OC - (21505) - β-adrenoceptor antagonists affect the establishment of traumatic

Memories and anxiety-like behaviour in a post-traumatic stress disorder mice model

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INTRODUCTION

Post-traumatic stress disorder (PTSD) is a psychiatric disorder originated from exposure to traumatic events, with associated limiting symptoms [1]. Studies indicate that catecholamines, possible though activation of peripheral β-adrenoceptors, are required for the formation of contextual traumatic memories[2,3].

AIMS

To evaluate the influence of β-adrenoceptor antagonists in a PTSD mice model by the administration of sotalol (peripheral β-adrenoceptor antagonist) and ICI-118,551 (ICI, selective β_2-adrenoceptor antagonist).

MATERIAL AND METHODS

Female mice (129x1/SvJ) were exposed to PTSD induction. Briefly, on days 0 and 1 mice were exposed to 15-foot shocks (10 s, 0.8 mA) followed by contextual reminder exposure on days 2, 7 and 14. Sotalol, ICI (2 mg/kg; i.p.) or vehicle (0.9% NaCl) were administered on days 2, 7, and 14, 30 minutes before context re-exposure. Other behavioural analyses were conducted. $P < 0.05$ was assumed to represent a significant difference.

RESULTS

On context days, sotalol- and ICI-treated mice showed decreased freezing behaviour when compared to vehicle-treated mice. Moreover, sotalol-treated mice showed decreased anxiety-like behaviour (elevated plus maze and light/dark transition test).

CONCLUSIONS

In conclusion, administration of sotalol and ICI was able to reduce PTSD symptoms and signs by weakening traumatic memories. Additionally, sotalol decreased anxiety-like behaviour, suggesting that while β_2-adrenoceptors may be more implicated with traumatic fear memory systems, β_1/β_3-adrenoceptors may be associated with anxiety-related circuits.

ACKNOWLEDGMENTS

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Keywords: β-adrenoceptors, antagonists, Post-traumatic stress disorder, contextual traumatic memories

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OC - (21507) - Contextual fear memory impairment in adrenaline-deficient mice may be related to downregulation of the m4 muscarinic receptor subtype in the hippocampus

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ABSTRACT

Adrenaline-deficient mice (mice lacking phenylethanolamine-*N*-methyltransferase function, Pnmt-KO) have impaired contextual fear memory[1,2], which is reverted by AD administration[2]. Our aim was to understand the role of muscarinic receptors in AD strengthening effect of contextual fear memory and respective molecular mechanism.

Wild-type (WT) and Pnmt-KO (129x1/SvJ) mice were submitted to the fear conditioning paradigm. Mice were administered with AD (0.1 mg/kg, i.p., 3 min), atropine (10 mg/kg, i.p., 5 min), methylatropine (0.5 mg/kg, i.p., 3 min), AD plus atropine, or vehicle (NaCl 0.9%). Relative quantification of *M1*, *M2,* and *M4* mRNA expression in hippocampus samples was evaluated. Results were

analyzed by Two-Way ANOVA (post-hoc Sidak's or Tukey's test) or Students' t-test.

There was a decrease in hippocampus mRNA expression of muscarinic M4 receptor subtype in Pnmt-KO mice compared with WT. In AD-treated Pnmt-KO mice it was observed an increase in hippocampus mRNA expression of muscarinic M4 receptor subtype compared with vehicle-treated Pnmt-KO mice. No differences were observed in mRNA expression of M1 or M2 receptor subtype between groups. In context day, atropine-treated WT mice showed a decrease in freezing behaviour when compared to methylatropine or vehicle-treated WT mice. Furthermore, it was observed a decrease in freezing behaviour in AD plus atropine-treated Pnmt-KO mice when compared to AD-treated Pnmt-KO mice.

In conclusion, contextual fear memory impairment in Pnmt-KO may be related to the downregulation of M4 muscarinic receptor subtype in the hippocampus, which is reverted by AD administration. Contextual fear memory strengthening by AD is attenuated by the central action of a muscarinic receptor antagonist, and not by a peripheral antagonist.

This work was supported by FCT (Ana Oliveira, SFRH/BD/138984/2018; Raquel Martinho, SFRH/BD/133860/2017).

Keywords: Fear conditioning, Contextual fear memory, Adrenaline-deficient mice, Adrenaline, Muscarinic Receptors

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Theme: Other

OC - (21433) - WWOX inhibition by Zfra1-31 ameliorates brain mitochondrial dysfunction and oxidative stress in a mouse model of type 2 diabetes

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Cristina Carvalho is a doctorate investigator interested in exploring the mechanisms underlying type 2 diabetes-associated (brain) complications. The ultimate goal is to identify new targets for therapeutic intervention. Her CV comprises >50 papers published in peer-reviewed journals, including a publication in Cellular and Molecular Life Sciences (2022; IF=9.2). In 2021, she won an Exploratory Research Grant from European Society for Clinical Investigation and a FCT Exploratory Research Project.

ABSTRACT

Type 2 diabetes (T2D), a chronic metabolic disorder, is the 2nd leading cause of dementia in the elderly. It is of utmost importance to decipher the mechanisms underlying T2D-associated brain damage to develop effective strategies to avoid/delay its development/progression. Recently it was shown that WW domain-containing oxidoreductase1 (WWOX) overexpression/overactivation plays a key role in several metabolic disorders. So, this study is aimed to assess the role of WWOX in T2D brain and the therapeutic potential of Zfra1-31

peptide, a specific inhibitor of WWOX. We used a high fat diet (HFD)-induced T2D mice treated or not with 2mM Zfra1-31 for 4weeks (4x; 1injection/week via tail vein). We performed behavioral and cognitive tests and assess glucose tolerance and insulin levels; brain cortical mitochondria function and oxidative stress (OS) levels were evaluated. HFD induced a phenotype of T2D, with an increase in body weight and peripheral blood glucose levels and decreased glucose tolerance. T2D mice also showed increased levels of anxiety and impaired cognitive function. Brain mitochondria isolated from T2D mice presented defects in mitochondrial function, decreased calcium buffering capacity and increased OS levels. Interestingly, Zfra1-31 treatment decreased blood glucose levels, anxiety-like behaviour, and memory impairment; improved mitochondrial function and calcium buffering capacity and decreased OS levels. In conclusion, our results showed that HFD induces behavioral/cognitive and brain mitochondrial defects and supports the role of WWOX in in the diabetic brain and the therapeutic potential of Zfra1-31 against T2D-associated brain damage.

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Keywords: Type 2 diabetes, mitochondrial dysfunction, WWOX, Zfra1-31, neurodegeneration

OC - (21495) - Physiology of body composition – How do vegetarians and omnivores differ?

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ABSTRACT

Plant-based diets are characterized by a reduction or elimination of animal product consumption and are believed to exert beneficial effects concerning the incidence and clinical course of different chronic diseases especially those related to overweight and obesity. We aimed to examine the differences in total body composition as well as in metabolic markers among vegetarians-vegans and omnivores individuals. The present study was a cross-sectional analysis consisting of 274 healthy participants, 95 vegetarian-vegan, and 179 omnivores (67% of women, presenting a mean age of 32 years old). Body composition was assessed using a dual-energy x-ray absorptiometry (DXA), and dietary habits were collected using a Food Frequency Questionnaire. Specific biochemical parameters were obtained (LINX DUO, Menarini Diagnostics) from capillary blood. Our results suggest that vegetarian-vegan individuals presented higher values (p-value>0.05) of bone, tissue, lean, and total masses. Also, these individuals presented lower levels of fat mass, nevertheless higher values of visceral and subcutaneous adipose tissue (p-value>0.05). Statistically significant differences were observed for total,

LDL, and non-HDL cholesterol, being these metabolic markers higher for omnivorous. These results may be explained by the fact that the omnivorous participants reported practicing less vigorous physical activity and also walking ($p<0,05$). Another explanation can come from the diet since vegetarian-vegan individuals seem to consume more nuts, whole-grain cereals, legumes, vegetables, and fruits. In conclusion, adherence to a vegetarian-vegan dietary pattern was related to healthy dietary habits and physical exercise practice. Nevertheless, this dietary pattern does not seem to automatically mean a healthier body composition, mainly regarding visceral and subcutaneous adipose tissue distribution.

Keywords: Body Composition, metabolic markers, Vegetarianism, Dietary pattern

Posters

Theme: Education

PO - (21487) - Autonomic nervous system: Evaluation methods

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ABSTRACT

Autonomous nervous system (SNA) is a major regulator of various internal organs contributing to physiological homeostasis. A tuned balance between sympathetic and parasympathetic functions is fundamental for internal organ regulation and provocative manoeuvres may be used to evaluate their normal function (deep breath, position changes, cold test, handgrip).

This topic is fundamental for undergraduate students to highlight the importance of SNA in the organism and teach them how these evaluations can be performed. The methods used to teach this topic are both online videos (Valsalva manoeuvre, tilt test and sudomotor tests) and the evaluation of cardiac frequency and determination of blood pressure in the supine versus orthostatic position. The description and discussion of several methods for the evaluation of cardiovagal, adrenergic and sudomotor function is important in the clinical practice enabling the identification of different types of dysautonomia.

Keywords: Autonomous nervous system, Deep breath, Valsalva manoeuvre, Tilt test, Sudomotor tests, Teaching physiology

PO - (21488) - Electroencephalography: The basics

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ABSTRACT

The human brain is very complex and attractive. Brain activity can be recorded both when we are awake or asleep, collecting and processing your surroundings and absorbing data. There are several tools available to study the processes underlying human behaviour consciousness, but one of the most versatile and affordable technique is electroencephalography (EEG).

EEG records non-invasively the electric activity of the cerebral cortex. Typical clinical EEG waveforms recorded using scalp electrodes (International Federation of EEG Societies 10-20 system) can be identified. The methodology and clinical applications of this diagnostic tool are discussed. This activity changes and the frequency bands and individual waveforms found in the normal adult EEG are described for both the waking and sleeping states. Correlations exist with specific brain states (e.g., wakefulness, sleep) and specific pathologies associated with abnormal EEG waveforms. The features of sleep and some activation procedures are typically discussed. A recording and interpretation of some EEG are performed in the classroom using the Biopac System. In the awake state, in a well-organized EEG, there is a well-formed posterior dominant rhythm occipitally, which attenuates with eye opening. In sleep, there are distinct sleep states with sleep structures (e.g., K-complexes, vertex waves) specific to each state.

Overall, EEG is an important diagnostic tool in clinical neurology, psychiatry and in polysomnography, among others but more recently a different application of EEG has emerged, as a brain-computer interface where EEG signals represent control signals for prostheses of extremities.

Keywords: EEG, Wakefulness, Sleep, Teaching physiology

PO - (21489) - Electromyography as a tool to teach skeletal muscle physiology to undergraduate students

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ABSTRACT

Electromyography (EMG) is the record of the electric activity of the muscle. Surface and deep EMG in conjunction with nerve conduction studies are known as the electrodiagnostic methods and enable the diagnose and location of neurologic disorders. These tests are essential in neurophysiology, physical rehabilitation, and neuromuscular medicine. EMG techniques study neuromuscular activity of striated muscles using a recording electrode that is inserted into or placed on the surface of a muscle. These methods can be used as a tool in physiology lectures to show and elucidate several features of skeletal muscle function. The aim of this teaching approach was to make the learning of skeletal muscle physiology more interesting by using the EMG to demonstrate the various aspects of muscle physiology.

Nerve conduction studies are used to assess motor and sensory nerves, while EMG enable to characterize the muscle innervated by the nerve. In nerve conduction studies several topics will be covered including the measurable features of the sensory nerve action potential, compound muscle action potential, F-response, and H-reflex. Normative values for commonly performed nerve conduction studies (ex. Median nerve) will be discussed. Normal patterns of EMG in muscle at rest, EMG features of voluntary motor activity, including duration, polyphasia, amplitude, and recruitment will be addressed (Biopac and Powerlab Systems).

Overall, EMG and nerve conduction studies enable the real-time dynamic study of the peripheral nerves and associated muscular system. These diagnostic methods, used in clinical neurophysiology, can be utilized as didactic tools to improve understanding and interest of muscle physiology concepts in a practical classroom setting.

Keywords: EMG, Teaching muscle physiology, Nerve conduction studies, Neuromuscular junction, Motor unit, Recruitment

PO - (21490) - Endothelial function/dysfunction: Methods of evaluation

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ABSTRACT

Endothelium is a fundamental physical and functional barrier with the ability to produce vasoactive and protective mediators under physiological conditions. It regulates vascular tone, coagulation, remodelling, vascular inflammation, and angiogenesis. Several vascular diseases commence with the endothelial dysfunction emphasizing the importance to monitor its function towards prevention and reduction of vascular dysfunction. Endothelial cells are an important biomarker and a therapeutic target in preventive and personalised medicine. The development of new non-invasive techniques to determine endothelial dysfunction in combination with existing clinical imaging modalities delivers a viable opportunity to reduce the burden of vascular disease.

This topic introduces the principles of endothelial function evaluation and gives a summary of invasive and non-invasive techniques to determine vascular function and their major advantages and drawbacks. The students are introduced to the mechanisms underlying the regulation of vascular function and dysfunction and potential new biomarkers of endothelial damage. Identifying and acknowledging these biomarkers is crucial towards a shift from reactive to preventive, personalised medicine. The student will be sensibilized to this important topic. Pinpointing vascular dysfunction earlier enables predictive diagnostics reducing the burden of vascular disease.

Keywords: Vascular function and endothelium, Invasive and non-invasive techniques, Biomarkers of vascular disease, Teaching physiology

PO - (21491) - Exercise physiology: Major challenges

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ABSTRACT

Exercise physiology is a major topic essential in the medical curriculum. The basic contents regarding this topic are introduced to undergraduate students emphasizing the impact of physical exercise in muscle, respiratory and cardiovascular physiology. This integrative approach is essential in the end of these three major topics in physiology to help student to consolidate and integrate the functions. The concept and differences between Exercise *versus* physical activity are discussed. In addition, the Frequency, Interval, Time, and Type (FITT) of exercise are discussed in the context of American College of Sports and Medicine (ACSM) guidelines. Major adaptations to exercise (chronic *versus* acute) are discussed and acute adaptations to exercise are observed, measured, and discussed in a practical approach in the classroom. Performing aerobic exercise and determining changes in respiratory, cardiovascular, and metabolic functions when compared to control (at rest) enables the teaching of exercise physiology with more efficacy and positive enthusiasm achieving better results in undergraduate students. The importance of physical exercise to preventive and personalized medicine is also addressed.

Keywords: Exercise physiology, FITT, Adaptations to exercise, Physical activity, Teaching physiology

PO - (21603) - Teach physiology with flipped laboratories

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ABSTRACT

Teaching physiology is challenging and continues to evolve to meet students' needs and expectations. Our students learn when they do a practical task or lecture activity. They also learn when read to prepare lectures or watch online video/webinar. Learning achievements increase when they work in small groups doing tutorials which facilitate discussion / evaluation. Writing or presenting an essay or a group discussion will further increment the learning goals and will increment the ability to remember a concept. The model of flipped laboratories is student-focussed and accessible to all but involves more screening time. This concept is applied to small groups where an introduction to a concept and equipment is need. Achievements are high allowing both the teacher/facilitator and the students to be engaged and fully motivated to the tasks. These methods of teaching physiology are quite rewarding, particularly in the practical classes and the feedback from students is very positive.

Keywords: Physiology, Teaching methods, Flipped laboratories

PO - (21627) - Empathy profiles in medical physiology students: A cross-sectional study using the interpersonal reactivity index tool

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BACKGROUND

Medical education constitutes an unparalleled opportunity to comprehend students' empathy profiles.

AIMS

To characterize empathy features in first- and second-year medical undergraduates, exploring correlations with personal characteristics and academic performance.

METHODS

A single-faculty cross-sectional study of medical students enrolling in 2018/2019 first-semester Physiology courses was conducted. Participants were divided into three groups: Musculoskeletal Physiology (MSP, first-year students), Cardiovascular Physiology (CVP) and MSP+CVP, both second-year students. Students filled an online form, providing biographic and academic information. Empathy was assessed using the Interpersonal Reactivity Index (IRI) questionnaire, under four subscales: Perspective taking (PT), Empathic concern (EC), Personal distress (PD) and Fantasy (F). Independent t-tests, ANOVA and Pearson's correlation were used.

RESULTS

From 685 students enrolled, 558 (81.5%) participated in the study, with a predominance of female participants (70.1%), and a mean age of 19.4 ± 3.4 (MSP), 20.2 ± 2.6 (CVP) and 22.1 ± 4.1 (MSP+CVP). Female students exhibited a statistically significant higher EC and F subscale scores in MSP group, and higher PT, EC and F scores for CVP ($p<0.01$ for all). A higher Physiology grade was associated with superior EC and F for MSP+CVP. Working-student status was correlated with a higher EC in MSP+CVP. No asymmetries were found for empathy subscales in the three groups. Admission grade and age didn't correlate with IRI scores. PT and EC skills were positively correlated ($r=0.526$, $p<0.001$), as well as EC and F ($r=0.448$, $p<0.001$). In contrast, PT and PD were negatively correlated ($r=-0.148$, $p<0.001$).

CONCLUSIONS

Female gender, higher Physiology grades and working-student status are, in some contexts, associated with superior empathy. Empathic skills were no different between study groups, and did not vary from first-year to second-year medical students.

Keywords: Empathy, Medical students, Physiology

PO - (21637) - The impact of digital flashcards on physiology academic performance in a medical course – A consistent dose-dependent effect between the amount of training and academic success

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INTRODUCTION

Digital flashcards help review factual knowledge through active-recall and spaced-repetition. Is this study method associated with superior musculoskeletal (MSP) and cardiovascular physiology (CVP) grades, through a dose-dependent effect?

METHODS

A single-faculty cohort study of 1st- and 2nd-year medical MSP and CVP students was conducted, and 155 and 676 flashcards (respectively) were created

through Moodle®. An exploratory analysis examined three exam results (2019), the latter being optional and performed 1 month after the course's end. A confirmatory study used a fourth exam (2021) in another CVP cohort. Flashcard-users were determined as having reviewed ≥5% cards. One-sample t-tests, Pearson's correlation and multiple and simple linear regressions were applied.

RESULTS

Of 685 students enrolled, 557 participated in the exploratory analysis – 319 (69%) for MSP, and 311 (83%) for CVP, with 200 MSP flashcard-users and 265 CVP flashcard-users. Flashcard-users scored higher versus non-users (0-20 scale): 14.2±3.9 vs. 10.9±5.3, p<0.001; 12.4±4.6 vs. 10.4±5.1, p=0.02; 7.5±4.5 vs. 5.2±4.8, p<0.001; 1st, 2nd and 3rd MSP exams, respectively; 11.8±3.6 vs. 9.5±3.6, p<0.01; 12.5±3.0 vs. 11.5±3.2, p=0.225; 10.2±4.7 vs. 7.5±4.5, p=0.041; 1st, 2nd and 3rd CVP exams, respectively. The training amount was positively correlated with grades (r=0.254-0.331 for MSP and r=0.310-0.396 for CVP, p<0.001). Multiple linear regression models showed a statistically significant and dose-dependent association between results and the number of flashcards studied – for every 100 MSP cards reviewed, exam grades increased 0.44-0.75 (p<0.001), and for every 1000 CVP flashcards, results raised 0.81-1.08 values (p<0.05). The positive impact of flashcards was confirmed in the 2021 CVP cohort of 269 participants, of which 67% used flashcards.

CONCLUSION

Digital flashcards' revision has a positive consistent dose-dependent effect on MSP and CVP grades, both in short- and medium-terms.

Keywords: Flashcards, Physiology, Medical education, Academic success

PO - (21649) - Empathy in portuguese medical students: A cross-sectional study using the jefferson scale of physician empathy

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BACKGROUND

Empathy is a multi-factorial concept that plays a vital role in a patient-centered healthcare, and is a soft skill often overlooked in medical education.

PURPOSE

Analyze the empathy of medical undergraduates, and explore its association with personal and academic characteristics.

METHODS

A cross-sectional study of first- and second-year medical students enrolling in Physiology courses during 2018/2019 was conducted in a Portuguese faculty. The Portuguese Version of Jefferson Scale of Physician Empathy Student Portuguese Version (JSPE-spv) was distributed and completed through an online form, and the total score on this tool (from 20 to 140) was obtained for each participant. Independent sample t-test, Pearson's correlation, ANOVA and Bonferroni tests were used to assess empathy's association with collected personal and academic information.

RESULTS

From 685 students enrolled, 539 (79%) agreed to participate, and scored 92.4±11.7 (mean±standard deviation) in JSPE. Female students exhibited higher scores when compared to males (94.2±10.5 vs. 88.3±13.3, $p<0.001$). Participants with previous failure of a Physiology course exhibited higher total empathy scores when compared to students enrolling for the first time (94.3±9.9 vs. 91.9±12.1, $p=0.035$). A positive correlation was found between the mean medical course grade and JSPE score ($r=0.142$, $p=0.015$). No statistically significant associations were found between empathy scores and first versus second medical course year, previous enrollment in a public or private high school, or full time versus working students. No correlation was found between empathy and age, admission grade to the faculty, or Physiology exam grades.

CONCLUSIONS

Female gender, history of previous failure and a higher mean course grade are associated with superior empathy scores among medical students. Further efforts should be made in better comprehending empathy evolution in Portuguese students, and how can it be properly trained.

Keywords: Empathy, Medical students, Physiology, Jefferson Scale of Physician Empathy

Theme: Endocrine, Reproduction and Development

PO - (21632) - Cymbopogon citratus extract improved endothelial dysfunction in type 2 diabetes

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ABSTRACT

Type 2 diabetes significantly impairs both endothelium and perivascular adipose tissue (PVAT) in the vasculature. PVAT loses its vasodilatory and anti-inflammatory phenotype under diabetic conditions. Previous studies have suggested that extracts of *Cymbopogon citratus* (DC.) Stapf (CC) have antioxidant, anti-inflammatory and anti-diabetic properties. This work aimed to study the therapeutic efficacy of extracts from CC on endothelial and perivascular dysfunction associated with type 2 diabetes. Non-obese type 2 diabetic Goto-Kakizaki (GK) rats were divided in two groups: (1) control group; (2) group treated with 175 mg/kg CC. CC was given orally for 4 months. Several *in vivo* parameters and endothelial function were studied in aorta with PVAT (+) or without PVAT (–). CC improved insulin resistance, the intraperitoneal

glucose tolerance test, endothelial function, reduced the contractile phenotype of diabetic PVAT and did not change lipid profile in diabetic GK rats. In addition, hepatic function was normal indicating a reduced toxicity of the extracts from CC. In summary, CC improved vascular dysfunction in part due to its antidiabetic properties.

Keywords: Type-2 diabetes, Endothelium, Vascular dysfunction, Cymbopogon citratus, Antidiabetic properties

PO - (21634) - Pterospartum tridentatum as a novel therapeutical strategy for the treatment of endothelial dysfunction in type 2 diabetes

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ABSTRACT

Type 2 diabetes promotes endothelial and perivascular adipose tissue (PVAT) dysfunction leading to vascular disease. Extracts of Pterospartum Tridentatum (L.) Willk. (PT) have antioxidant, anti-diabetic, and anti-inflammatory properties. This work aimed to study the therapeutic efficacy of PT on endothelial and perivascular dysfunction associated with type 2 diabetes. Non-obese type 2 diabetic Goto-Kakizaki (GK) rats were divided in two groups: (1) control group; (2) group treated with 175 mg/kg PT. PT was given orally for 4 months. Several in vivo parameters and endothelial function were studied in aorta with PVAT (+) or without PVAT (–). PT improved the intraperitoneal glucose tolerance test and did not change lipid profile in diabetic GK rats. The toxicity of PT was very low not affecting hepatic function. In addition, PT improved endothelial dysfunction and recovered the vasodilating phenotype of perivascular adipose tissue. In conclusion, PT exhibited anti-diabetic properties ameliorating glucose tolerance test curve and significantly improved vascular function in type 2 diabetes.

Keywords: Pterospartum tridentatum, Endothelial dysfunction, Type 2 diabetes, Perivascular adipose tissue

Theme: Gastrointestinal physiology

PO - (21480) - Personalised treatment for cystic fibrosis patients with rare CFTR mutations

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I am a young researcher with a BSc and MSc degree in Biochemistry and I am currently doing a PhD at BioISI/FCUL, Lisboa. My work is focused on improving Cystic Fibrosis (CF) diagnosis in cases of atypical CF. I have used Ussing chamber to measure CFTR-mediated chloride secretion in rectal biopsies and performed forskolin-induced swelling assays in patient-derived intestinal organoids to predict the response to currently available CFTR modulators.

BACKGROUND

Cystic Fibrosis (CF) is an autosomal genetic disease caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. Therapies that rescue defective CFTR (CFTR modulator drugs) have now reached the clinic, however these drugs are mutation-specific and have been developed for people with CF (pwCF) with common genotypes. Accordingly, pwCF with rare mutations do not have access to these treatments.

OBJECTIVE

Bring personalised therapies to pwCF with rare CFTR mutations.

METHODOLOGY

CFTR-mediated chloride secretion was assessed by Ussing chamber intestinal current measurements in native rectal biopsies from pwCF with rare CFTR mutations. In parallel, intestinal organoids were generated [Dekkers et al (2013) Nat Med]. CFTR function was assessed through the Forskolin Induced Swelling assay. CFTR modulators tested included: potentiator VX-770 (Ivacaftor) alone or in combination with correctors VX-661(Tezacaftor) and/or VX-445 (Elexacaftor), all from Vertex Pharmaceuticals®.

RESULTS

Our data show that intestinal organoids from pwCF with rare mutations including Y1092X, P205S, R334W and Q1100P exhibit CFTR rescue by the VX-661/VX-770 combination, while 2789+5G>A, M1137R, Y1092X, P205S, G85E, N1303K, Q1100P, S4X and 3272-26A were only rescued by the triple combination VX445/VX-661/VX-770.

CONCLUSION

Altogether, our results demonstrate how intestinal organoids can be used to assess responsiveness to CFTR modulator drugs in a personalized therapy/theranostics approach, as well as to extend the label of approved CFTR modulator drugs so that additional pwCF can benefit from those drugs.

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Keywords: Cystic Fibrosis, Intestinal Organoids, CFTR, CFTR Modulators, Rare Mutations

PO - (21599) - More evidence on the gut-skin axis modulation by kefir

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ABSTRACT

The interaction between the gut microbiota and immune system has been an attractive thematic in many areas, from nutrition and well-being to medicine. Evidences of multiple links between dysbiosis and skin inflammatory processes have accumulated suggesting that microbiome is a critical component of immunological homeostasis. In this exploratory study we focus on the potential interest of kefir an old food with probiotic properties, on the gastrointestinal (GI) status of atopic skin (AD) subjects. Participants (n = 18, mean age 32.1 $\pm$ 12.2 years old, females) previously diagnosed with AD were included either in the kefir intake (K) group or in the control (C) group. Protocol and procedures fully respected the principles of GCP. Intervention consisted on the daily consumption of kefir for eight weeks exclusively in the K group. Severity of AD was assessed using the Scoring Atopic Dermatitis Severity Index (SCORAD). GI symptoms were self-reported. Results have shown a significant improvement on AD severity ($p<0.001$) in the K group individuals. In this group GI symptoms, such as constipation and abdominal distension

were also improved (p=0.046 and p=0.058, respectively). No significant differences were observed in the control group during the study. AD severity improvement was also correlated with abdominal distension improvement (rho=0.484, p=0.042). Therefore our results suggest that the regular intake of kefir improves the gastrointestinal status of our participants potentially due to the modulatory effect of kefir over the gut-skin axis. From the skin physiology perspective it seems these results reinforces this concept of gut–skin axis and its interest for further investigation.

Keywords: Gut-skin axis, Kefir, Probiotics, Atopic Dermatitis

Theme: Heart, Circulation and Respiration

PO - (21483) - The prompt adaptive hemodynamical response depends on age – Data from the wavelet components' correlations of LDF curves

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BACKGROUND

The Prompt Adaptive Hemodynamical Response (PAHR) has been identified as a component of cardiovascular homeostasis. To recognize the mechanism behind PAHR, we modulated perfusion signals measured by laser Doppler flowmetry (LDF) in healthy human participants. The aim of this study is to evaluate how the PAHR evolves with age and identify which LDF signal components are involved.

METHODS

The study involved 56 participants divided into two groups: Young (n=34; 19.8 ± 1.6 y/o) and Aged (n=22; 52.6 ± 6.2 y/o). The protocol consisted of registering the perfusion increase evoked by a 5min low-intensity massage (phase II) of one lower limb compared with baseline (phase I) and recovery (phase III). Perfusion was measured by LDF in both feet and decomposed into their spectral components - cardiac, respiratory, myogenic, sympathetic, endothelial- by the Wavelet transform (WT). Statistical analysis was performed in jamovi version 2.2.5. and a 5% significance level adopted.

RESULTS

In the test foot of the younger group a positive correlation was found between phases II-I for cardiac and respiratory components. Also, the myogenic component was significantly associated with both cardiac and respiratory components (p=0.002 and p=004). Endothelial components were differently associated with the cardiac component; in the aged group endothelial components were positively associated with the sympathetic and myogenic components.

CONCLUSION

Although this PAHR seems to be similar in both groups, WT analysis suggests that their mechanisms differ. Cardiac and respiratory components seem to be predominant but different intensities are clear. Probably, the mechanical and sensory receptors activated by massage evoke different intensity spinal-supraspinal responses, apparently more intense and wider in the younger group. However, the final result – perfusion recovery, seems to be the same. This suggests that PAHR might be used as an endpoint with clinical relevance.

Keywords: Prompt Adaptive Hemodynamic Response – PAHR, microcirculation, cardiovascular function, Wavelet transform

PO - (21499) - New perspectives from erythromelalgia

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ABSTRACT

Erythromelalgia (EM) or Mitchell's disease is a rare orphan disease, poorly understood. We compared the perfusion profiles of the hands of one female EM patient, 35 years old and noother clinical history, with healthy individuals. Ongoing medication was interrupted one week prior to the study. Current lab markers were all normal, and peripheral neuropathy wasabsent. Nailfold capillaroscopy revealed a decreased capillary density (6/mm) and dilated giant capillaries. Our convenience reference group included five healthy women (31.3+11.7 years old). Perfusion was recorded in both hands (phase 1), during reduction of skin temperature (~20%) in one hand by contact with cooling material (phase 2) and recovery to room temperature (phase 3). Perfusion was measured by laser Doppler flowmetry (LDF) to assess deeper plexus and non-contact polarized light spectroscopy (PS) for superficial measurements. At rest, the EM patient exhibited reduced perfusion at deep and much higher perfusion at the skin surface compared with healthy participants. Cooling the skin reduced deep perfusion in all participants in both hands,

especially noticed in the EM patient and remaining in phase 3. No changes were seen in the superficial perfusion in the EM patient contrary to the healthy group. Component analysis of LDF signals (Wavelet transform) revealed lower myogenic and sympathetic activities during rest in the EM patient compared to the reference group. Cooling dramatically reduced all components' activity, more significantly in the patient. Here, full recovery was unachieved and only the sympathetic component seemed to be more effective than the control group. This approach brings a new functional perspective to EM that should be explored.

Keywords: microcirculation, erythromelalgia, capillaroscopy, laser Doppler flowmetry, polarized light spectroscopy, Wavelet transform

PO - (21600) - Ventricular-arterial coupling the silent indicator of efficiency- Effect of a personalized physical exercise program in cardiac efficiency of older aduts

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ABSTRACT

Ventricular-Arterial Coupling the silent indicator of efficiency- Effect of a Personalized Physical Exercise Program in Cardiac Efficiency of Older Aduts.

INTRODUCTION

This paper aims to disseminate findings on the impact of implementing a multidisciplinary intervention program, comprising a tailored physical exercise (PE) component, on the Ventricular-Arterial Coupling (VAC).

METHODS

Non-randomized pilot study, enrolling 21 old adults aged above 65 years (mean: 81 years). Participants were divided into two groups (G1 and G2), both subject to a multidisciplinary diagnostic evaluation. We used transthoracic echocardiography and pulse wave analysis to evaluate central and peripheral Blood Pressure (BP) and hemodynamic parameters related to cardiovascular efficiency. We implemented a tailored intervention program for 3 months. G2's program included a component of tailored exercise training. Participants were re-evaluated after the program. Self-efficacy for exercise scales, handgrip strength and nutritional status were also evaluated at baseline and after intervention.

RESULTS

Baselines were similar in both groups and no significant changes were observed in G1. However, significant changes were observed in G2 post-intervention. We found a reduction of BP, arterial stiffness, and stroke work in G2, as well as increased cardiovascular efficiency, VAC and left ventricle efficiency parameter. We also found an improvement in handgrip strength and self-efficacy for exercise. The results of this pilot study highlight the positive modulation provided by a tailored PE approach of the old adult, increasing cardiac efficiency (CE).

CONCLUSION

The findings constitutes a factor for improving overall well-being. Now the focus on this field is finding what are the variability of VAC during PE, which type, and intensity of PE is better for cardiac efficiency and what are the differences between adult athletes and non athletes.

Keywords: Exercise, Cardiac efficiency, Ventricular-Arterial Coupling

PO - (21641) - Comparative analysis of the success of atrial fibrillation cryoablation in patients with sleep apnea syndrome – A retrospective study

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INTRODUCTION

Atrial Fibrillation (AF) is the most common arrhythmia and Sleep Apnea Syndrome (SAS) is a highly prevalent sleep disorder. Evidences claim that the two entities are interconnected and patients with SAS are at high risk of developing AF. As one of the therapies for AF is cryoablation, it is pertinent to clarify whether the presence of SAS and/or its correction is a strong predictor of the effectiveness of cryoablation.

OBJECTIVES

To compare the effectiveness of cryoablation in patients with AF with concomitant SAS.

METHODS

Clinical data were collected about the medical history, cryoablation procedure and follow-up of all patients undergoing this procedure in the Electrophysiology and Pacing Laboratory of the Coimbra University Hospital. Data were statistically analyzed, in an anonymized form, to investigate whether there is an association between SAS and the effectiveness of AF cryoablation.

RESULTS

Were included in this study 38 patients with AF, over 18 years of ag, of both genders,subjected to cryoablation and divided into two groups: 14 patients with diagnosed SAS and 24 patients without. In this study population, patients

diagnosed with SAS have increased body mass index, longer cryoablations and a greater tendency to long-term AF recurrence. The presence of SAS seems to be the only predictor of long-term success in the study.

CONCLUSION

There is a tendency for patients without SAS to have more long-term success compared with patients diagnosed with SAS for AF cryoablation, however, further studies are needed to confirm this relation.

Keywords: Atrial Fibrillation, Sleep Apnea Syndrome, Cryoablation

PO - (21642) - The impact of nutritional ketosis in gut microbiome and the cardiovascular function in a rat model of heart failure with preserved ejection fraction

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PURPOSE

Heart failure with preserved ejection fraction (HFpEF) affects more than half of the patients diagnosed with heart failure. Presently no effective therapeutic options are available for HFpEF. There is growing evidence to support the therapeutic potential of ketones on cardiac diseases, however any beneficial impact of the ketogenic diet remains highly controversial. In this study, we aim to characterize the impact of a ketogenic diet on the gut microbiome and cardiac function in HFpEF by using rat model.

METHODS

Sixteen week-old male ZSF1 rats lean (CT) and obese (HFpEF) were randomly allocated to receive standard diet (ND), standard diet+ ketone salts supplementation in drinking water (KS) or ketogenic diet (KD). The animals were subjected to glycemia and ketonemia assessment as well as insulin resistance (IR) and oral glucose tolerance testing. Faecal samples were collected fourteen weeks later, the microbial DNA extracted and 16S V4 rRNA microbiome was sequenced on Illumina Miseq. The targeted microbiome sequences were processed and analysed using R.

RESULTS

Both KD and KS were able to reduce glycemia in HFpEF while KD alone significantly increased ketonemia. Even though IR test showed no significant difference since these rats are extremely diabetic, a slight improvement was seen in glucose tolerance with KD on HFpEF rats. Regarding the gut microbiome, ND rats showed decreased Actinobacteria and increased Lactobacillaceae and Ruminococcaceae, while the rats on KD and KS showed increased Proteobacteria, Verrucomicrobia, and Erysipelotrichaceae. At the genus level, Allobaculum were decreased in ND rats, while Romboutsia were increased in KD rats.

CONCLUSION

The present study demonstrates that KD ameliorates some of the metabolic dysfunction commonly associated with HFpEF as suggested by changes in glycemia levels and glucose tolerance. Such a diet resulted in changes in the gut microbiome, mainly in bacteria associated with ketogenic metabolism.

Keywords: heart failure, cardiovascular risk, obesity, hypertension, diabetes, ketones, gut microbiome

PO - (21645) - Myosin-inhibitor mavacamten acutely enhances diastolic compliance in a rat model of heart failure with preserved ejection fraction

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PURPOSE

Diastolic dysfunction with increased ventricular passive stiffness is a hallmark of heart failure with preserved ejection fraction (HFpEF), a prevalent and deadly syndrome with limited therapeutic options available. Recently, mavacamten, a first-in-class cardiac myosin inhibitor, has been successfully used for the treatment of hypertrophic cardiomyopathy, in large part due to its effect in decreasing diastolic stiffness. We therefore sought to test the effects of mavacamten on the sarcomere in an animal model of HFpEF.

METHODS

Single cell preparations from the left ventricular-free wall of hearts (n=5 cells per animal) from 25 weeks-old ZSF1 obese (OB- HFpEF model), ZSF1 lean (LN- hypertensivecontrol) and Wistar Kyoto (WKY- wild-type control) rats (n=5 animals per group) were chemically permeabilized and attached to a force-measuring apparatus and a motor to perform functional studies. Passive tension (PT) and Ca^{2+}-activated tension (AT) were measured at sarcomere lengths 1.8-2.3μm and Ca^{2+} sensitivity (pCa50) was determined in the presence or absence of 0.5μM mavacamten.

RESULTS

Skinned cardiomyocytes from OB rats exhibited increased PT compared to LN and WKY rats. mavacamten decreased PT in myocytes from both LN and OB rats, particularly in the latter. mavacamten also significantly decreased both AT and pCa50, as well as the rate of force redevelopment and decreased residual force in OB rat cells. The length-dependent activation response was not significantly decreased in OB rat cells in the presence of mavacamten.

CONCLUSION

Our data suggest that mavacamten decreases myocardial stiffness in a rat model of HFpEF. This effect may offset the decrease in contractile potential, preserving length-dependent activation and overall improve tolerance to hemodynamic load. Mavacamten may therefore become a useful therapy for HFpEF patients.

Keywords: heart failure, hfpef, mavacamten, diastolic dysfunction

PO - (21647) - Impact of overweight/obesity in cardiac remodelling and reverse remodelling induced by pregnancy

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ABSTRACT

I: During pregnancy occurs cardiac remodelling (CR) characterized by left ventricle (LV) hypertrophy and left-atrium enlargement. After delivery, the woman's heart undergoes reverse remodelling (RR). The impact of cardiovascular risk (CVR) factors in CR and RR remains to clarify.

M: Women [healthy and with CVR factors (obesity/hypertension/gestational diabetes)], were evaluated by transthoracic echocardiography during gestation [10-15 weeks,1T; 30-35 weeks,3T] and in postpartum period [1st and 6th mo after delivery,RR]. Kruskal-Wallis and Friedman tests were used.

R: Pregnant women (n = 125) developed from 1T to 3T eccentric hypertrophy, characterized by a significant increase of LV mass index (LVMi, p<0.001), relative wall thickness (RWT, p=0.034), and atrial (p<0.001) and ventricular enlargement (p<0.001). A significant rise in filling pressures was also seen during gestation (E/e', p<0.001).

LVMi regression and indexed left atrial and ventricular volumes normalized at 1-mo after birth (p=0.012, p<0.001 and p<0.001, respectively), as well as, ventricular filling pressures (p<0.001).

Structural adaptations during CR and RR were accompanied by a reduction of PCR (p<0.001), IL33/ST2 (p<0.001) and PICP (p<0.001) from 3T to 6-mo after delivery.

CVR factors promoted higher RWT in postpartum, with similar values of indexed cardiac volumes. They also displayed elevated values of LVMi when compared with healthier women at 6-mo after delivery (p=0.036) and deterioration of diastolic function as shown by higher values of E/e' during postpartum (1st-mo, p=0.002; 6th-mo, p=0.010).

Higher values of PCR (p=0.016), IL33/ST2 (p=0.021) and PICP (p=0.005) were seen in CVR factors group when compared with healthier one at 3T.

C: All cardiac parameters seemed to recover as 1-mo after delivery, associated with reduction of cardiac hypertrophy and biomarkers. Pregnant women with CVR factors showed higher RWT and diastolic deterioration when compared with healthy women.

Keywords: Overweight, Obesity, Pregnancy, Postpartum, Cardiac Remodelling, Reverse Remodelling

PO - (21650) - Cardiac remodelling and reverse remodelling in pregnancy: Impact of cardiovascular risk factors

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ABSTRACT

I: During pregnancy occurs cardiac remodelling (CR) characterized by left ventricle (LV) hypertrophy and left-atrium enlargement. After delivery, the woman's heart undergoes reverse remodelling (RR). The impact of cardiovascular risk (CVR) factors in CR and RR remains to clarify.

M: Women [healthy and with CVR factors (obesity/hypertension/gestational diabetes)], were evaluated by transthoracic echocardiography during gestation [10-15 weeks,1T; 30-35 weeks,3T] and in postpartum period [1st and 6th mo after delivery,RR]. Kruskal-Wallis and Friedman tests were used.

R: Pregnant women (n = 125) developed from 1T to 3T eccentric hypertrophy, characterized by a significant increase of LV mass index (LVMi, p<0.001), relative wall thickness (RWT, p=0.034), and atrial (p<0.001) and ventricular enlargement (p<0.001). A significant rise in filling pressures was also seen during gestation (E/e', p<0.001).

LVMi regression and indexed left atrial and ventricular volumes normalized at 1-mo after birth (p=0.012, p<0.001 and p<0.001, respectively), as well as, ventricular filling pressures (p<0.001).

Structural adaptations during CR and RR were accompanied by a reduction of PCR (p<0.001), IL33/ST2 (p<0.001) and PICP (p<0.001) from 3T to 6-mo after delivery.

CVR factors promoted higher RWT in postpartum, with similar values of indexed cardiac volumes. They also displayed elevated values of LVMi when compared with healthier women at 6-mo after delivery (p=0.036) and deterioration of diastolic function as shown by higher values of E/e' during postpartum (1st-mo, p=0.002; 6th-mo, p=0.010).

Higher values of PCR (p=0.016), IL33/ST2 (p=0.021) and PICP (p=0.005) were seen in CVR factors group when compared with healthier one at 3T.

C: All cardiac parameters seemed to recover as 1-mo after delivery, associated with reduction of cardiac hypertrophy and biomarkers. Pregnant women with CVR factors showed higher RWT and diastolic deterioration when compared with healthy women.

Keywords: Cardiovascular risk factor, Arterial Hypertension, Obesity, Gestational diabetes, Pregnancy, Postpartum, Cardiac Remodelling, Reverse Remodelling

Theme: Integrative physiology

PO - (21593) - The CCR2 inhibitor propagermanium as a novel therapeutic approach for the treatment of endothelial dysfunction in type 2 diabetes

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ABSTRACT

Perivascular adipose tissue (PVAT) exerts vasodilatory and anti-inflammatory functions changing under pathologic conditions. Propagermanium (PG) has immune modulating activity and anti-inflammatory properties. This work aimed to study the therapeutic efficacy of PG on endothelial and perivascular dysfunction associated with type 2 diabetes. Non-obese type 2 diabetic Goto-Kakizaki (GK) rats were divided into four groups: (1) control group; (2) group treated with 50 mg/kg PG; (3) group fed a high-fat-diet (GKHFD) and (4) group of GKHFD treated with 50 mg/kg PG. PG was given orally for 3 months. Several in vivo parameters and endothelial function were studied in aorta with PVAT(+) or without PVAT(–). We also evaluated vascular inflammation and levels of cytokines in PVAT. PG improved fasting glucose levels, insulin resistance, endothelial function and recovered the anti-contractile effect of perivascular adipose tissue reducing its inflammation and did not change lipid profile and the intraperitoneal glucose tolerance test in diabetic GK rats. PG improved endothelial dysfunction and recovered the vasodilating phenotype of perivascular adipose tissue probably due to its anti-inflammatory properties.

Keywords: Endothelial dysfunction, Type 2 diabetes, Inflammation

PO - (21594) – Cinnamaldehyde supplementation reverts endothelial dysfunction in diet induced obesity rats

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ABSTRACT

We aimed to determine whether activators of NFE2-related factor 2 (Nrf2) can be used to reduce oxidative stress and improve endothelial dysfunction in metabolic syndrome animal models. In this study we investigate cinnamaldehyde (CN) as a therapeutic intervention in endothelial dysfunction associated with obesity in both aorta and mesenteric arteries.

Normal Wistar (W) rats were divided in eight groups: (1) Wistar (W) rats, (2) W rats fed with high fat diet (WHFD), (3) W rats fed with sucrose diet (WS), (4) WHFD fed with sucrose diet (WHFS), (5) W+CN, (6) WHFD+CN, (7) WS+CN, (8) WHFS+CN. CN treatment with 20 mg/kg/day was administered for 8 weeks. At the end of the treatment, nitric oxide (NO)-dependent and independent vasorelaxation in isolated aorta and mesenteric arteries were evaluated. Metabolic profile, NO bioavailability, inflammation, and vascular oxidative stress were also assessed.

The metabolic dysfunction was more exacerbated in WHFD and WHFS rats accompanied by significantly higher levels of oxidative stress, inflammation, and endothelial dysfunction (associated with decrease NO bioavailability). CN significantly improved endothelial dysfunction, in aorta and mesenteric arteries of all groups. In addition, CN also decreased vascular oxidative damage (accumulation of anion superoxide and 3-nitrotyrosine in arteries) and inflammation (levels of monocyte chemoattractant protein-1) in arteries. CN

up-regulated Nrf2 expression and transcription activity that was reflected by increased Nrf2 nuclear accumulation and phosphorylation. Furthermore, CN significantly improved metabolic profile in WHFD and WHFS rats.

In summary, we provide experimental evidence indicating that cinnamaldehyde, an activator of Nrf2, can be used therapeutically to improve metabolic profile and relieve endothelial dysfunction in obesity and metabolic syndrome.

Keywords: Obesity, Endothelial dysfunction, Oxidative stress

PO - (21630) - Carotid body modulates catecholaminergic signaling in the adipose tissue

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ABSTRACT

Obesity is an epidemic worldwide. Adrenergic signaling in white (WAT) and brown (BAT) adipose tissues promotes lipolysis and glucose uptake and activates BAT thermogenesis with contribution of dopamine signaling. During obesity this effect of catecholamines is blunted. The carotid bodies (CB), metabolic sensors involved in energy homeostasis, have key function in dysmetabolism by regulating adipose tissue through the modulation of catecholaminergic activity. We investigated how obesity is associated with decreased catecholaminergic signaling in the WAT and BAT and the effects of CB modulation. Male Wistar rats were assigned to a HF group (60% fat) or a control group fed with a standard diet (NC). After 10 weeks, half the groups were submitted to bilateral carotid sinus nerve (CSN) resection or to

a sham procedure. 9 weeks after, WAT and BAT depots were collected and kept at -80ºC for western blot analysis of proteins from catecholaminergic system and to measure catecholamines by HPLC. Experiments followed the 2010/63/EU European Union Directive and were approved by NMS Ethics Committee and Portuguese Authority for Animal Health. Differences between means were calculated using One-Way ANOVA and considered significantly for $p<0.05$. HF diet decreased norepinephrine (NE), epinephrine (Epi) and dopamine (DA) in WAT. In WAT, HF diet did not change D2R or b3R but decreased D1R, an effect not changed by CSN resection, and increased b2R, an effect abolished with CSN resection. In BAT, HF diet or CSN resection did not change D1R and D2R, but HF diet decreased b3R, an effect abolished by CSN resection. HF diet show a tendency to decrease TH levels in both WAT and BAT, reversed by CSN resection. HF diet differentially altered catecholaminergic signaling in WAT and BAT, with major roles for D1R and b2R on WAT and b3R on BAT. CSN resection restored adrenergic and catecholaminergic signaling in both tissues, unraveling a mechanism to overcome catecholamines resistance in obesity.

Keywords: carotid body, adipose tissue, catecholamines, obesity

PO- (21646) - Ketogenic diet modulates glucose management and physical endurance in a sex-dependent manner

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ABSTRACT

Ketogenic diet (KD) has already been established as a therapy for epilepsy, and shown benefic effects for several other disorders, namely in glycemic control in diabetes, and weight loss without compromising exercise capacity in obesity. Regarding healthy individuals, KD-induced effect and sexual dimorphism remain poorly understood or controversial. Hence, we hypothesized that KD modulates glucose management and physical endurance in a sex-specific way in healthy adult rats. Accordingly, we aimed to peripherally characterize *in-vivo* glucose management and physical endurance-related parameters, in standard or KD-fed adult male and female Wistar rats.

Three-month-old male and female Wistar rats were randomly assigned to be fed with standard or KD. Two-months later, rats were subjected to: 1) glycemia, glucose tolerance and insulin resistance tests to evaluate glucose management; 2) metabolic cages to analyze food/water intake; 3) and treadmill running test to evaluate endurance and VO_2 max.

As expected, KD-fed rats had higher blood ketone levels compared to respective controls. KD significantly increased blood glucose levels and the vulnerability to glucose intolerance specifically in male rats, while increased the risk of insulin resistance in the female cohort. Despite lower food and water intake in rats fed with KD, their caloric intake and body weight remained similar to their controls. While KD did not affect VO_2 max levels, it decreased the RQ value in male rats, suggesting a higher percentage of fat-based metabolism at VO_2max. Energy expenditure and total speed and distance run were only (tendentially) decreased by KD in female rats, suggesting a decrease in their physical endurance.

In summary, ketogenic diet induced sex-specific alterations in healthy adult rats regarding glucose management and physical endurance. Still, further studies are needed.

Keywords: ketogenic diet, glucose management, physical endurance, sexual dimorphism

PO - (21648) - Chronic caffeine intake ameliorates white adipose tissue adenosine signaling and its metabolism alterations in dysmetabolic states

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INTRODUCTION

Adenosine (Ado) is involved in the regulation of white (WAT) adipose tissue and implicated in obesity and related diseases. Herein, we characterized alterations in Ado receptors (AdoR) and metabolism in WAT investigating the underlying mechanisms. Additionally, we explored the impact of chronic caffeine intake on these mechanisms.

METHODS

Expression of AdoR was evaluated in WAT samples from obese and stratified in insulin sensitive (IS) vs insulin resistant (IR) groups. Study was approved

by the Ethics Committee and in accordance with the Helsinki Declaration. Written informed consent was obtained. For the animal experiments, 3 groups of Wistar rats were used: a control (NC, 25 weeks standard diet), a HFHSu (25 weeks, 60% lipids+35% sucrose) and a HFHSuCAF group submitted to HFHSu diet plus caffeine intake (1g/kg) in the last 11 weeks of diet. Rats were evaluated for weight gain, insulin sensitivity and glucose tolerance. WAT depots were collected for Ado quantification and analysis of the AdoR and proteins involved in the pathways evaluated in the human study.

RESULTS

A2A and A2B expression in WAT was lower in IR patients in comparison with IS group. The expression of A_{2A} and A_{2B} receptor was positively correlated with genes that code for proteins involved in immunity, thermogenesis and angiogenesis ($p<0.0001$). In animals, HFHSu diet decreased A2A and A2B levels by 33.7% ($p<0.01$) and 15% ($p=0.061$), with no changes in A1. These effects were rescued by caffeine. HFHsu diet did not change ENT1 or CD73 levels, but caffeine intake in HFHsu rats increased by 38.15% ($p<0.01$) CD73 levels in comparison with HFHSu rats. Diet-induced alterations in WAT occurred in parallel with an increase in WAT depots and adipocytes perimeter, effects attenuated by caffeine treatment.

CONCLUSION

Alterations in AdoR and metabolism in WAT are associated with metabolic dysfunction both in rats and humans. Modulation of AdoR in WAT can be useful to improve dysmetabolic states.

Keywords: Adenosine, Caffeine, Adipose Tissue, Dysmetabolism

Theme: Locomotion | Exercise | Muscle | Active | Living

PO - (21409) - Relationship between symmetry of muscle group loads and spinal deformities

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ABSTRACT

The aim of this study was to examine the relationship between the load on muscle groups in different sports with the development of spinal deformities. The study was conducted on 60 volunteers aged 20 - 40, 17 women and 43 men. Of all volunteers, 22 were professional athletes and 38 were recreational athletes. All volunteers were classified into two groups, the athletes who play sports with a predominantly symmetric load and the athletes who play sports with a dominant asymmetric load. Bare's vertical axis test was used to determine the position of the spine. The deviation of the spinal column

from the physiological position was determined using the Posturokit system, which consists of a laser with a tripod. Considering all subjects, the deviation of the spinal column from the ideal physiological position was found in 16 (27%). Athletes from group of sports with asymmetric load had a statistically significant difference in the frequency of deformities ($p < 0.001$) compared to group of sports with symmetric load. In sports with an asymmetric load, 56.5% had spinal deformities, while, in sports with a symmetrical load, 8.1%. Considering the age, in subjects younger than 26, the presence of deformity was found in 30%. In the group of older than 26 years, the deviation of the spinal column was found in 10%, without statistically significant difference. Deformities were found in 25.6% of men and 29.4% of women, without statistically significant difference in relation to the sex of the subjects. Professional athletes had a spinal deformity in 9.1% of cases, while recreational athletes had spinal deformities in 36.8% of cases, with statistically significant difference in relation to these two categories of athletes ($p < 0.05$). The results of this study support the fact that sports with an asymmetric load lead to a significantly higher incidence of deformities compared to sports with a symmetrical load, as well as that deformities are more common in recreational athletes.

Keywords: spinal column, sport, symmetrical load, asymmetric load

PO - (21427) - The regular practice of light physical activity at home improves lower limb hemodynamics

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ABSTRACT

In elderly, mobility and self-sufficiency are important complementary determinants of health. To that, it is important to maintain adequate levels of performance specially in the lower limb through physical activity. The aim of this study was to identify changes in the lower limb perfusion in senior sedentary individuals (with some comorbidities associated to aging) after a daily regular unsupervised physical activity program at their homes. Ten participants were selected (five women and five men) mean age 62.4$\pm$5.6 years old, with similar lifestyles, body mass index (BMI) values compatible with overweight, ankle-brachial index (ABI) and mean arterial pressure within normal range. The study respected all aspects of good clinical practice being approved by the institutional Ethics Committee. After adapting to room conditions, both feet perfusion was evaluated for five consecutive minutes with laser Doppler flowmetry (LDF) and contactless polarized spectroscopy (PSp). Evaluations took place at days zero (D0) and thirty (D30). Baseline measurements at D0 and D30 revealed no perfusion differences between right and left foot nor

between sexes. For 30 days participants repeated, every day, a set of three sequential activities, whose impact on distal perfusion had been identified in previous studies (five minutes "step in place"; one-minute plantar flexion; five minutes walking). At D30 a significant increase in perfusion ($p=0.005$) and decrease in MAP ($p=0.037$) was noted, with a significant expression in the male group ($p=0.042$). A strong correlation between the increase in perfusion and the weekly activity time was found in both sexes ($p=0.043$). This simple approach suggests that regular unsupervised activity improves distal perfusion and global hemodynamics. circulatory conditions. The clinical interest and practicability of this home-health strategy should be further investigated.

Keywords: Foot perfusion, LDF, home activity program

PO - (21501) - The impact of exercise on prevention of sarcopenia after bariatric surgery: The study protocol of the expobar randomized controlled trial

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My name is Claudia, I'm a PhD Student, MSc in Exercise and Wellness and Specialist Nurse. My entire professional life has been dedicated to the follow-up of patients with severe obesity, proposed for surgical treatment. The long-term maintenance of the results of the surgery became a challenge and the search for the best results and the best care centered on each patient is my main focus.

INTRODUCTION

Bariatric surgery is one of the treatments for obesity, with proven efficacy in reducing weight and diseases associated with obesity. Weight loss associated with bariatric surgery is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, which leads us to induce that after bariatric surgery, patients incur an increased risk of sarcopenia. The need for prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. The aim of this randomized clinical trial will be to study the effects of a 16-week supervised exercise intervention program on the prevention of sarcopenia, in patients undergoing bariatric surgery. As a

secondary purpose, it is also intended to characterize metabolic risk factors, physical fitness, and quality of life in post-bariatric surgery patients.

METHOD

A total of 45 patients on the waiting list for bariatric surgery and who underwent surgery later will be included in EXPOBAR (EXercise POst BARiatric) and randomized into 2 groups, experimental and control. The intervention starts one month after the surgery, totaling 16 weeks. Body composition parameters, metabolic risk, quality of life, physical activity, physical fitness and sedentary behavior will be determined. For each participant, results are measured at five different times: before surgery, before the exercise program, after the exercise program, six and twelve months after the exercise program.

RESULTS

This study will provide the effects of physical exercise on sarcopenia in patients after bariatric surgery.

STUDY REGISTRATION

The study was registered at Clinicaltrials.gov NCT03497546

Keywords: exercise, bariatric surgery, fat-free mass, sarcopenia, metabolic risk factors, quality of life

PO - (21608) - Acute effects of inspiratory muscle training combined or not combined with moderate-intensity treadmill walking on blood pressure and related variables in hypertensive subjects

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ABSTRACT

Aerobic exercise is a widely used non-pharmacological strategy for prevention and treatment of hypertension. Inspiratory muscle training with breathing devices is also pointed as beneficial. However, the physiological hemodynamic acute effects are not known in participants with hypertension. The aim of this study is to analyze the acute effect of 3 sessions with a breathing device (POWERbreathe, Southam, England) combined, or not combined to treadmill walking on systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), mean blood pressure (MAP) and rate pressure product (RPP). Nine hypertensive participants with non-beta-blockers medication were recruited (age= 53.4$\pm$10.1yr; body mass= 75.1$\pm$12.6kg). The study included a combined session (COMB) characterized by 30-min walking at moderate intensity (40-59% of heart rate reserve) combined with 3-sets of 15 breathing cycles at 40% of maximal inspiratory pressure (MIP), an isolated session (IMT) with 3-sets of 15 breathing cycles at 40% of MIP and a control session (SHAM)

with 3-sets of 15 breathing cycles at 5% of MIP. During and up to one hour after exercise, SBP, DBP and HR were measured and MAP and RPP were derived from standard equations. The ANOVA reveal that during exercise, the HR in the COMB was significantly higher compared to the SHAM and IMT in all sets and RPP values in the COMB were higher compared to the SHAM (1st set= 9821±2101 vs 8677±1690 bpm.mmHg, p=0.013). No differences were found in SBP, DBP and PAM. After exercise, the COMB promoted a lower SBP compared to SHAM and to IMT (post 15'= 114±11 vs 126±16 vs 129±19 mmHg, p=0.014; post 45'= 120±13 vs 129±15 vs 134±17 mmHg, p=0.003). SBP was also lower in the COMB compared to SHAM (post 60'= 122±11 vs 132±15, p=0.049). The SHAM and IMT promoted a similar response during and after exercise in all variables. The COMB promoted greater expression of hypotension compared to the SHAM and to IMT. The breathing sessions were well tolerated.

Keywords: Inspiratory Muscle Training, POWERbreathe®, Treadmill Walking, Blood Pressure

PO - (21615) - Effects of different types of muscle contraction on cardiovascular, haemodynamic and near-infrared spectroscopy derived-parameters during back squat exercise

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ABSTRACT

Exercise monitoring is essential for enhancing performance and reaching the set goals. With the back squat being one of the most popular exercises in training, understanding physiological changes in real time has become indispensable. This pilot study compared the effect of a dynamic contractions protocol (DYN) and an isometric contractions protocol (ISO) on cardiovascular, haemodynamic, and near-infrared spectroscopy (NIRS) derived-parameters. Seven participants (age: 26.4±6.1 years old; height: 176.6±9.7cm; body mass: 76.7±9.6kg) with back squat experience were recruited. The DYN was constituted by 3 sets of 16 repetitions at 50% of 1RM (57.14±19.23kg), with 120 seconds of rest interval between sets and 2 seconds per cycle of movement. The ISO was composed by 3 sets of 1 isometric contraction with the same total length and conditions as DYN. Throughout the protocol, heart rate (HR),

mean arterial pressure (MAP), double product (DP) and NIRS parameters, i.e., deoxygenation percentage change (Deoxy %Δ), and reoxygenation time to 50% ($t\text{SmO}_{2\ 50\%\ reoxy}$) in four muscles (*vastus lateralis*, *soleus*, *longissimus*, and *semitendinosus*) were assessed. Cardiovascular and haemodynamic parameters were higher in DYN in all sets, being significantly different in the 3rd set in HR and DP (*ES*=0.65 and *ES*=0.86, respectively), and in the last sets in MAP (2nd set: *ES*=1.13; 3rd: *ES*=0.98). The DYN also induced a higher Deoxy %Δ in most of the muscles (related to muscular stress), however it was only significant different in *soleus* muscle. The $t\text{SmO}_{2\ 50\%\ reoxy}$ was significantly lower in *vastus lateralis* in DYN in the 3rd set, showing a faster recovery. The results suggest that the use of different types of contraction can induce distinct cardiovascular, haemodynamic and muscular responses. This may be an interesting line of research regarding acute exercise adaptations, where back squat dynamic contractions promoted greatest effect both in central and peripheral physiological variables.

Keywords: muscle oxygen saturation, dynamic contractions, isometric contractions

PO - (21636) - Effect of a combined session of aerobic and isometric exercise on acute heamodynamic response and 24-hour ambulatory blood pressure

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ABSTRACT

The short-term effects of a single aerobic and isometric exercise session on ambulatory blood pressure (BP) are not well known in medicated hypertensives. So, this study aims to evaluate the acute effect of treadmill walking exercise combined with 3 strength exercises focusing on isometric contractions on Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Blood Pressure (MAP) and heart rate (HR) during exercise and for up to 24h after the exercise session. A total of 8 hypertensive participants (age= 53,125 years old) with controlled BP by proper medication without beta-blockers held a control and an exercise session. The exercise session consisted of 30 minutes of treadmill walking exercise, at a moderate intensity (between 40% and 60% of HR reserve), followed by 3 sets of 1 isometric contraction of 60 sec in each of the 3 strength exercises: the unilateral handgrip (30% of maximal voluntary contraction), the plank and the wall-sit (at a self-perceived

moderate intensity). During the exercise session, SBP, DBP and perceived exertion (RPE) were registered at 10, 20 and 30 minutes of treadmill walking and immediately after each isometric set and HR was continuously measured (in order to record all the necessary data and guarantee the safety of the participants). After the sessions the participants used the TensioDay ambulatory BP monitor (TensioMED, Budapest, Hungary) for 24 hours.

The t-test revealed no differences in all studied variables between the control and the combined exercise sessions (p=0.001), except for DBP (p=0.056). The plank exercise promoted a significant (p£0.05) higher HR, SBP and MAP response. The unilateral Handgrip was associated to lowest BP values, probably very dependent on the smaller amount of muscle mass involved. There were no differences in ambulatory BP variables between the sessions studied, revealing that this dose of exercise was inefficient in promoting a reduction in BP in medicated hypertensive participants.

Keywords: static contraction, blood pressure, handgrip exercise, plank exercise, wall-sit exercise

PO - (21640) - Acute effects of unloaded squat variations on muscle oxygen saturation and local perceived exertion

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ABSTRACT

Assessment of muscle oxygen saturation (SmO2) during exercise provides information related to local blood flow and muscular oxygenation. This study aimed to compare the SmO2 of the vastus lateralis (VL) and soleus (SL) muscles and local perceived exertion (RPELocal) during six squat variations (Deep/Jump/Uneven/Wall/Unstable/Pistol). Eight healthy adults (age=26.9±2.8 yr; BMI=24.8±3.1 kg/m2; VL skinfold=14.2±4.8 mm; SL skinfold=12.7±3.3 mm), after a familiarisation session, completed in random order six squats for 90 sec, interspersed with 5-min rest (cadence 40-60 bpm). The squat variations were chosen according to motion, level of stability and foot position. The SmO2 was measured in VL and SL of both legs and expressed in percentage (%) using four MOXY monitors (Fortiori Design, Hutchinson, USA). The RPELocal (Borg 6-20) was collected immediately after each variation. A repeated measures

ANOVA revealed differences in RPELocal between exercise variations. A higher RPELocal was reported during Jump squat (18.6±0.9) which was the variation with the lowest levels of SmO2. No changes in mean SmO2 were identified on right and left VL. Differences in right SL mean SmO2 ($\eta 2$=0.298) were seen in Deep vs Pistol. Left SL ($\eta 2$=0.456) showed significant differences in Jump (42.77%) vs Deep (65,59%), Uneven (67.24%) and Pistol (65.59%); Unstable (54.54%) vs Uneven, Wall (65.11%); Pistol and Deep; Deep vs Pistol. In the last 30 sec of exercise, no differences were found in right SL. In turn, in the left SL ($\eta 2$=0.520) SmO2 was lower in Unstable (49.87%) compared to Deep (60.97%), to Uneven (67.38%) and to Wall (58.22%), in Jump (30.61%) compared to Uneven and Wall, in Wall was lower than Deep. Lower SmO2 both in VL and SL, during Jump as well higher RPELocal, indicates higher physiological stress during this unloaded squat variation. Further studies are needed to better understand the complex puzzle of how the muscle system responds to the execution of different movements.

Keywords: Bodyweight squat, NIRS, Muscle Oxygen Saturation, Perceived Exertion

PO - (21643) - Muscle oxygen saturation kinetics, heart rate and perceived exertion during six variations of push-up exercise

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ABSTRACT

Near-infrared spectroscopy (NIRS) has been used to assess changes in muscle oxygen saturation (SmO_2), which helps in exercise characterization. This study compared in *triceps* (TRI) and *deltoideus* (DEL) muscles,SmO_2 kinetics, heart rate (HR) response and perceived exertion (RPE) in six push-up variations.After a familiarisation session, ten males (age:25.2$\pm$3.2 yr), performed six push-ups randomly (diamond, declined, inclined, knuckles with one foot, spartans, and unstable terra-core platform) over 60 sec, with 5-min rest. Minimum SmO_2, percentage of oxygen saturation loss ($\Delta\%SmO_2$) and deoxygenation$_{slope}$ were assessed by NIRS. HR (Garmin monitor) and RPE (local and general) using Borg scale (6-20). Data were compared using a repeated-measures ANOVA

and correspondent effect sizes. For HR and RPE_{local} no differences were found. Regarding $RPE_{general}$, spartans variation exhibited the highest values (18.7±1.2), and significant differences were observed between spartans and declined/diamond/unstable/knuckles, and between inclined (17.5±2.5) and diamond (16.3±3.6). The minimum SmO_2 in TRI and DEL were lower in diamond compared to other variations. Significant differences were observed in diamond (15.9%) vs inclined (21.7%), declined (30.8%), unstable (26.1%), and knuckles (26.7%) in TRI minimum SmO_2 (η^2 =0.23). For DEL (η^2 =0.300) significant differences were observed between inclined (44.2%) vs declined (25.0%), inclined vs diamond (24.9%), inclined vs knuckles (31.4%) and declined vs unstable (39.8%). A greater Δ%SmO_2 in TR was identified for inclined (-62.2±13.7%), while in DL for diamond (-48.7±25.2%). The $deoxygenation_{slope}$ was higher in TR during diamond (1.9% SmO_2 s^{-1}) and in DL during spartans (2.2% SmO_2 s^{-1}), which suggests an initial superior demand. The variation in hand position and body posture during the push-ups contributes to different muscular adaptations in TRI and DEL. Besides, the spartans require a higher RPE and SmO_2 change compared to other variations.

Keywords: NIRS, push-ups exercise, muscle oxygen saturation, physiological adaptations

Theme: Neurophysiology

PO - (21498) - Glucose may revert contextual fear memory impairment observed in adrenaline-deficient mice through an increase in Nr4a3 and Bdnf hippocampus expression

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ABSTRACT

The release of adrenaline (Ad) into the bloodstream during stress strengthens contextual fear memory[1,2]. Glucose is one of the purposed mechanisms by which Ad, that does not cross the blood-brain barrier, affects contextual fear memory[3]. We aimed to detach the effect of glucose from Ad and evaluate its impact on contextual fear memory. Wild-type (WT) and Ad-deficient (129x1/SvJ) mice were submitted to the fear conditioning procedure and freezing was evaluated on training and context days. Mice were treated with Ad (0.01 mg/kg, i.p., 3 min), glucose (30 or 10 mg/kg, i.p., immediately before), or vehicle (0.9 % NaCl). Blood glucose was quantified by coulometry. *Nr4a1*, *Nr4a2*, *Nr4a3* and *Bdnf* mRNA expression were evaluated in hippocampus samples.

Results were analysed by Two-Way ANOVA (post-hoc Sidak's or Tukey's test), One-Way ANOVA or Students' t-test. In Ad-deficient mice, glucose administration (30 mg/kg) increased freezing compared with vehicle-treated mice. It was observed an increase in the hippocampal mRNA expression of *Nr4a3* and *Bdnf* genes of glucose-treated Ad-deficient mice compared to vehicle-treated mice. Treatment with a sub-effective dose of glucose (10 mg/kg) and Ad (0.01 mg/kg) did not increase freezing in Ad-deficient mice compared to vehicle-treated mice. However, when given simultaneously, Ad-deficient mice showed an enhancement in contextual fear memory. In conclusion, our data suggest that glucose alone is capable to revert the contextual fear memory impairment observed in Ad-deficient mice possibly due to modulation in the hippocampal expression of *Nr4a3* and *Bdnf* genes. When both Ad and glucose are present, they appear to act synergically to strengthen contextual fear memory.

Keywords: adrenaline, glucose, adrenaline-deficient mice, fear conditioning, contextual fear memory

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PO - (21508) - Evidence of altered enteric GABA receptor modulation in high fat diet induced type 2 diabetes

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ABSTRACT

Worldwide the prevalence of type 2 diabetes (T2D) is alarming, with current global average incidence of 9%. It is associated with increased mortality and severe comorbidities. The discovery of T2D remission after Roux-en-Y gastric bypass spotlighted the proximal small intestine as possible culprit in the aetiology of T2D. Changes in gut hormones such as the incretin GLP-1, and the gut microbiome have been suggested to explain diabetes remission after gastric bypass but remain inconclusive. Our preliminary in silico analyses, indicated disruption of neurotransmitter GABA (gamma-aminobutyric acid) signalling in T2D. GABA is normally involved in regulated dampening of nerve excitability by causing hyperpolarization and is present in the gut, implicating GABA-mediated signalling in the regulation of physiological functions within the gastrointestinal tract. GABA mediates its effects via GABA receptors, including the metabotropic hetero-dimeric $GABA_B$ G-protein coupled receptors.

Signalling through these receptors is regulated by homo-oligomers of auxiliary subunits termed potassium channel tetramerization domain (KCTD) proteins that can specifically negatively regulate presynaptic voltage-activated Ca2+ channels and cAMP signalling and positively regulate postsynaptic inwardly rectifying K+ channels. Gut signalling in response to ingested nutrients involves enterocytes, diverse enteroendocrine cells, networks of enteric glia, and intrinsic and extrinsic nerves that communicate with the peripheral and central nervous systems. We investigated GABAB receptors and their potassium channel tetramerization domain (KCTD) auxiliary subunits in the enteric nervous system of a mouse model of high fat diet induced T2D using immunofluorescence microscopy. Significant differential expression and cellular localization of distinct KCTD subunits was observed in the proximal small intestine of our T2D model, which supports enteric GABAergic signalling as a possible novel target for T2D.

Keywords: enteric nervous system, diabetes, GABAergic signalling

PO - (21591) - Non-convulsive status epilepticus and the salzburg criteria: Does clinical practice agree?

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INTRODUCTION

Non-convulsive status epilepticus (NCSE) is a neurological emergency whose misdiagnosis or delayed diagnosis can have serious consequences, including death. The Salzburg consensus criteria for non-convulsive status epilepticus (SCC) are based on electroencephalographic and clinical criteria and classify patients as definite NCSE (D-NCSE), possible NCSE (P-NCSE) or no NCSE (N-NCSE). Despite the high precision in the first two groups, the possible NCSE group complicates clinical decision-making because it makes the diagnosis uncertain and therapeutic escalation is potentially iatrogenic. There are several validation studies on SCC, but few studies based on patient outcomes.

OBJECTIVES

Comparison of outcomes and mortality by each of the SCC classification groups and additional characterisation of patients in the P-NCSE group.

METHODS

Retrospective study of a sample of patients with altered state of consciousness without accompanying motor phenomena and without defined aetiology who underwent EEG between January 2019 and April 2021. Patients were functionally assessed using the modified Rankin Scale (mRS) at 3 different time points: baseline, hospital discharge and follow-up.

RESULTS

79 patients (37 women and 43 men, mean age 69.5 years) were included, 18 of whom had a previous diagnosis of epilepsy. According to SCC, 59 N-NCSE, 11 P-NCSE and 9 D-NCSE cases were identified. The most common clinical suspicion of NCSE was cerebrovascular disease and the most common lesion on MRI was of ischaemic origin. Age and mRS score at hospital discharge were found to be predictors of mortality, in contrast to epilepsy diagnosis, which appears to be a protective factor.

CONCLUSIONS

In this study, the P-NCSE group appears to be more similar to the D-NCSE group than the N-NCSE group in several aspects, including outcome, although the small sample size does not allow for statistically significant results to support this tendency.

Keywords: Non-convulsive status epilepticus, Salzburg Consensus Criteria, Outcome, modified Rankin Scale, EEG

PO - (21638) - Decreased vip expression and AMPA GluA1 phosphorylation underly the postweaning developmental shift of endogenous $VPAC_1$ modulation of hippocampal CA1 LTP

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ABSTRACT

Long-term potentiation (LTP) induced by theta-burst stimulation (TBS) undergoes postweaning developmental adaptations, likely relying on GABAergic circuit maturation[1]. We have recently shown that modulation of LTP by endogenous VIP acting on $VPAC_1$ receptors involves regulation of GABAergic transmission[2] and is gradually diminishing during postweaning development (3- to 12-week-old), while global hippocampal $VPAC_1$ receptor expression is gradually increasing during the same developmental period[3]. This is accompanied by GABAergic circuit and synapse maturation. In this work we investigated whether hippocampal VIP, $VPAC_1$ and $VPAC_2$ receptor expression is increasing specifically in synaptic membranes and if enhanced LTP is due to altered AMPA receptor basal GluA1 subunit phosphorylation. Both $VPAC_1$ and $VPAC_2$ receptor remained unaltered in juvenile (3-week-old), young adult (7-week-old) or adult (12-week-old) rats. VIP expression decreased in hippocampal synaptosomes while AMPA GluA1 subunits

increased from weaning (3-week-old) to adulthood (12-week-old). Conversely, basal phosphorylation of AMPA GluA1 subunits in Ser831 and Ser845 was progressively enhanced during postweaning development. Taking into account the recently described involvement of VIP interneurons in several aspects of hippocampal-dependent learning, neurodevelopmental disorders and epilepsy[4,5], these findings could provide important insights into the role of VIP modulation of hippocampal synaptic plasticity in normal and altered brain development and in epileptogenesis.

Keywords: LTP, VIP, VPAC1 R, VPAC2 R, cognition, synaptic plasticity

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PO - (21639) - Carotid sinus nerve activity in rats is differently modulated by nutritional status and diet interventions

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I am graduated in Molecular and Cellular Biology (2010) and obtained my master's in Biotechnology (2012). In 2019, I finished my PhD (NOVA Medical School, UNL), on the modulation of carotid body activity as a therapeutic intervention in metabolic diseases. After my PhD, I spend 8 months at the Institut de Pharmacologie Moléculaire et Cellulaire, France. Since 2020, I am a Junior Researcher and I am dedicated to the decoding of carotid sinus nerve activity to treat type 2 diabetes.

ABSTRACT

Carotid bodies (CB), peripheral O_2 sensors, are also metabolic sensors involved in energy homeostasis, since resection or electric modulation of carotid sinus nerve (CSN), the CB sensitive nerve, prevents and reverses pre-diabetes and type 2 diabetes (T2D) in rats. Also, CB-CSN activity augmented with the increase in caloric intake, one of the major causes of dysmetabolism. Aiming to selectively modulate CB-CSN activity to treat diseases associated with overnutrition, as T2D and obesity, we characterized CSN neural activity in different nutritional status and submitted to different nutritional interventions in rats.

Three groups of male Wistar rats were used: control (normal chow diet, NC), high-fat group (HF, 60% lipid-rich diet, 3 weeks) and high-fat/high-sucrose group (HFHSu, 60% fat+35% sucrose, 25 weeks). CSN *ex vivo*recordings in normoxia and in response to hypoxia were performed in CB-CSN preparation collected from rats in fasting state, *ad libitum* or after the ingestion of Fortimel, a high protein nutritional supplement (1,46g/2ml). Spike sorting and clustering were performed.

Four different types of CSN action potentials (AP) were detected. In NC animals, basal CSN activity increased by 47 and 44% in postprandial and *ad libitum* states, respectively, when compared with fasted animals, an effect characterized by an increase in type 2 AP in the postprandial state. Also, hypoxia-evoked CSN response increased significantly in postprandial and *ad libitum* NC animals *vs* fasted animals. In *ad libitum* rats, HF and HFHSu diets increased by 195 and 301% CSN basal activity, respectively, effect characterized by increased type 2 and 4 AP, and correlated with insulin resistance but not with fasting glycemia. Also, hypercaloric diet did not alter the CSN response to hypoxia.

We conclude that nutritional status and interventions modulate differently CSN neural activity. CSN neural signatures might be a good parameter to distinguish overnutrition states.

Keywords: Carotid body, Carotid sinus nerve, Diet interventions, Neural activity

PO - (21652) - Plastic rearrangements of mcpo parvalbumin-immunoreactive neurons in the kainate model of epilepsy - preliminary results

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INTRODUCTION

Temporal lobe epilepsy (TLE) is the most common form of refractory epilepsy in adults. Besides all the efforts to understand the underlying mechanisms, there are some morphological changes that remains unknown in TLE patients' brains. The amygdala, however, is a cerebral region that has been identified as the core of the cognitive and emotional changes of these patients. Basal forebrain is composed by different subregions, all comprising cholinergic, GABAergic and glutamatergic neurons. Magnocellular preoptic nucleus (MCPO) is a structure of BF that receives inputs from basolateral amygdala, where different neuronal populations might contribute to the neurochemical reorganization in this type of epilepsy.

OBJECTIVES

The main goal of our work was to evaluate the plastic rearrangements of inhibitory neurons of MCPO in a model of TLE.

METHODS

Adult Wistar rats received a 12.5 mg/kg injection of kainic acid to induce *status epilepticus*. The development of chronic epilepsy was documented with the monitorization of spontaneous recurrent seizures weeks later. Changes in inhibitory neurons of MCPO nucleus were investigate using an antibody against parvalbumin (PARV). Mann-Whitney test was used for statistical comparison, at a significance level of .05.

RESULTS

A total of six animals (3 per group) were analysed. A 59% increase in volume of MCPO PARV-stained cells in epileptic rats was observed (771 ± 303 vs. 485 ± 94 μm^3), although not statistically significant ($Z=1.53$, $p=.127$).

CONCLUSIONS

These results illustrate that in the presence of spontaneous seizures PARV-stained neurons in the basal forebrain show a tendency to increase in size, reflecting the plastic rearrangements known in TLE. Our previous work showed significant changes in the cholinergic populations in different regions of the basal forebrain that project to amygdala, which might relate to the above described findings.

Keywords: Temporal lobe epilepsy, Magnocellular preoptic nucleus, Parvalbumin, Basal forebrain, Animal model

PO - (21653) - Hippocampal volumetric changes in temporal lobe epilepsy: A systematic review with meta-analysis

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INTRODUCTION

Hippocampal sclerosis (HS) is the morphological hallmark of the neuropathological process in mesial temporal lobe epilepsy (mTLE), which is found in more than 50% of the patients. HS is recognized using magnetic resonance imaging (MRI) by its characteristic neuron loss and synaptic reorganization. These changes may affect the volume of hippocampal formation (HV), leading to cognitive and emotional dysfunctions that occur in these patients.

OBJECTIVES

The aim of our study is to quantify the volumetric changes in the hippocampal formation in patients with mesial temporal lobe epilepsy.

METHODS

In this study PubMed®, Embase®, Scopus®, Web of Science™, Cochrane Library and SciELO databases were used. Several trial registers were also consulted. Controlled and non-controlled terms were used to increase sensitivity. A total of 733 records were screened with a total of 127 publications assessed for eligibility. Studies were analysed by two authors, and data collection was reviewed by both. Meta-analysis was performed using jamovi's METAFOR package.

RESULTS

Twenty-nine articles regarding a total of 1247 mTLE patients and 812 age- and sex-matched controls were included. Brain MRI was acquired in 1.5-7T equipment. Meta-analysis estimated a mean difference of 933 ± 95.5 mm^3 between controls and mTLE ipsilateral HV ($Z=9.77$, $p<.001$), with a significant heterogeneity ($p<.001$). Also, a significant volume difference was observed between controls and mTLE contralateral HV (200 ± 33.5 mm^3, $Z=5.96$, $p<.001$), with a significant heterogeneity ($p<.001$).

CONCLUSIONS

This systematic review shows a significant decrease in HV both ipsi- and contralaterally in mTLE patients. The large heterogeneity might account different HV anatomical definitions between studies.

Keywords: Temporal lobe epilepsy, Hippocampal atrophy, MRI, neuropathology, mesial temporal sclerosis

PO - (21666) - Effect of systemic inflammation on memory, depression and anxiety in rodents

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ABSTRACT

Neurodegenerative and neuroinflammatory diseases such as Alzheimer's disease, depression, and anxiety are of multisystem etiology where non-genetic risk factors play an important role in the progression of these conditions. Among the non-genetic factors, peripheral inflammatory events are associated with cognitive decline and progression of these diseases as they are mainly related to inflammatory mediators released by microglial cells, considered the primary mechanism underlying the development of neurodegeneration symptoms in response to systemic inflammation. In this scenario, in recent years the hypothesis that correlates plasma endotoxin levels, microglial activation, and the development of neurodegenerative and neurinflammatory diseases has gained prominence. Thus, the central nervous system (CNS) and the enteric nervous system of the gastrointestinal tract (GI tract) are intimately connected via hormones, neuromodulators, and neurotransmitters related to efferent/ afferent nerves, which further drives investigations of the brain-intestinal axis in the progression and contribution of this diseases. To observe the behavioral changes exerted by a condition of systemic inflammation, female Swiss mice of 25 to 35g, from the central vivarium of UNIVALI (Brazil), were used. The study was approved by the Ethics Committee on Animal (approval no. 029/22). The animals were subjected to the acute inflammatory bowel disease (IBD) protocol where they were divided into groups according to treatment and received 3% dextran sulfate sodium (DSS - MW: 40,000) dissolved in drinking water for 7 days. After this time, the DSS was replaced by water until day 10, and behavioral tests were conducted from day 11 to 13. It was possible to observe that the animals that consumed DSS (vehicle group) developed a cognitive deficit when compared to the naive group (group that did not consume DSS) ($p<0.001$) and evaluated in the novel

object recognition test (NOR), a memory test. When evaluated in the elevated plus maze (EPM) test, animals in the vehicle group decreased their time in the open arms compared to the naive group ($p<0.05$), indicating an anxiety-like behavior. Finally, when evaluated in the tail suspension test (TSC) the animals in the vehicle group increased the immobility time when compared to the naive group ($p<0.001$), interpreted as a depressive-like behavior of the animal. In conclusion, the colitis model by ingestion of DSS alters behavioral parameters of mice exposed to this agent, suggesting that this condition may exert an important influence on the central nervous system.

Keywords: Neuroinflammation, inflammatory bowel disease, behavior

Theme: Other (miscellaneous)

PO - (21414) - Reparo de defeitos ósseos críticos na calvária de ratos após a aplicação de ondas mecânicas vibratórias

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INTRODUÇÃO

As fraturas ósseas representam grande causa de morbidade e geram custos para o serviço de saúde. A vibração de baixa magnitude e alta frequência foi proposta como um tratamento alternativo e seguro para aumentar a massa óssea.

OBJETIVO

Avaliar histomorfologicamente o potencial osteogênico das ondas vibratórias no reparo de defeitos ósseos críticos.

MATERIAIS E MÉTODOS

Utilizou-se 12 *Rattus norvegicus*, da linhagem Wistar albinus, machos, com massa corporal entre 350 e 450g, que foram distribuídos de aleatoriamente à composição de dois grupos: Grupo Controle (GC) e Grupo Experimental de Vibração Imediata (GEVI). Animais do grupo experimental foram submetidos a ondas vibratórias de 60 Hz e aceleração vertical de 0,3 g. As ondas vibratórias foram aplicadas três vezes por semana, durante 20 minutos. Após 15 dias a partir do ato operatório, os animais foram eutanasiados para a realização da análise histomorfométrica.

RESULTADOS

Observou-se neoformação de matriz osteoide reparativa, restringida às bordas ósseas, em ambos os grupos. A média de extensão linear do defeito ósseo do GEVI (5,83 ± 0,79mm) foi menor em relação ao GCDO (6,62 ± 0,63mm), porém, de maneira não estatisticamente significante (U=8,00, z=-1,604, p=0,132).

DISCUSSÃO

Ao se estimular a via de sinalização canônica Wnt nas células osteoprogenitoras ainda não comprometidas com a linhagem osteoblástica, ao invés de ajudar, há prejuízo da osteogênese. Diante do fato de que um possível mecanismo pelo qual as ondas vibratórias obtêm suas respostas é justamente através da estimulação desta via, o pós-operatório imediato pode não ter sido momento oportuno para o início da intervenção.

CONCLUSÃO

A elucidação do melhor momento no pós-operatório para se realizar a intervenção com ondas vibratórias deve ser objetivada em futuros trabalhos, sendo tão relevante quanto a definição dos protocolos ideias de regime vibratório.

Keywords: reparo osso osteogênese ondas mecânicas

PO - (21424) - A proof-of-concept setup for neurosecurity

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BACKGROUND

One of the goals of neurosecurity is to protect users' personal information from being manipulatively used. Tailoring media communication strategies to a user or group of users, based on their personality characteristics, is called microtargeting (currently based on digital footprints). Microtargeting can exploit users' vulnerabilities to enhance biases that shape how users process information, posing a threat to free will; studies show that commercials tailored to viewers' personality type can be up to 50% more persuasive. A need arises to develop tools to prevent psychological manipulation.

METHODS

In this work we explore physiological responses, namely, Electrodermal Activity (EDA), Photoplethysmography (PPG) and motion, for neurosecurity evaluation. Data is collected during an experiment devised to elicit both positive (happiness) and negative (fear, disgust) emotions using two short

videos, one comedy (positive) and one horror (negative) film, with a duration of approximately 15 minutes each and viewed by groups of participants in an audience setting. A total of 24 participants (8 female) of ages 24.0±5.0 volunteered to participate in the study, divided in 6 groups of 4 individuals. The neurosecurity technique consists on assessing the personality type of each participant using the Big Five Factor Structure, which is disclosed to certain groups of participants.

DISCUSSION

We expand the state-of-the-art by collecting data in a real-world group setting, based on the analysis of emotional responses through physiological data and self-report annotation during visualization of short films in a neurosecurity framework. The collected data is annotated in terms of SAM self-reporting, and is used as a tool to investigate and protect users against microtargeting using a cognitive approach of boosting their awareness on the type of psychological targeting being. The use of a group setting is relevant to explore affective phenomena of collective emotions.

Keywords: Affective Computing, Neurosecurity, Physiological Data, Wearable Devices

PO - (21494) - Adipose tissue and its relation to cardiometabolic biomarkers

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ABSTRACT

Excess body fat, as well as increased levels of subcutaneous adipose tissue (SAT) or visceral adipose tissue (VAT), are linked to higher risk for metabolic syndrome, type 2 diabetes mellitus, and cardiovascular disease, among other several non-communicable chronic diseases. However, it is not only the level but also the distribution of body fat that contributes to increased disease risk.

The present study was a cross-sectional analysis consisting of 165 healthy participants, 61 men, and 104 women, presenting a mean age of 33.58 years old. Body composition was assessed using a dual-energy x-ray absorptiometry (DXA), and specific biochemical parameters were obtained from capillary blood using LINX DUO (Menarini Diagnostics).

Our results indicate that those participants presenting ≥17.86kg of total adipose tissue also showed higher levels of glycated hemoglobin (HbA1c) and fasting glycemia, total cholesterol, LDL cholesterol, non-HDL cholesterol, triglycerides/HDL cholesterol ratio, and systolic and diastolic blood pressure

(p<0.05). Additionally, participants in the highest category of VAT levels (≥232.00 g) presented the highest levels of the above-mentioned metabolic markers (p<0.05) and also statistically significant lower levels of HDL cholesterol. Finally, participants showing more than 894.00 g of SAT showed statistically significant lower levels of HDL-cholesterol, higher levels of LDL-cholesterol and triglycerides/HDL cholesterol ratio, and diastolic blood pressure. In all analyses performed, these participants presented higher body weight (and consequently higher BMI) and higher abdominal circumference (p<0.05). Similar results were obtained when analyses by sex were performed.

In conclusion, this study suggests that individuals presenting higher levels of total adipose tissue but also SAT and VAT, show unfavorable metabolic markers distribution which may represent an increased risk factor for the development of cardio-metabolic diseases.

Keywords: Body Composition, Metabolic markers, Adipose Tissue

PO - (21502) - Repair of critical bone defects in rat calvary afterthe application of vibratory waves

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INTRODUCTION

Bone fractures represent a major cause of morbidity and generate costsfor the health service. Low-magnitude and high-frequency vibration was proposed as analternative and safe treatment to increase bone mass.

OBJECTIVE

To evaluatehistomorphologically the repair of critical bone defects after the application of vibratorymechanical waves.

MATERIALS AND METHODS

10 Rattus norvegicus were used. Surgical protocol was used to perform the critical defect of 8.5 mm diameter in the calvaria ofthe rats. The animals were randomly divided into two groups: the Bone Defect Control Group (GCDO) and the Immediate Vibration Experimental Group (GEVI). GEVI animals weresubmitted to vibration waves of 60 Hz and vertical acceleration of 0.3 g. Vibrating waveswere applied three times a week for 20 minutes. After 15 days from the surgery, the animalswere euthanized for the histomorphometric analysis.

RESULTS/DISCUSSION

Osteoid matrixneoformation, restricted to bone edges, was observed in both groups. The mean linearextension of the bone defect, in millimeters, of the GEVI was 5.83 (SD=0.79); the GCDOmean was 6.62 (SD=0.63). There was no statistically significant difference between themeans (U=8.00, z=-1.604, p=0.132).

CONCLUSION

The present study fulfilled its objective, since it evaluated histomorphologically the effect of the vibratory waves in therepair of critical bone defects. In the qualitative analysis, an osteogenic response wasobserved from the use of the therapy, however it was not demonstrated in a statisticallysignificant way.

Keywords: Osteogenesis, Bone Regeneration, Bone Fracture, Vibration

PO - (21596) - Urolithin B rescues IAPP- induced metabolic changes in pancreatic β-cells

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ABSTRACT

Altered Ca^{2+} levels have been described in many cell types from type 2 diabetes patients. In pancreatic β-cells, toxic oligomers of Islet Amyloid Polypeptide (IAPP) are known to destabilize cellular membrane structure, potentially disrupting cytosolic Ca^{2+} homeostasis and consequently impairing insulin secretion.

Reports of (poly)phenols (PP) interfering with IAPP and other amyloidogenic proteins are vast. However, search has been focused on compounds with little to no bioavailability. Here, we screened a library of PP-derived metabolites towards their ability to modulate IAPP aggregation and consequently improve β-cell functionality. Docking studies of putative interactions between PP metabolites and IAPP were performed using Auto Dock Vina software. The PP metabolite Urolithin B (UroB) was narrowed as one of the best hits.

In cell-free systems, UroB delayed the aggregation kinetics of synthetic IAPP and altered the size and complexity of IAPP fibrils. UroB-mediated protection was investigated in INS-1 832/13 pancreatic β-cells challenged with *in vitro* pre-formed IAPP aggregates for 24h. In viability assays, UroB prevented IAPP-induced cytotoxicity. Transcriptomic analysis indicated Ca^{2+}-signaling as a central mechanism underlying UroB protective action. Consistently, UroB treatment improved intracellular calcium mobilization in response to KCl stimulus in cells damaged by IAPP insult. Noteworthy, UroB improved insulin secretion under hyperglycaemia conditions. Regarding oxidative phosphorylation, UroB was shown to decrease mitochondrial membrane potential and to rescue intracellular ATP levels impaired by IAPP exposure. In these cells, UroB also improved mitochondrial respiratory function.

Overall, our data reveal that UroB modulates Ca^{2+} homeostasis helping β-cells to better cope with IAPP aggregates toxicity. These promising results pointed out UroB as a potential molecule for therapeutic interventions against cellular and metabolic dysfunction in diabetes.

Keywords: Calcium signaling, Insulin secretion, IAPP-induced toxicity, Pancreatic β-cells, (Poly)phenol metabolites

PO - (21613) - New perspectives in the approach to skin barrier dysfunction - Using lipid nanoparticles based on insect biomass to improve dexamethasone delivery

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ABSTRACT

Dysfunctions in the cutaneous barrier are behind many pathologies, resulting in clinical manifestations as inflammatory processes. Some of these disorders are related to alterations or depletion of the SC lipidic matrix. In addition to ceramides, fatty acids (FA) are critical in skin barrier function; thus, the lipid fraction from *Hermetia illucens* larvae biomass, mainly composed of saturated FA, can be a potential biomaterial for the development of innovative nanodelivery systems for drugs or bioactives, as well to provide barrier recovery and act as emollient in topical formulations. The aim of this work was to assess their cytotoxicity using in vitro assays conducted in human keratinocytes and to characterize and evaluate the stability of these formulations. The human keratinocyte HaCat cell line was used as model. The MTT assay was used

to assess cell viability upon exposure to dexamethasone, the lipid extract, unloaded lipid nanoparticles, and lipid nanoparticles loaded with dexamethasone, at previously selected concentrations for 24h. The nanoformulations were characterized during 60 days at room temperature in terms of particle size, polydispersity index (PDI), zeta potential (ZP), and pH. The encapsulation efficacy (EE) of dexamethasone and loading capacity (LC) of the nanoparticles were also evaluated. The lipid nanoparticles loaded with dexamethasone displayed particle sizes under 185 nm, a PDI<0.26, and promising ZP values (< -34 mV) during the 60 days. Satisfactory results were obtained in terms of EE (around 84%), LC (1.3%) and pH (compatible with the skin). Finally, the results of the MTT assay showed that none of the compound's concentrations tested, demonstrate a significant effect in terms of cytotoxicity. In fact, wells treated with the highest concentration of the lipid extract demonstrated an increase in cell proliferation, being therefore a promising biomaterial for future cutaneous formulations, potentially at high concentrations.

Keywords: Skin barrier impairment, Lipid nanoparticles, Larvae extract

PO - (21614) - Overcoming the skin barrier - optimization of transfersomes for ibuprofen delivery

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ABSTRACT

The skin physiology has been extensively studied, since it can offer an advantageous route of administration. However, skin still presents some safety concerns, such as the local adverse effects, since the formulation can negatively affect the skin condition, depending on the type and composition of the delivery system used. In this context, nanotechnology-based delivery systems have been appointed to improve the compatibility of skin formulations and reduce unwanted adverse effects. Many of these encapsulation systems are based on lipids, which are well known to contribute to the skin barrier. This work aimed to develop and optimize a transfersomal formulation for the skin delivery of a model drug - ibuprofen. For that, a Box-Behnken Design (BBD) was performed to provide the optimum values for lipid concentration, surfactants ratio and ibuprofen concentration, according to predefined desirable criteria for transfersomal properties. The impact on skin cells was also

evaluated in vitro in 3D HaCaT cell cultures. Storage stability studies were also conducted. In agreement with the BBD predictions, the optimized transfersomes revealed promising properties: *ca.* 160 nm (size), <0.25 (PDI), <-40 mV (ZP), *ca.* 30% (EE) and 1% (LC), validating the experimental design used. Furthermore, the transfersomes produced did not reduce cell viability, both in the presence and absence of ibuprofen. Regarding the storage stability studies, transfersomes have proven to be stable for at least 2 months under refrigeration. To conclude, the optimized transfersomes have favorable properties both regarding skin drug delivery and compatibility. Further studies are ongoing to ascertain the efficacy of this encapsulation system.

ACKNOWLEDGEMENTS

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Keywords: Transfersomes, Ibuprofen, Skin barrier, Box-Behnken Design

PO - (21654) - Probing the impact of transferomils containing rutin in skin physiology- cytotoxicity studies

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ABSTRACT

Antioxidants are well known to impact skin physiology through the scavenging of free radicals. But their use may be limited due to the low aqueous solubility of many of these compounds, such as rutin. Thus, their loading in delivery systems is also conditionate.

Transfersomes are considered biocompatible nanosystems with several interesting properties, such as elasticity and deformability, making them suitable

for cutaneous delivery. Their overall properties and performance may still be improved. Ionic liquids (ILs) have been studied as valuable tools to enhance the performance of several formulations, because of their ability to improve several physicochemical properties of formulations and/or drugs. So, it may be interesting to continue studying their incorporation into nanosystems, such as transfersomes. Though, since there are reports in the literature of cytotoxicity associated with ILs, the biocompatibility of these systems must be ascertained.

Our aim was to develop new TransfersomILs to load rutin and their physicochemical properties were evaluated. A Box–Behnken factorial design was performed to obtain the optimized formulation of the TransfersomILs. The impact of imidazole and choline-based ILs, their combinations, as well as of the TransfersomILs systems on the viability of HaCaT cells and on the solubility of rutin, were studied.

The TransfersomILs with rutin presented a smaller size and showed an enhanced association efficiency, loading capacity, and total amount of drug release compared to the transfersomes without IL. Furthermore, ILs promoted the colloidal stability of TransfersomILs, upgrading the storage stability. The *in vitro* biocompatibility assays were performed and TransfersomILs were compatible with the skin at the studied concentrations. Overall, the incorporation of the ILs, to produce TransfersomILs, allowed to improve the rutin loading and enhance the performance of the nanosystems, without compromising the viability of skin cells.

Keywords: Vesicular nanosystems, Ionic liquids, Rutin, TransfersomILs

PO - (21656) - Extracts from plectranthus SPP. and evaluation of their ability to promote tissue protection

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ABSTRACT

Tissue damage occurring in chronic processes is known to heavily affect the extracellular matrix (ECM) by several different mechanisms. For example, UV radiation is recognized as a major aggressor to human skin, thus producing connective tissue alterations (via the formation of lipid peroxides) and reactive oxygen species (ROS), and altering cell enzymatic defense systems.

In recent years, natural products have been widely studied for their potential application in the protection of tissues. As well, plant extracts have been reported as inhibitors of proteinases and as antioxidants, suggesting their roles in tissue remodeling, both in physiological and pathological conditions.

On these bases, we focused our interest in *Plectranthus* extracts as bioactive ingredients, since their content in polyphenols (i.e., rosmarinic acid) could exert some antioxidant activity on human skin against photo-aging caused, in particular, by ultraviolet radiation. All the extractions were performed using methanol and the resulting extracts were screened to assay their potential bioactivity as antimicrobials, antioxidants and on skin-related enzymes, as well as their general toxicity. The results showed only a moderate effect against bacteria, but a very promising antioxidant activity, and no relevant general toxicity. Good tyrosinase inhibition was observed, together with an excellent inhibitory activity on collagenase, making these extracts a promising raw material to be used for the development of dermocosmetic formulations,

especially those with antiaging activity. Considering their potential applications for internal and topical uses, further studies are currently ongoing to investigate about other relevant biological activities and ascertain their safety.

Keywords: Plectranthus, natural products, skin, skin products

Theme: Renal and Urinary physiology

PO - (21407) - Immunohistochemical expression of heme oxygenase-1, 4- hydroxynonenal and hypoxia inducible factors (1α, 1β, 2α) after apocynin treatment in postischemic acute kidney injury induced in spontaneously hypertensive rats

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ABSTRACT

Renal ischemia/reperfusion injury (IRI) is common cause of acute kidney injury (AKI). Antioxidant and anti-inflammatory effects of apocynin have been shown in many experimental models, so the aim of this study was to examine those effects in renal IRI performed hypertensive conditions. Rats were randomly selected in 3 groups: sham-operated group (SHAM, n=7), AKI group (AKI, n=9) and AKI group with apocynin treatment (AKI+HBO, n=11). AKI was induced by

removal of the right kidney and atraumatic clamp occlusion of the left renal artery for 45 minutes. Apocynin was applied 5 min before clamp removal. AKI induction significantly decreased creatinine, urea and phosphate clearances with significant improvement after apocynin treatment. HO-1 expression in SHAM group, was diffuse with weak intensity on the apical surface of the proximal tubular cells. In AKI group, the expression was moderate and diffuse in the cytoplasm of the proximal tubular epithelial cells, with strong expression in some tubules. In AKI + APO group, the intensity of HO-1 expression was diffuse, but with weak intensity in the cytoplasm and on the apical surface of the proximal epithelial tubular cells, as previously noticed in SHAM group. Sham-operated rats did not express 4-HNE in any parenchymal structure. AKI induced abundant and strong glomerular expression of 4-HNE along with expression in interstitial compartment. Apocynin treatment significantly decreased 4-HNE expression both in glomeruli and interstitium. Expression of hypoxia inducible factors: HIF 1α, HIF 1β and HIF 2α, in SHAM group were minimal, with expression in glomeruli and interstitium. AKI caused a pronounced and abundant expression in the glomeruli and interstitium. Apocynin treatment significantly reduced the expression of these parameters, restoring to the expression pattern noticed in SHAM group. Considering our results, even in hypertensive conditions, we can expect protective effects of apocynin in experimental model of AKI.

Keywords: acute kidney injury, apocynin, hypertension

PO - (21485) - The food bioactive erucin impacts on kidney cells migration mechanisms

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ABSTRACT

The consumption of cruciferous vegetables is associated with reduced risk of several pathologies, such as cardiovascular disease and cancer. Erucin can be generated *in vivo* by reduction of sulforaphane or by hydrolysis of glucoerucin, which is present at high levels in rocket salads. This work aims to study the effects of this bioactive compound in the physiology of kidney cells and to explore the underlying mechanisms. Vero-E6 cells, a cell model of non-tumor origin, were used in this study. Erucin decreased cell viability only at 100 mM. Non-cytotoxic concentrations of erucin modestly reduced the intracellular levels of reactive oxygen species, induced cell a cycle arrest at G2/M, and decreased collective cell migration. After erucin treatment, kidney cells revealed a concentration-dependent alteration in their morphology, changing from their initially more elongated form towards a smaller spherical form.

Erucin also affected cell adhesion. The cytoskeleton analysis revealed profound effects in microtubule network and an increase of actin stress fibres upon exposure to erucin. Tubulin polymerization was also impaired. These results are in line with the observed decrease in cell migration and G2/M arrest. Overall, this work contributed to understand some of the cellular physiological mechanisms affected by erucin, which can be involved in the biological activities associated with this compound.

Keywords: erucin, renal cells, cell migration, cytoskeleton

Theme: Skin Physiology

PO - (21481) - The regular intake of kefir improves epidermal barrier in atopic dermatitis

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ABSTRACT

Kefir, an ancient food with probiotic characteristics is known to present several health benefits including a positive impact on the general condition of the digestive system, and intestinal microbiota. Atopic Dermatitis (AD), a chronic inflammatory skin disease, is associated to both skin barrier dysfunction and intestinal dysbiosis. This exploratory study aimed to assess the potential relationship between the ingestion of kefir and the skin barrier function of atopic skin subjects. Our volunteers (n = 18) were all females with a diagnosis of AD, mean age 32.1 $\pm$ 12.2 years, assigned to either the kefir intake (K) or the control (C) group, according to their preference. All participants were given instructions on how to proceed during the study. The kefir group intervention consisted on the daily consumption of kefir for eight weeks. The control group did not consume kefir. Skin measurements were made by reference technology (CK electronics G) in the forearm. AD severity was assessed using the Scoring Atopic Dermatitis Severity Index (SCORAD). Regular consumption of

kefir for 8 weeks was associated to a significant improvement on skin barrier parameters, TEWL and hydration ($p<0.001$ and $p<0.001$, respectively) and AD severity ($p<0.001$). No similar differences were observed in the control group. Both TEWL and hydration improvement correlated with AD severity decrease ($rho=0.532$, $p=0.023$ and $rho=0.766$, $p<0.001$, respectively), which supports the skin physiology improvement. Despite the small number of participants this study was able to find a beneficial effect of kefir intake in cutaneous conditions. A correlation between AD severity and skin barrier function was found in previous observations supporting the potential modulatory capacity of kefir on the gut-skin axis. To our knowledge no similar information on the effect of kefir intake on skin barrier function of AD individuals was published. These results justify this interest on kefir as a gut-skin axis modulator.

Keywords: Axis, Gut, Kefir, Probiotics, Skin

PO - (21484) - The cis isomer of the skin chromophore urocanic acid decreases keratinocytes viability and collective migration

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ABSTRACT

Urocanic acid (UCA) is a skin chromophore that has been identified as an important immunosuppression mediator after its photoisomerization from trans to cis, induced by ultraviolet radiation (UVR) exposure. Once UCA is isomerized in the skin it persists in the stratum corneum for, at least, two weeks, progressively returning to initial levels. The cis-UCA is systemically released into the bloodstream and is eliminated in the urine for two weeks. Cis-UCA affects immune cells not only in the stratum corneum and epidermis, but also in the dermis, blood, lymph nodes, spleen, thymus, and bone marrow. Cis-UCA has been proposed as a biomarker of UVR exposure and previous reports have associated it with the etiology of skin cancer. However,

these interactions and the molecular mechanisms involved have not been completely elucidated yet. The objective of this study was to evaluate the effects of UCA cis and trans isomers in the viability and collective cell migration in a human keratinocyte cell model (HaCaT cells). Both UCA isomers at concentrations up to 100 µg/mL did not show cytotoxic effects, while cis-UCA at the highest concentration tested (500 µg/mL) decreased HaCat cells viability after a 48 h-exposure. Collective cell migration was measured by the wound healing assay after 24 h. At 10 mg/mL trans-UCA did not modify cell migration, while cis-UCA slightly decreased migration of HaCat cells. Previous studies by our group showed that 10 mg/mL is a physiologically relevant concentration, found in skin after sun exposure. Furthermore, UVR was previously demonstrated to delay the wound healing progress and, particularly, to affect keratinocyte motility. Our data suggest that the generation of cis-UCA might be implicated in the skin regeneration impairment induced by UVR exposure.

Keywords: Urocanic acid, keratinocytes, cell viability, cell migration

PO - (21590) - Optoacoustic imaging provides new insights into vascular physiology

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ABSTRACT

Multi-spectral optoacoustic tomography (MSOT) is regarded as an advanced instrument for vascular functional imaging. To explore its applicability, we studied the impact of the suprasystolic Reactive Hyperemia (RH) in the forearm of healthy participants.

Ten healthy participants, different ages were selected after informed written consent. The protocol was previously approved by the institutional ethical committee (CE.ECTS/P10.21). RH was applied in one forearm by occluding the brachial artery with an inflated cuff (200 mmHg) for 1 minute. Videos were continuously recorded at the flexor forearm with the system from iThera Medical (Germany) at 900 nm for HbO_2, and 760nm for Hb during rest, occlusion, and recovery after the cuff release. Statistical analysis was performed in Graphpad Prism version 9 and a 95% confidence level adopted. Image reconstruction allowed the quantification of HbO_2 and Hb within our defined 15mm^3 volume regions of interest (ROI). The mean saturation of oxygen (mSO_2) and total Hb (HbT) could also be calculated. The MSOT system

permitted to characterize the occlusion effect in the skin upper plexus where smaller vessels were practically occluded while in the deeper plexus larger vessels showed a high level of congestion. After the cuff deflation HbO_2 Hb and mSO2 showed opposite evolutions in both plexus. MSOT made clear that the classical RH obtained with single point measurement technologies such as laser Doppler flowmetry only access a portion of the response. This functional imaging system gave us real-time access to the complete adaptive response occurring with the perfusion modification. Therefore, this system seems to have an interesting potential to bring new insights and perspectives to microvascular physiology.

Keywords: optoacoustic tomography, functional imaging, skin microcirculation

PO - (21598) - About the cymbopogon citratus essential oil anti-inflammatory potential – Data from the human in vivo methylnicotinate model

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ABSTRACT

Cymbopogon citratus leaves preparations are used in traditional medicine to mitigate inflammatory processes but a strong science demonstration to support these properties is still missing. Methylnicotinate (MN) is often used to imitate an inflammatory process in human skin. Here we investigate the antioxidant and anti-inflammatory properties of a formulation containing *C. citratus* essential oil (EOCC) using this MN- model. The study involved 14 healthy participants (9 women and 5 men; mean age 32.9 $\pm$ 17.6 years old). All procedures respected the principles of good clinical practice previously approved by the Ethics Committee (P. 04/13). Three areas were drawn on both forearms (3cm x 3cm). One randomly chosen area was treated for 14 days, 2 times/day with polyacrylic acid gel containing 5% EOCC (0.1 mL of the formulation). The other were used as controls. The study was carried out in a single-blind manner. By the end of the application period the MN model was applied (0.5% methylnicotinate for 1 minute) and skin reaction measured in terms of blood perfusion, erythema, transepidermal water loss, and edema. High-resolution sonography images were also obtained. Results revealed a significant decrease in TEWL, blood perfusion, erythema, and edema in the areas treated with EOCC, suggesting that formulations containing EOCC could prevent and mitigate skin inflammatory disorders. Besides, the methodology here developed is also an innovative safe approach to study the clinical impact of some topical substances of natural origin in human skin.

Keywords: Cymbopogon citraus, essential oil, citral, lemongrass

PO - (21610) - Assessment of formulations cutaneos enzymatic activity of topical formulations with moisturizing and antioxidant properties

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ABSTRACT

The skin is the main protective organ against the exposome. Besides natural aging, UV radiation and pollution are the main exposome factors that lead to skin senescence. This process contributes to the decrease of the fibroblasts synthesis, consequently, of collagen and elastin, leading to the reduction of elasticity, characteristic of mature skin. The damage caused to the skin by photoaging is more aggressive than chronological aging, as it leads to thinning of the stratum corneum, changes in the size and organization of collagen, elastic fibers degeneration, skin dryness, reactive oxygen species exacerbated production, increased pigment heterogeneity, which can cause stains, and even malignancies changes, such as carcinoma. In this context, the need for antioxidant, moisturizing, skin barrier repair cosmetics that can inhibit enzymes that degrade important skin components is evident. D-panthenol is

known for its hygroscopic and emollient capacity, thus, it is able to hydrate, recover the hydrolipidic mantle of the skin and stimulate cell renewal, while ascorbyl tetraisopalmitate has antioxidant capabilities when hydrolyzed in the skin into ascorbic acid. Thus, the aim of the present work was to provide further insights into the mechanism of action of cosmetic formulations containing the active substances ascorbyl tetraisopalmitate and D-panthenol by assessing their potential in enzymatic reactions. For this, L-tyrosine and FALGPA substrates were used to evaluate the ability of the formulations to inhibit tyrosinase and collagenase enzymes, respectively. The wavelengths used were 450 and405 nm, respectively (SynergyHTX). The results obtained were promising, indicating that these cosmetic formulations can be effective in skin care, maintaining its eudermia by protecting it against the effects of the exposome.

Keywords: Skin enzymes reactions, D-panthenol, ascorbyl tetraisopalmitate

PO - (21655) - Dietary patterns and skin physiology

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ABSTRACT

The impact of dietary patterns on skin functions is still unclear. We examined cutaneous physiology characteristics between vegan-vegetarian (VG) and omnivorous (OM) participants, involving 122 healthy participants, both sexes, 82 OM (32.0 ± 13.1 y.o.) and 40 VG (34.0 ± 9.62 y.o) with similar Body Mass Indices. The protocol was previously approved by the institutional Ethical Commission. Main indicators were transepidermal water loss (TEWL), hydration, and biomechanics skin parameters in five anatomical sites (forehead, cheek, neck, hand, and leg). Carotene skin content was determined in the hand palm by Multiple Spatially Resolved Reflection Spectroscopy. The food group intake was assessed using a validated Food Frequency Questionnaire. The dietary patterns and their impact on the skin were compared using Mann–Whitney test and correlations were investigated by the Spearman rank correlation coefficient ($p<0.05$). The carotenoid content was significantly higher in the VG group . TEWL has shown higher values in the VG group but significant differences could only be detected in the neck and leg. Concerning skin biomechanical parameters and hydration we could not find significant differences between the two groups. Looking for a potential relationship between the most frequent foods consumed by the two groups and skin physiology we found that vegetables, vegetable drinks, milk, yogurt, and cheese had a significant positive relationship with epidermal water balance. Alcoholic beverages and fast food showed a significant negative relationship with the same variables. Other significant correlations included a VG group positive correlation with the carotenoid content, and a OM group a negative correlation with red meat, viscera, alcoholic beverages, and sugar-sweetened beverages consumption. These results clearly suggest that skin physiology can be influenced by regular dietary patterns and should be further investigated.

Keywords: Skin physiology: Vegan-vegetarian, Omnivorous, Dietary patterns

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