FIZIOLOGIA
physiology

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http://www.ebscohost.com/titleLists/a9h-journals.pdf

Fiziologia (Physiology) is issued quarterly
Printed at Editura **EUROSTAMPA**
www.eurostampa.ro
Bd. Revoluției din 1989 nr. 26, Timișoara
Tel/fax: 0256-204816
ISSN 1223-2076

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(b) Monographs; Matthews DE, Farewell VT: *Using and Understanding Medical Statistics.* Basel, Karger, 1985.

(c) Edited books: Hardy WD Jr, Essex *M:.FeLV-inducted feline acquired immune deficiency syndrome: A model for human AIDS;* in Klein E(ed): Acquired Immunodeficiency Syndrome. Prag Allergy, Busel, Karger, 1986, vol 37,353 - 376.

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From brain to heart and back

September 29th - October 1st, 2022

Venue:

Faculty of Medicine,

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National Neuroscience Society of Romania (SNN)

The National Neuroscience Society of Romania (SNN) was founded in 2000 in Bucharest.
From the very beginning, SNN was affiliated to the Federation of European Neuroscience Societies (FENS) and to the International Brain Research Organization (IBRO), through its former "Central and East European Regional Chapter" (CEER), presently part of the "Pan-European Regional Chapter" (PERC), aimed at helping neuroscience in the region. SNN is continuing to win the support of IBRO for organizing its national meetings with international participation.
SNN webpage: www.snn.ro

SRF
Romanian Society of Physiological Sciences

The Romanian Society of Physiology (SRF) was founded in 2009 in Cluj-Napoca.
SRF is affiliated to the Federation of European Physiological Societies (FEPS) and to the International Union of Physiological Sciences (IUPS).
SRF webpage: www.fiziologie.org

The largest Romanian conference of Neuroscience and Physiology with international participation:
***From brain to heart and back*, Bucharest, September 29th - October 1st, 2022**

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The largest Romanian conference of Neuroscience and Physiology with international participation: From brain to heart and back, Bucharest, September 29th - October 1st, 2022

Organizers**:**
National Neuroscience Society of Romania & Romanian Physiology Society
in partnership with Carol Davila University of Medicine and Pharmacy and IBRO

Venue:

Faculty of Medicine, Carol Davila University of Medicine and Pharmacy
8 Eroii Sanitari Boulevard, Bucharest

Event type: onsite
Event official languages: Romanian and English; presented materials in English

Program

Thursday, 29.09.2022

13:00 - 14:00 **Onsite registration and poster mounting**

14:00 - 15:00 **Satellite workshop –** *Dizzy Workshop – investigating vestibular system. Organizers: Daniela Cîrpaciu, Cristina Maria Goanță*

15:00 - 15:30 **Opening Ceremony**

15:30 – 17:15 ***Session 1***, *Chairs: Marius Sabău, Dan Dobreanu*

Marius Sabău – "Gheorghe Arsenescu" Lecture
Ruxandra Drăgoi-Galrinho - Experimental echocardiography
Alkora-Ioana Balan – Impact of chronic ivabradine administration on autonomic nervous system
Vasile Bogdan Halațiu – Impact of Bisphenol A on the cardiovascular system
Florentina Pluteanu – Altered subcellular Ca^{2+} signaling in atrial myocytes of hypertensive rats
Andreas Rinne - Allosteric modulation of GPCR signaling by the membrane potential

17:15 – 17:30 Coffee break

17:30 – 19:30 ***Session 2****, Chairs: Mihai Moldovan, Tibor Szilágyi*

Mihai Moldovan - "Mircea Steriade" Lecture. The infraslow brain activity matters
Andrei Barborică - Validation of EEG source localization algorithms through simultaneous scalp-intracranial EEG recordings in patients with drug-resistant epilepsy
Miralena Tomescu - Oxytocin modulates salience associated resting EEG microstates
Tudor Badea - Selective molecular markers for Retinal Ganglion Cell anatomy, physiology and function
Mihai Stancu - Acoustic stimulation tunes axonal conduction speed by regulating radial growth of myelin on an individual axon-to-axon basis

19:30 – Welcome cocktail

Friday, 30.09.2022

8:30 – 9:00 **Onsite registration and poster mounting**

09:00 - 10:30 ***Session 3**, Chairs: Carmen Panaitescu, Ana-Maria Zagrean*

Bogdan Pavel - "Nicolae C. Paulescu" Lecture - Do we need near infrared spectroscopy and end-CO_2 monitoring during hyperventilation test?
Constantin Căruntu - Neuro-endocrine factors in the skin - from physiology to pathological conditions
Carmen Panaitescu – Allergies in a changing world
Carmen Tatu - Prediction of allergic response based on molecular components
Gabriela Tănasie - Aeroallergens impair the barrier function of the bronchial epithelial cells - an in vitro study
Michael Bogdan Mărgineanu - Consensus strategy for B cell epitope prediction in allergen IgE epitope mapping studies

10:30 - 11:00 Coffee break

11:00 – 12:30 ***Session 4**, Chairs: Leon Zăgrean, Ionela Lăcrămioara Șerban*

Ionela Lăcrămioara Șerban - "Ion Haulică" Lecture
Dragomir Șerban - Endothelial function vs. oxidative stress: molecular mechanisms
Radu Iliescu - Neural control of blood pressure: therapeutic target for hypertension
Minela Mărănducă - News in the renin-angiotensin system
Andrei Neamţu - Applications of computer simulation methods in molecular physiology
Ionuţ Tudorancea - The role of inflammatory cytokines in obesity hypertension

12:30 - 12:45 ***Sponsor presentation***

12:45 - 13:30 Lunch

13:30 - 15:00 - ***Poster session &*** **Young investigators blitz presentations**

15:00 - 16:30 ***Session 5**, Chairs: Gabriela Adriana Filip, Dana-Carmen Zaha*

Simona Clichici - "Mircea Doroftei" Lecture
Mihai Lupu - Effect of iron redistribution in an experimental model of cardiac hypertrophy
Iuliana Nenu - Trusting your gut – a new paradigm in hepatocellular carcinoma therapy
Irina Camelia Chis - Quercetin restores endothelial dysfunction in diabetic rat aortic rings
Nadina Liana Pop - Magnetic nanoparticles functionalized with chitosan: between nerve regeneration of peripheral nerve injuries and hepatotoxicity
Diana Valentina Tudor - Celecoxib: a double-edged sword in metastatic melanoma

16:30 – 17:00 Coffee break

17:00 – 18:30 ***Session 6**, Chairs: Alexandru Babeș, Violeta Ristoiu*

Maria Luisa Flonta - "Dimitrie Călugăreanu" Lecture
Beatrice Radu - Assessing the safety profile of a drug - an itinerary from heart to brain
Bogdan Amuzescu - Infrared laser effects on excitability of primary sensory neurons and gating of Nav1.5 ion channels

Debora-Elena Huțanu - The antimalarial artemisinin is a non-electrophilic agonist of the Transient Receptor Potential Ankyrin type 1 receptor-channel
Roxana-Olimpia Gheorghe - Switch of macrophages to M2 phenotype after cytoskeleton alteration reduces SNL induced neuropathic pain
Tudor Șelescu - TRPM8-dependent 'wet dog shake' behaviour in mammals and birds

18:30 - 19:30 - **General Assembly of SRF**

19:30 - 20:30 - **General Assembly of SNN**

Saturday, 01.10.2022 – Brain Day – IBRO Sessions

09:00 – 10:30 ***Session 7 – IBRO session,*** *Chairs: Aurel Popa-Wagner, Tudor-Adrian Bălșeanu*

Tudor-Adrian Balseanu - "*Valeriu Neștianu" Lecture.* Obesity as a risk factor for cerebrovascular disease: biomarkers and back-translation into animal models for development of novel therapies
Bogdan Catălin - The Impact of Acute Sepsis on Amyloid Formation in a Mouse Model of Alzheimer's Disease
Roxana Surugiu - Brain exosomal vesicles as serum biomarkers of stroke
Aurel Popa-Wagner - Long-term treatment with chloroquine increases lifespan in middle-aged male mice possibly via autophagy modulation, proteasome inhibition and glycogen metabolism
Dirk Hermann - Injury development and therapeutic responses to small extracellular vesicles in the aged ischemic brain

10:30 – 10:45 Coffee break

10:45 – 12:30 ***Session 8,*** *Chairs: Beatrice Radu, Tudor Badea*

Leon Zăgrean - "Gheorghe Marinescu" Lecture
Ana-Maria Zăgrean – Brain response to perinatal asphyxia in experimental paradigms
Sebastian Isac - The impact of general anesthesia on the developing brain previously exposed to perinatal asphyxia
Mara-Ioana Iesanu - The impact of gestational gut microbiome alteration on neurodevelopment in rat offspring exposed to perinatal asphyxia
Violeta-Maria Caragea - Dopaminergic modulation of hippocampal synaptic plasticity and spatial memory
Diana Rotaru - MR spectroscopy of GABA and glutathione: advancements in data acquisition, preprocessing and analysis.
Gabriel Crumpei - The information paradigm in neuroscience

12:30 – 12:45 Coffee break

12:45 - 14:00 **Session 9** (**SNN SRF Roundtable) - *Brain Day - IBRO event,*** *Chairs: Ana-Maria Zăgrean, Mihai Moldovan*

14:00 – 15:00 **Concluding remarks, Awards, and Closing Ceremony**

The sessions are scheduled in G.E. Palade Amphitheater, except Sessions 3 and 4 which will take place in the Council Hall.

ABSTRACTS - ORAL PRESENTATIONS

O1. Impact of chronic ivabradine administration on autonomic nervous system

Balan Alkora-Ioana (1,2), Halațiu Vasile Bogdan (1), Cozac Dan Alexandru (1,2), Mutu Cosmin Constantin (1), Comșulea Emilian (1), Perian Marcel (1), Scridon Alina (1,3)

(1) Department of Physiology, Faculty of Medicine, University of Medicine, Pharmacy, Science and Technology "George Emil Palade" of Târgu Mureș, Romania (2) Department of Cardiology, Emergency Institute for Cardiovascular Diseases and Transplantation, Târgu Mureș, Romania (3) Center for Advanced Medical and Pharmaceutical Research, Târgu Mureș, Romania

The mechanisms underlying the modulation of the I*f* current by the autonomic nervous system (ANS) are well understood. In contrast, the effects of chronic If blockade on the ANS are still largely unknown. We thus aimed to evaluate the effects of chronic ivabradine therapy on cardiac autonomic modulation. Adult male Wistar rats were randomized into two groups: Control (n = 6) and IVA (ivabradine 10 mg/kg/day, 3 weeks, n = 10). All rats were implanted with radiotelemetry ECG devices and 24-h continuous ECG monitoring was performed. Heart rate variability analysis was performed. The parameters that estimate the activity of the parasympathetic and sympathetic nervous systems, as well as the balance between the two components were analyzed. As expected, mean 24-h heart rate was significantly lower in the IVA compared to the Control rats ($p< 0.01$). Parameters reflecting vagal activity were significantly higher in IVA compared to Control rats (all $p >0.05$). In the IVA rats sympatho-vagal balance was shifted toward vagal dominance ($p = 0.04$). These changes were present both when the animals were awake and while asleep (all $p< 0.05$). Our study demonstrates that chronic administration of ivabradine increases vagal modulation and shifts ANS activity toward vagal dominance in healthy rats, bringing new insights into the mechanisms of ivabradine-related atrial proarrhythmia. By increasing parasympathetic tone in healthy rats, this study suggests that the vagal dominance induced by ivabradine extends beyond heart failure, and it can be used in other clinical conditions associated with increased sympathetic activity.

O2. Altered subcellular calcium signaling in atrial myocytes of hypertensive rats

Florentina Pluteanu (1); Jens Kockskämper (2)

(1) Department of Anatomy, Animal Physiology and Biophysics, Faculty of Biology, University of Bucharest, Bucharest, Romania; (2) Institute of Pharmacology and Clinical Pharmacy, Biochemical and Pharmacological Center (BPC) Marburg, Philipps-University Marburg, Marburg, Germany

Hypertension (HTN) is a major risk factor for cardiovascular complications, such as heart failure and atrial fibrillation. At the atrial level, the cellular and molecular mechanisms of HTN-induced functional remodeling are insufficiently understood. Our hypothesis was that altered calcium signaling occur in spontaneously hypertensive rats (SHR) and contribute to aggravation of the functional remodeling and AF susceptibility. Here, we characterized the calcium handling mechanisms in atrial myocytes isolated from SHR or age-matched normotensive Wistar-Kyoto (WKY) control rats, at different stages of HTN: (1) young with developing left ventricular hypertrophy (LVH), (2) mature with stable HTN and compensatory LVH, and aged rats (3) with no heart failure or (4) with heart failure. Confocal microscopy was used to investigate the subcellular calcium transients electrically evoked, while patch clamp was used to record the L-type calcium current and Na+/Ca2+ exchanger current during compensatory LVH stage. The functional measurements were correlated with the levels of calcium -handling proteins in the atria of the same experimental groups. Our results obtained from atrial myocytes of SHR showed that subcellular alterations of calcium signaling were mostly localized at sub-sarcolemmal and sarcolemma level and correlate with the expression and phosphorylation of the calcium-handling proteins. Experimental simulation of tachycardia induced significantly more arrhythmogenic calcium alternans in SHR than in WKY atrial myocytes. These data indicate that in the context of HTN, the subcellular changes in calcium signaling may represent an important substrate for the increased propensity of SHR to develop atrial tachyarrhythmias.

Funding: EUTRAF

O3. Allosteric modulation of GPCR signaling by the membrane potential

Andreas Rinne

Department of Biophysics and Cellular Biotechnology, UMFCD Bucharest, Bucharest, Romania

G-protein-coupled receptors (GPCRs) are one of the largest classes of cell surface receptors. They regulate multiple cellular functions and represent important drug targets. Allosteric modulation of GPCRs refers to a change of signaling of preactivated receptors induced by small molecules known as allosteric modulators (AMs). Classic AMs bind to the receptor at intracellular or extracellular sites different from the orthosteric binding site for agonists. AMs either facilitate activation of the receptor (positive allosteric modulation) or cause inhibition (negative allosteric modulation). It is now recognized that class A GPCRs are voltage dependent. By using fluorescent biosensors that resolve receptor activation (conformational changes) or receptor signaling (G-protein activation) we demonstrate that the novel phenomenon of voltage dependence serves as an allosteric modulator of GPCRs. Our data suggest that the molecular pathway that alters receptor activity in response to voltage involves intracellular and extracellular binding sites of known AMs. Remarkably similar to pharmacological allosteric modulation, a depolarization of the membrane modulated binding of the orthosteric agonist and affected G protein signaling. These effects translated into fine-tuning of cellular signaling events downstream of the receptors. Consequently, pharmacological properties and signaling of receptors expressed in electrically excitable cells differ from those observed in non-excitable cell types.
Funding: DFG (German Research Society).

O4. The infraslow brain activity matters

Mihai Moldovan (1,2,3)

(1) Department of clinical neurophysiology, Rigshospitalet, Copenhagen, Denmark; (2) Department of neuroscience, University of Copenhagen, Denmark; (3) Department of Functional Studies, Division of Physiology, Center for Excellence in Neuroscience, University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

An oscillatory activity can be recorded from many cortical networks across brain states and species. The resulting fluctuations in the scalp electromagnetic field recorded by electroencephalography (EEG) are typically described within the 1-30 Hz frequency band. Nevertheless, recordings from single cortical neurons revealed slower subthreshold oscillations of their membrane potential. Functional imaging studies found that multiple resting-state networks, among which the most notorious is the default mode network, present an infralow activity (ISA) within 0.01-0.1 Hz. It remains controversial whether the ISA is an epiphenomenon or whether it serves a physiological function. I propose a novel conceptualization of ISA as a modulatory rhythm of the faster neuronal activity. Data was aggregated from 3 sources: 1) cortical EEG recordings in rats under deep anesthesia subjected to intermittent photic stimulation or auditive stimulation; 2) scalp EEG recordings at rest from healthy volunteers and post-stroke comatose patients during photic or verbal stimulation and 3) in vivo Ca2+ imaging from the pyramidal neurons of the mouse prefrontal cortex during a go/no-go behavioral task. These data suggest that ISA coalesces the faster neuronal activity into oscillatory macrostates. The modulatory strength of ISA appeared stronger when the specific input was reduced. Such a subthreshold effect could matter for behavior in conditions of uncertainty.

The macrostate EEG analysis is protected under patent EP3646784B1

Funding: This project was partly supported by grants of the Romanian National Authority for Scientific Research, CNCS – UEFISCDI, project number PN-II-ID-PCE-2011-3-0847, PN-II-PT-PCCA-2011-3.2-1290 and PN-III-P2-2.1PTE-2016-0114.

O5. Validation of EEG source localization algorithms through simultaneous scalp-intracranial EEG recordings in patients with drug-resistant epilepsy

Andrei Barborică (1), Ioana Mîndruță (2), Irina Oane (2), Cristian Donoș (1), Felicia Mihai (1), Constantin Pistol (1)

(1) Physics Department, Bucharest-Măgurele, Romania; (2) Epilepsy Monitoring Unit, Neurology Department, Emergency University Hospital Bucharest, Bucharest, Romania

Funding: UEFISCDI COFUND-FLAGERA II-SCALES, PN-III-P4-ID-PCE-2020-0935

O6. Intranasal oxytocin modulates salience microstates as a function of social proficiency

Miralena I. Tomescu(1,2,3), Stephanie Van der Donck (4,5), Emanuela M. Perisanu (6,7), Valeria Kebets (8), Alexandru I. Berceanu (2), Kaat Alaerts (4), Bart Boets (4,5) and Ioana Carcea (1,2,9); Andrei Popescu (2)

(1) Faculty of Educational Sciences, Department of Psychology, University "Stefan cel Mare" of Suceava, Bucharest, Romania; (2) CINETic Center, National University of Theatre and Film "I.L. Caragiale" Bucharest, Bucharest, Romania; (3) Faculty of Psychology and Educational Sciences, Department of Psychology, University of Bucharest, Bucharest, Romania; (4) Center for Developmental Psychiatry, Department of Neurosciences, KU Leuven, Belgium; (5) Leuven Autism Research (LAuRes), KU Leuven, Leuven 6.Institute of Cardiovascular Diseases, Timisoara, Romania; (7) Faculty of Medicine, University of Sibiu, Sibiu, Romania; (8) Department of Electrical and Computer Engineering, National University of Singapore, Singapore; (9) Department of Pharmacology, Physiology and Neuroscience, Rutgers Brain Health Institute, Rutgers, The State University of New Jersey

Intranasal oxytocin (OXT) administration is considered as a potential treatment for social cognition as it modulates social behavior by possibly enhancing salience towards social stimuli as a function of social context. Inter-individual variability in expectations about the social context, social behavior patterns and associated intrinsic spontaneous brain activity might play an important role in salience attribution that drives behavior. With this goal we investigated modulatory effects of exogenous OXT on fast dynamics of spontaneous EEG activity as a function of self-reported social responsiveness, social phobia and adult attachment using multivariate partial least square (PLS) statistical analyses. For each condition we identified seven EEG microstates, very similar between conditions (OXT vs placebo (PLCB)) and to the prototypical EEG microstates previously reported in the literature. In line with Schiller et al., 2019 we confirm an increased stability for D but also F EEG microstates after OXT administration. However, we also found decreased duration and occurrence for C and E microstates. In the narrow frequency band analyses we found modulations for the A (delta 2-4Hz), B (low gamma 30-40Hz) and G (delta and low gamma) microstates. Effects of the OXT administration on the low gamma frequency band microstate dynamics (OXT-PLCB) showed that D and F increased duration and occurrence was most prominent in the low secure/high anxiety/high avoidance attachment style, and/or high social phobia, and/or low motivation self-reported social responsiveness. The opposite was true for C and E microstates, where decreased duration/occurrence was most prominent for high secure/low anxiety and avoidance, and/or low social phobia, and/or high social responsiveness individuals. These results suggest differential OXT effects on spontaneous dynamics of EEG microstates as a function of social attachment style and social responsiveness. Exogenous OXT might increase attention and salience related network dynamics (D and F microstate, respectively) in individuals with impaired social skills and difficulties in social attachment, and might decreased default-mode network dynamics (C and E microstate, respectively) for the socially high responsive, and secure attachment style individuals. This result supports the social salience enhancement hypothesis as a possible mechanism by which OXT is modulating behavior and, to a higher degree in socially less responsive individuals. Moreover, these results might partially explain contradictory behavioral effects of OXT that can act via different temporal patterns of spontaneous EEG microstate. Social motivation, attachment style, social phobia among other social traits might drive social expectations towards most likely social scenarios to ensure best adapted behavior by differentially modulating dynamics of EEG microstates after OXT administration.

Funding: The project "Developing a methodology of therapy through theater with an effect at the neurochemical and neurocognitive levels" (MET) is financed by the European Regional Development Fund (ERDF) through Competitiveness Operational Program 2014–2020, SMIS code 106688 and implemented by UNATC "I.L. Caragiale", CINETic center, LDCAPEI LAB. First author was also funded by an International Brain Research Organization (IBRO) fellowship. Additionally, the study was also funded by an European Economic Area (EEA)/Norway grant, EEA-ROsingle bondNO-2018–0606.ed

O7. Acoustic stimulation tunes axonal conduction speed by regulating radial growth of myelin on an individual axon-toaxon basis

Mihai Stancu, Conny Kopp-Scheinpflug

Division of Neurobiology, Department of Biology & Graduate School of Systemic Neurosciences, Ludwig-Maximilians University, Munich, Germany

Funding: *DFG SFB870 A-10*

O8. Do we need near infrared spectroscopy and end-tidal CO_2 monitoring during hyperventilation test?

Bogdan Pavel (1), Ștefan Șandru (1), Denise Carmen Mihaela Zahiu (1), Sebastian Isac (1, 2), Ana-Maria Zagrean (1)

(1) Division of Physiology, Department of Functional Sciences, "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania; (2) Department of Anesthesiology and Intensive Care I, 'Fundeni' Clinical Institute, Bucharest, Romania

Background: The purpose of this study was to assess the role of end-tidal CO2 ($ETCO_2$) monitoring during hyperventilation in predicting the occurrence of cerebral oximetry changes, recorded by near-infrared spectroscopy (NIRS). Materials and Methods: Forty-six healthy volunteers were enrolled in the study. All subjects were required to breathe at a baseline rate (8-14 breaths/min) for the first 2 minutes of the procedure and then to hyperventilate at a double respiratory rate for the next 4 minutes. The parameters monitored during the test were: the regional cerebral oxyhemoglobin and deoxyhemoglobin concentrations via NIRS, $ETCO_2$ and the respiratory rate. Results: During hyperventilation, each subject showed a decrease in $ETCO_2$ values comparing with baseline. Only the subjects (N=30) who registered a reduction (%) in $ETCO_2$ of 37.58% ± 10.34% presented changes in cerebral oximetry. These oximetry changes were represented by a decrease in total hemoglobin and oxyhemoglobin concentrations whereas reduced hemoglobin remained unchanged. Using the AUC-ROC analysis, an $ETCO_2$ decrease > 26% was identified as the optimal cutoff value for predicting the occurrence of changes in cerebral oximetry (AUC-ROC = 0.93, $p < 0.0001$). Conclusions: Cerebral vasoconstriction induced by hyperventilation cannot be effectively predicted by the rise in the respiratory rate alone. Therefore, the simultaneous $ETCO_2$ and cerebral oximetry monitoring could be used to validate this clinical test.

O9. Neuro-endocrine factors in the skin – from physiology to pathological conditions

Constantin Caruntu (1,2); Mihaela Adriana Ilie (3); Daniel Boda (2,4); Ana Caruntu (5,6)

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The structure of the skin is extremely complex, with separate layers, of different embryological origin, but functionally interdependent. The regulation of skin functions involves numerous mechanisms, with cellular and molecular details that still need to be unveiled. Various types of neurohormones, neuropeptides, neurotransmitters and neuromediators are released both by the cutaneous nerve fibers and by numerous skin cells. The activation of their receptors contributes to the modulation of physiological and pathophysiological processes that may remain local or may affect the entire body. Knowledge of the interconnections between the nervous system and the skin can contribute to the discovery of new functional mechanisms and new therapeutic targets. Moreover, it can have an important clinical impact through the development of new approaches in the treatment of skin diseases. This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CCCDI - UEFISCDI, project number PN-III-P2-2.1-PED-2021-2243, within PNCDI III

Funding: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CCCDI - UEFISCDI, project number PN-III-P2-2.1-PED-2021-2243, within PNCDI III

O10. Allergies in a changing world

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Background: A healthy immune response to allergen is characterised by allergenspecific T cell tolerance, induced spontaneously by dose-dependent exposure to allergens. Tolerance induction is maintained by regulatory T cells secreting IL-10 and TGF-β, IgG4 synthesis and inhibition of allergic effector cells. Allergic response is characterised by a Th2-immune response, especially in atopic individuals, under the influence of genes and environmental factors. Allergic sensitisation is driven by type 2 specific cytokines (including IL-4 and IL-13, essential for IgE isotype switch in B cells, and IL-5, essential for eosinophilic inflammation), allergen-specific IgE, and allergenspecific Th2 and B memory cells. The allergens have multiple epitopes, able to induce specific-IgE synthesis, each one favouring the allergic response to another epitope, in a process of “molecular spreading”. Ragweed pollen contains 12 molecular allergens, with Amb a1 and Amb a 11 as major allergens. The aim of our study was to investigate IgE reactivity profiles of ragweed allergic patients and to associate them with clinical symptoms. Methods: IgE sensitization profiles from clinically well-characterized ragweed allergic patients (n = 150) were analyzed using immunoblotted ragweed pollen extract. Immunoblot inhibition experiments were performed with two Amb a 1 isoforms and CCD markers, and basophil activation experiments were performed with IgE serum before and after depletion of Amb a 1-specific IgE. Results: 19 different IgE reactivity patterns with and without Amb a 1-sensitization were revealed by immunoblotting. Serum with and without Amb a 1-specific IgE induced basophil activation. Patients with complex IgE sensitization profiles developed more clinical symptoms.

O11. Prediction of allergic response based on molecular components

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Traditionally, the diagnosis of allergic diseases has been based on a thorough clinical history together with proof of sensitisation to allergens, either in vivo, by skin prick test and/or in vitro, by identification of serum specific immunoglobulin E. Both in vivo and in vitro evaluation of the sensitisation status are extract-based methods, which often fail to identify the molecules responsible for the allergic reactions, as the extract contains a mixture of allergenic molecules, some common to multiple sources (cross-reactive molecules or pan-allergens) while other allergenic molecules are specific to a singular source (genuine or species-specific allergens).Component resolved diagnosis developed in the last twenty years, has overcome most of these limitations, as it distinguishes molecular allergens responsible for symptom elicitation from those attributable to cross-reactivity. This diagnostic strategy is evolving towards the new concept of precision immunology for allergy diagnosis, which aims to improve the management of allergic diseases and asthma. The benefits of using molecular components are: better diagnosis for symptoms elicited by molecules of low abundance and/or weak stability thus missing in the extract; risk assessment in food and/or venom allergy; indicator of cross-reactivity; marker of genuine (species specific) sensitization. In addition, component-resolved diagnosis can support the choice of allergen immunotherapy based on patient sensitization profiles. Emerging applications of component-resolved diagnosis are focused on characterizing allergic diseases and asthma endotypes and in the diagnosis of occupational allergic disease.

O12. Aeroallergens impair the barrier function of the bronchial epithelial cells - an in vitro study

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The respiratory epithelium acts as a complex barrier at the interface between the ventilated air and the bronchial structures. Respiratory viruses and pollutants affect the integrity of the epithelial layer, causing inflammatory reactions and inducing hyper-reactivity of the bronchial smooth muscle. The present study investigated the in vitro interactions of aeroallergens with the bronchial epithelium, addressing the main indoor allergen, house dust mite (HDM), and one of the most effective outdoor allergens, ragweed pollen.A human bronchial epithelial cell line (NHBE) was cultured at the air-liquid interface and then exposed to different concentrations of standardized extracts of HDM and ragweed, as well as to the combinations of allergenic fragments with clinical relevance: Amb a 1, Amb a 11, Amb a 12 (from Ambrosia pollen), and Der p 1 (from HDM). The trans-epithelial electrical resistance (TEER) was measured every 30 min for the first 4 hours, then daily for 72 h. The cellular index of NHBE cells was monitored 72 h after allergen addition, using an xCELLigence system.The experiments revealed a substantial decrease in TEER values in the treated cells, with the largest decrease after continuous exposure to the combination of HDM and ragweed extracts. The alteration of the cellular index after the addition of combined allergenic fragments was noticed, especially if ambrosia allergens were tested after Drp1 exposure.In conclusion, the combined action of indoor and outdoor allergens can induce a cumulative effect on the bronchial epithelium, in this way initiating or maintaining the bronchial hyper-reactivity state.

INSPIRED Project (INnovative Strategies for Prevention, diagnosis and therapy of ragweed pollen Induced REspiratory Diseases) - cod SMIS 103662

O13. Consensus strategy for B cell epitope prediction in allergen IgE epitope mapping studies

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One of the most promising and novel strategies for allergy immunotherapy employs non–IgE-reactive peptides that are derived from the IgE-binding sites (B-cell epitopes) of the major allergens of a given allergen source. This therapeutic strategy is based on the induction of blocking IgG antibodies, which prevent the interaction between IgE antibodies and the allergen. In silico B-cell epitope prediction methods could help reduce time and cost of peptide synthesis as typically overlapping synthetic peptides spanning the entire length of the protein are constructed and evaluated in vitro to identify the IgE-binding sites. Based on the prediction results, one can exclude specific peptide sequences that do not contain any B-cell epitopes predicted in silico and thus reduce the number of candidate peptides that will be synthetized.In this study, we have compared two different consensus strategies employing two or three of the five prediction methods Bepipred, BCPreds, ABCPred, Emini, Kolaskar-Tongaonkar, which exploit the inherent physicochemical properties of B-cell epitopes in their algorithms, or are based on algorithms trained on epitope and non-epitope data. We have used for validation experimental IgE binding inhibition results obtained for Amb a 8-derived peptides in our group, and reports on other allergen-derived peptides from literature. The consensus method employing two tools predicted epitopes in peptides for which highest IgE inhibition scores were obtained, and did not predict potential epitopes in peptides with lowest IgE inhibition, suggesting that this strategy can help reduce the number of peptides required for experimental screening for allergen-specific vaccine development.

O14. Endothelial function vs. oxidative stress: molecular mechanisms

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There is ongoing wide interest in endothelial function and dysfunction, in oxidative stress, and in their inter-relations. We have been working on such subjects for over ten years. Here we present some of the most recent advances in these areas. We discuss the cardio-vascular physiological responses to stimuli and stress, referring to their variability and reset and also to their homeostatic, adaptive, and integrative goals. We focus on the microcirculation, because resistance arteries and arterioles together provide the fine adjustment of local tissue blood flow to the tissue needs and the main contribution to peripheral resistance (thus to systemic arterial blood pressure). Endothelium-dependent relaxation (EDR) of vascular smooth muscle is known to be mediated by nitric oxide (NO), but the major EDR mechanism in resistance arteries and arterioles is independent of NO-synthase and cyclooxygenase and it is mediated by endothelium-dependent hyperpolarization (EDH). EDH-mediated EDR relies on endothelial Ca2+-activated K+ channels with small and intermediate conductance. EDH-mediated EDR is: counter-regulator of sympathetic vasoconstriction; important in flow autoregulation, myogenic response, and vasomotion; compensatory in endothelial dysfunction, but also involved in its pathogenesis. H2O2 has a special role in EDH-mediated EDR, so here we discuss our very recent studies on small arteries and the effects of: H2O2, vitamin C, Mg2+. We also discuss the most recent progress in: NO-mediated EDR, endothelial dysfunction of large arteries, and atherosclerosis. Therein, our recent clinical studies and reviews have their own major focuses: (a) cerebral circulation and function; (b) chronic kidney disease.

O15. Effect of iron redistribution in an experimental model of cardiac hypertrophy

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Iron dysmetabolism affects a great proportion of heart failure patients, while chronic hypertension is one of the most common risk factors for heart failure and death in industrialized countries. Serum data from reduced ejection fraction heart failure patients show a relative or absolute iron deficiency, whereas cellular myocardial analyses field equivocal data. An observed increase in organellar iron deposits was incriminated to cause reactive oxygen species formation, lipid peroxidation, and cell death. Therefore, we studied the effects of iron chelation on a rat model of cardiac hypertrophy. Suprarenal abdominal aortic constriction was achieved surgically, with a period of nine weeks to accommodate the development of chronic pressure overload. Next, deferiprone (100 mg/kg/day), a lipid permeable iron chelator, was administered for two weeks. Pressure overload resulted in increased inflammation, fibrotic remodeling, lipid peroxidation, left ventricular hypertrophy and mitochondrial iron derangements. Deferiprone reduced cardiac inflammation, lipid peroxidation, mitochondrial iron levels, and hypertrophy, without affecting circulating iron levels or ejection fraction. In conclusion, metallic molecules may pose ambivalent effects within the cardiovascular system, with beneficial effects of iron redistribution, chiefly in the mitochondria.

O16. Trusting your gut - a new paradigm in hepatocellular carcinoma therapy

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Introduction: Hepatocellular carcinoma (HCC) has become a worldwide burden and its incidence is rising. The intestinal microbiota is responsible for inducing resistance to antitumoral drugs. The present study investigated the effects of the combined treatment of Regorafenib (Rego) and probiotic Streptococcus rhamnosus (Pro) on HCC bearing mice. Main methods: We have induced cirrhosis and hepatocellular carcinoma on two week Swiss male mice using diethylnitrosamine (DEN) 1 mg/kg one intraperitoneal injection following carbon tetrachloride (CCl4) 0.2 ml/kg intraperitoneal administration two times per week for six weeks. Abdominal ultrasound was performed to validate the presence of cirrhosis and liver tumors. Afterward, the mice were divided into four groups: in the first group (control group), the mice were only monitored, the second group received Regorafenib, in the third group probiotic was administered, and the last group received the combination of Rego and Pro. Tumour and intestinal inflammation performed by ELISA and western blot, apoptosis markers, necrosis rate and oxidative stress markers were assessed. Results: Although without statistical significance ($p>0.05$), levels of both Il-6 and Il-1 decreased in the groups where the probiotic was administered. Similarly, malondialdehyde levels dropped when Pro was added. Tumor necrosis factor-alpha (TNF-α) and TLR-4 have a decreased activity in the combined regimen ($p<0.05$) and in the Rego group ($p<0.05$) when compared to the control group and correlate with the histological findings. Likewise, nuclear factor-κB (NF-κB) and IKKα expression decreased in the combined regimen. Intestinal inflammation assessed by determination of lipopolysaccharide (LPS) is reduced in the groups where probiotic was administered compared to the control and Rego group ($p<0.05$). In addition, inducible nitric oxide synthase activity determined from the intestine diminishes in Rego and Rego associated with the probiotic group. Conclusion: The administration of the Streptococcus rhamnosus probiotic with Regorafenib improves the antitumoral activity of the multikinase inhibitor. Tumoral resistance and systemic adverse effects might be diminished when systemic and intestinal inflammation is lowered. Our results confirmed that the association of Regorafenib with probiotic proves a novel and promising approach. Manipulating and trusting your gut has never been so facile than in the present day for the oncology field.

O17. Quercetin restores endothelial dysfunction in diabetic rat aortic rings

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Background: Cardiovascular disease is one of the leading causes of death in diabetes mellitus. Most of the complications in diabetes are due to increased serum glucose and increased generation of oxygen-derived free radicals, which lead to endothelium dysfunction. Methods: We examined the effect of quercetin administration on the endothelial NO-dependent relaxation (NO-EDR) in the aorta of the streptozotocin (STZ)-induced diabetic rats. Methods: STZ-induced diabetic rats were treated with quercetin (30 mg/kg body weight/day). Relaxation response to acetylcholine (ACh) and sodium nitroprusside (SNP) was measured in the rat aortic rings at the end of this study. Results: ACh-induced EDR was significantly decreased in Phenylephrine (PE) pre-contracted aorta of diabetic rats. Quercetin administration preserved Ach induced EDR, but did not influence SNP-induced endothelium-independent relaxation in diabetic rat aorta. Conclusions: Diabetes induced an endothelium dysfunction. In vitro functional assessment of aortic rings showed that quercetin administration restored aorta endothelial function of the STZ-induced diabetic rats. This improvement of the aorta endothelial function may be due to the antioxidant mechanisms.
Keywords: acetylcholine; endothelium; diabetes; quercetin; aorta

O18 Chitosan functionalized magnetic naopartices: between neural regeneration after peripheric nerve injury and hepatotoxicity

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Chitosan is a natural polysaccharide, hydrophilic, non-toxic, with a good chemical and thermic stability. Chitosan functionalized magnetic oxide iron nanoparticles (CMNPs) appear to have a reduced cytotoxicity and chitosan protects and stabilizes the magnetic nanoparticle, making it non-detectable for the immune system. Our study evaluated the effects of CMNPs on peripheral nerve injuries' rehabilitation by using an in vivo experimental model. CMNPs treatment was administrated daily, orally, for 21 days to rats subjected to right sciatic nerve lesion and compared to the control group (no treatment) by analyzing the sciatic functional index, pain level, body weight, serum nerve growth factor levels and histology, TEM (transmission electron microscopy) and EDX (Energy-Dispersive X-ray Spectroscopy) analysis at different times during the study. Animals treated with CMNPs had a statistically significant functional outcome compared to the control group regarding all studied parameters. In the study we also assessed the potential adverse effects of CMNPs treatment on animals' liver. Hepatic histological modifications observed in the animals that received CMNPs consisted in significant periportal inflammation, with no relevant modifications regarding oxidative stress parameters and with a tendency of an antioxidant effect. In conclusion, oral administrated CMNPs in a dosage of 2.5mg/kg for 21 days produced peripheral nerve regeneration, confirmed by histological studies, TEM and TEM-EDX, which suggest that CMNPs can be a promising treatment method for peripheral nerve injuries. Moreover, CMNPs treatment did not generate hepatic oxidative stress and appeared to had an antioxidant effect on the liver.
Funding: This research was partially funded by Iuliu Hatieganu University of Medicine and Pharmacy, Cluj Napoca, Romania, as a research grant for the first author's PhD thesis.

O19. Celecoxib: a double-edged sword in metastatic melanoma

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Introduction: Emerging therapies are changing melanoma approach. Targeting inflammation markers using celecoxib seemed a valuable strategy in preclinical studies. Thus, we assessed for the first time how celecoxib impacts on the phenotype switching phenomenon in metastatic melanoma cells treated with dabrafenib. Methods: The in vitro experiments used BRAF positive SK-MEL-28 human melanoma cell line, treated with dabrafenib and celecoxib drug combination, for 72 h. Of main interest was the WB evaluation of key molecules expressed during the proliferative-invasive phenotype switch (TGF – β, MITF, YAP, TAZ, AXL). Results were correlated with cell death and oxidative stress-related mechanisms. Results: On one hand, celecoxib increased the apoptotic effect of dabrafenib compared to dabrafenib single agent therapy ($p<0.0001$). On the other hand, celecoxib decreased MITF expression and increased AXL levels ($p<0.0001$). Celecoxib and dabrafenib therapeutic combination increased oxidative stress compared to the dabrafenib group ($p < 0.0001$). Conclusion: Celecoxib might promote MITFlow/AXLhigh expression in SK-MEL-28 cutaneous melanoma, a suggestive hallmark for an invasive state. This finding could limit its use in future clinical trials. Further assessment of celecoxib in melanoma is warranted.
Keywords: melanoma, celecoxib, dabrafenib, MITF, AXL.

O20. Assessing the safety profile of a drug - an itinerary from heart to brain

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Drug safety is an essential concept in medical practice. Pharmacological safety regulations are permanently improved for both ‚old' classical and newly-approved drugs. In accordance with these continuously adapted regulations it is mandatory to evaluate the pro-arrhythmogenic risk for each drug. In this respect, according to the Comprehensive in vitro Proarrhythmia Assay (CiPA) paradigm there are several proarrhythmogenic risk predictors that can be assessed based on patchclamp recordings of human cardiac channels activity. Another important aspect is the ability of a drug to penetrate the blood brain barrier (BBB), whether or not it is psychoactive. Moreover, for brain active drugs it is highly relevant to evaluate their capacity to activate drug-resistance mechanisms. To this purpose, our project is widespread approach from heart to brain that assesses drug safety by in vitro methods on human induced pluripotent stem cell-derived cardiomyocytes or BBB cells, and HEK293T cells stably or transiently transfected with human ion channels. Methods include manual and automated patch-clamp recordings, mathematical computing, immunofluorescence, transendothelial electrical resistance measurements, Western blot and qRT-PCR. So far, we analyzed the drug safety profiles of several drugs belonging to different pharmacological classes in terms of proarrhythmogenic risk predictors and we are further extending our study to their interactions with BBB. In conclusion, pharmacological safety regulations are constantly improved and our study brings relevant informations that can be further exploited to obtain rapid, reproducible and patient-personalized drug safety profiles.

B.M. Radu and B. Amuzescu are the owners of the EP18465611.4A/23.12.2020 patent.

Funding: This study was funded from Competitiveness Operational Programme 2014–2020 project P_37_675 (contract no. 146/2016), Priority Axis 1, Action 1.1.4, co-financed by the European Funds for Regional Development and Romanian Government funds and by the Romanian Executive Agency for Higher Education, Research, Development and Innovation Funding, grant PN-III-P4-PCE-2021-1422.

O21. Infrared laser effects on excitability of primary sensory neurons and gating of Nav1.5 ion channels

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Photobiomodulation is a relatively new therapy that have been proved effective in several neurological/psychiatric disorders such as stroke, brain trauma, depression, dementia, and particularly Parkinson's disease. Clinical trials provided positive and encouraging results using either transcutaneous or deep invasive application of near-infrared laser light, although the complex cellular and molecular underlying mechanisms are far from being completely understood. Therefore we performed a series of manual whole-cell patch-clamp experiments on dissociated rat primary sensory neurons (ruptured or gramicidin-perforated approach) and HEK293T cells stably transfected with hNav1.5 voltage-gated Na+ channels. In each setting a series of voltage/current-clamp protocols was applied initially and after 3 min since start of exposure to a 808.5 nm solid-state laser radiation guided through a multimodal optical fiber connected to a transparent tip micropositioned above the cell. In neurons laser exposure produced over the 3-min interval slight resting potential depolarization and an increase in excitability (lowered stimulus current threshold and increased number of action potentials at highest stimulus amplitude using a multistep current injection protocol up to 500pA 100ms). In hNav1.5-expressing cells laser exposure kept unchanged the peak Na+ current amplitude (101.4%±16.7% relative to initial values, mean±SEM, n=10 vs. 70.6%±10.4%, n=10 control experiments), slow (103.3%±4.5% vs. 130.7%±17.8% control) and fast inactivation time constants (105.3%±6.0% vs. 131.2%±11.4% control). Laser exposure induced no significant changes relative to control in activation time constant, half-activation/half-inactivation potential, but decreased the slow time constant of recovery from inactivation to 86.3%±16.3%, while in control the fast recovery time constant increased to 153.5%±14.1%.

O22. The antimalarial artemisinin is an agonist of the Transient Receptor Potential Ankyrin type 1 receptor-channel

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Introduction. Artemisinin and its derivatives comprise the most important class of drugs used in medical practice to treat malaria. When administered, it has been found that moderate side effects may occur, such as dizziness, nausea or vomiting. Based on these considerations, we investigated the possible effects of artemisinin on three ion channels: TRPM8, TRPV1 and TRPA1.MethodsNon-ratiometric calcium microfluorimetry experiments were performed on HEK293T cells, transiently transfected with human TRPA1, human TRPM8 or human TRPV1, as well as primary sensory neurons from adult mice. For patch clamp recordings, HEK293T cells transiently transfected with hTRPA1 and GFP were plated on 35-mm treated Petri dishes and used within 24 hours. Calcium assay on FlexStation3 was performed on HEK293T cells transiently transfected with hTRPA1 and G5A.ResultsApplication of artemisinin induced an influx of Ca2+ into hTRPA1-HEK293T cells and the response was reversibly inhibited by the specific TRPA1 antagonist A967079. When artemisinin was applied in calcium-free conditions, the response was reversibly suppressed, resulting that the source of calcium is extracellular. Artemisinin acts as a non-electrophilic TRPA1 agonist, activating the channel in a similar manner to carvacrol. Artemisinin activates whole-cell currents in HEK293T-hTRPA1 cells mediated by TRPA1 channels and it activates a subpopulation of mouse dorsal root ganglion neurons which also respond to the TRPA1 agonist AITC. Conclusion: Based on our data obtained on heterologous expression systems and on primary sensory neurons from adult mice, we conclude that artemisinin acts as a TRPA1 agonist, which could explain the side effects of the drug.

Funding: This work was supported by a grant of the Romanian Ministry of Education and Research, CCCDIUEFISCDI, project number PN-III-P2-2.1-PED-2019-5179, within PNCDI III.

O23. Switch of macrophages to M2 phenotype after cytoskeleton alteration reduces SNL induced neuropathic pain

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Traumatic nerve injury such as SNL (spinal nerve ligations) is accompanied by clustering of Iba1 (+) macrophages around DRG (dorsal root ganglia) neurons, presumably activating them and facilitating neuropathic pain development. Previously we have shown that intra-ganglionic L5 injection of naked siRNA directed against Iba1 significantly inhibited spinal nerve ligation-induced mechanical and cold allodynia, 5 days after the lesion. In this study we investigated whether the siRNA-induced analgesia is due to a switch in the activation phenotype of macrophages from M1 pro-inflammatory to M2 anti-inflammatory accompanied by a reduced mobility of macrophages, and complemented by a pro-regenerative profile of DRG neurons with reduced excitability. The results have shown that the analgesic effect of Iba1 silencing in DRG macrophages is due to their functional switch towards an M2, antiinflammatory state accompanied by an increased secretion of anti-inflammatory cytokines and pro-regenerative mediators which, however, doesn't seem to alter significantly the electrophysiological properties of L5 DRG neurons. This data are in line with a reduced contribution of L5 DRG neurons to pain pathogenesis after SNL, and suggest an extended influence of the immune mechanism to neighboring nonlesioned DRG neurons, possibly responsible for the Iba1 siRNA-induced analgesia.

Funding: This research was funded by Executive Agency for Higher Education, Research, Development and Innovation Funding (UEFISCDI), grant number PN-III-P2-2.1-PED-2019-3103.

O24. TRPM8-dependent "wet dog shake" behaviour in mammals and birds

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Funding: CNCS/UEFISCDI through grant PN-III-PI-I.I-TE-202 I-1354

O25. The Impact of Acute Sepsis on Amyloid Formation in a Mouse Model of Alzheimer's

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O26. The impact of general anesthesia on the developing brain previously exposed to perinatal asphyxia

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Funding: This research was funded by the Romanian Minister of Education, Project No. PN-III-P1-1.2-PD-2019-1219

O27. The Impact of Gestational Gut Microbiome Alteration on Neurodevelopment in Rat Offspring exposed to Perinatal Asphyxia

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O28. Dopaminergic modulation of hippocampal synaptic plasticity and spatial memory

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Dopamine is a well-known modulator of cognitive functions, playing an important role in hippocampal information processing through means of synaptic plasticity. In this respect, dopamine acts on two families of receptors: the D1-like receptors (D1 and D5) - positively coupled to adenylyl cyclase (AC) and the D2-like receptors (D2, D3, and D4) - negatively coupled to AC. On one hand, D1-like receptors seem to play an important role in regulating the duration and stability of hippocampal synaptic plasticity for multiple synapses, as reported by numerous studies from our laboratory. On the other hand, the role of the D2-like receptors (D2R) in regulating hippocampal synaptic plasticity is less understood and controversial. Recently, we explored the influence of D2R blockade on synaptic plasticity at Schaffer collateral - CA1 synapses and on spatial memory in freely moving rats. Here, we show that intracerebral pharmacological antagonism of D2R prevented the in vivo expression of both short-term and long-term potentiation, as well as the expression of short-term depression at CA1 synapses. The same dose of D2R antagonist also altered the retention of a semantic-like spatial memory task and significantly impaired retention of recent spatio-temporal aspects of an episodic-like memory task. Taken together, these findings indicate that the D2-like receptors bidirectionally modulate synaptic plasticity in the hippocampal CA1 region and play an important role in enabling cumulative and episodic-like forms of spatial memory.

Funding: This work was funded by the Deutsche Forschungsgemeinschaft (SFB 874/B10, project number: 122679504).

O29. MR spectroscopy of GABA and glutathione: advancements in data acquisition, preprocessing and analysis

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Until recently, neuro-metabolites like the main inhibitory neurotransmitter, GammaAminobutyric Acid (GABA) and the antioxidant found throughout the brain, glutathione (GSH)) were unresolvable using standard Magnetic Resonance Spectroscopy (MRS) techniques due to their low concentrations and weak MR signals. Based on recent work on data acquisition schemes, discrimination and quantification of GABA and GSH became possible. However, improving the acquisition solely is not enough as despite the high-quality GABA results, GSH still suffers from poor spectral discrimination that translates into poorer concentration estimates. We propose a new analysis approach for the simultaneous assessment of GABA and GSH spectra: Concatenation Of Hadamard Encoded and Reconstructed spectra of Edited NeuroChemicals Estimates (COHERENCE). Our novel analysis pipeline was successfully implemented for simultaneous modeling of GABA and GSH HERMES data. While GABA results were similar to those of the traditional GABA difference single-spectrum analysis, for GSH, COHERENCE has shown a better agreement between scanning sessions. The repeatability of COHERENCE was comparable to traditional singlespectrum modeling.

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O30. The information paradigm in Neuroscience

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Nowadays, information is a notion present everyday, both in common language and in research and scientific works. Trying to define information is difficult because it is present at all levels of reality, from the quantum level to the cosmic one, and the definitions so far capture only certain aspects of what we call information. A coherent theory of information was developed by Shannon and Weaver over 70 years ago, but this is rather a theory of communication in electronic systems. Information technology and research in robotics and artificial intelligence increasingly highlight the need to define and integrate information in theories related to physical and biological reality. There are some attempts in neuroscience to build physical-mathematical models of reality, which include information. We have some theories developed in the last part of the 20th century and the beginning of the 21st century related to fractal geometry, topology, complex systems theory and network science, which are used in this offensive to define and integrate information in our theories about the world and life. The evolution in these fields is strictly linked to establishing the role of information, along with matter and energy, in the construction of reality. It is necessary to determine if information has a fundamental character in nature, if it is a ubiquitous universal aspect of reality and what are the relationships between substance, energy and information, starting from the immaterial nature of information.

ABSTRACT - POSTER PRESENTATIONS

POSTERS WITH BLITZ ORAL PRESENTATIONS

B01. Alteration of sleep stages in a murine model of temporal lobe epilepsy

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Epilepsy is a common condition that affects the brain causing multiple seizures. The disease is diagnosed by correlation of the clinical manifestation with the hypersynchronous wave on EEG known as epileptic spike. However, epileptic spike capture is inconsistent in the early stages, thus increasing the need for further research. This study aims to validate an alteration of the sleep stages in a temporal lobe epilepsy murine model, as a hypothetical approach for epilepsy early diagnosis methods. We induced epilepsy in C57Bl/6 mice using kainic acid administration in the hippocampus. Concurrently, we surgically implanted a headstage to the experimental lot (n=3) and control (n=2). The mice were ECoG, EMG (4+1 channels) recorded and video tracked for 24 hours. Data was split in 30-second epochs and plotted into raw ECoG tracings and power spectrum. The epochs were classified by sleep stage and epileptic activity using both visual inspection and entrainment of a machine learning model. The data revealed an increased time spent in wake, during which most epileptic spikes were captured. Furthermore, the sleep fragmentation was reduced in the epileptic mice, compared to control, suggesting a similar mechanism of the epileptic spikes and K-complexes in maintaining the sleep stage. Although the results are preliminary, the alteration of circadian rhythm and decrease in sleep fragmentation could be linked to temporal lobe epilepsy and might facilitate further diagnostic methods.

B02. Assessment of the rat ischemic brain by burst-suppression EEG reactivity

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Aim: The electroencephalographic (EEG) assessment of the diffuse ischemic brain injury remains methodologically challenging. The aim of this study was to investigate the impairment in EEG reactivity to intermittent photic stimulation (IPS) following experimental global cerebral ischemia. Rather than focusing on continuous EEG measures, we tested the reactivity of the discontinuous burst-suppression (BS) patterns induced in deep anesthetic coma. Methods: Male Wistar rats were surgically exposed to a mild global cerebral ischemia by electrocauterization of the vertebral arteries and the subsequent clamping of both common carotid arteries for 5 minutes under laser doppler control. A group of rats exposed to sham surgery served as controls. Cortical EEG recordings were carried out at 48 hours after surgery when all rats appeared clinically recovered. The BS patterns, induced by an overdose of Chloral hydrate, were quantified by the suppression ratio (SR), measuring the fraction of time spent in suppression, over 1-minute intervals. The IPS was delivered to one eye at 0.5 Hz in 1-minute epochs. The BS reactivity index (BSRI) was defined as the reduction in the ipsilateral SR that occurred during IPS, relative to the baseline SR recorded just prior to IPS. Results: At a baseline SR of 40%-80%, the mean BSRI was 0.27 seconds. In contrast, the mean BSRI was about 3-fold smaller in the rats exposed to GCI. The amplitude of the visual evoked potentials was similar between the groups. Conclusion: Our data suggest that measures of the burst-suppression EEG reactivity are sensitive to detect the post-ischemic brain injury.

The work with Termobit Prod SRL RO is protected under patent EP3646784B1 Funding: This project was supported by grants of the Romanian National

Authority for Scientific Research, CNCS – UEFISCDI, project number PN-II-ID-PCE-2011-3-0847, PN-II-PT-PCCA-2011-3.2-1290 and PN-III-P2-2.1PTE-2016-0114 to Mihai Moldovan.

B03. Burst-suppression EEG reactivity in a genetic model of absence epilepsy

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Aim: The burst-suppression (BS) patterns emerging on the electroencephalogram (EEG) in deep anesthetic coma are reactive to external stimulation. We aimed to investigate whether this BS reactivity is increased in the epileptic brain. Methods: Acute experiments were carried out in adult Wistar Albino Glaxo Rijswijk (WAG/Rij) rats, a commonly used genetic model of absence epilepsy which presents characteristic episodes of spike-and-wave discharges (SWD) lasting about 6 seconds on the wake EEG. Age-matched Wistar rats served as control. Cortical EEG recordings were carried out during isoflurane anesthesia. The BS patterns were quantified by the suppression ratio (SR), measuring the fraction of time spent in suppression, over 1-minute intervals. Investigations were carried out at a baseline SR of 40% – 80%. Intermittent photic stimulation (IPS) was delivered to one eye at 0.5 Hz in 1-minute epochs. Given the predominantly crossed visual pathways, the SR was assessed ipsilaterally to minimize the confounding effect of the visual evoked potentials. A BS reactivity index (BSRI) was defined as the reduction in SR that occurred during IPS, relative to the baseline SR recorded just prior to IPS.Results: The IPS under deep anesthesia did not trigger SWDs. The mean BSRI was 0.2 in controls. In WAG/Rij the mean BSRI was increased by 55%. The difference was reduced after ethosuximide and paradoxically increased after carbamazepine at doses that had no effect on controls.Conclusion: Our data suggest that measures of burst-suppression EEG reactivity could be useful to assess the hyperexcitability of the epileptic brain.

The work with Termobit Prod SRL RO is protected under patent EP3646784B1

Funding: This project was supported by grants of the Romanian National Authority for Scientific Research, CNCS – UEFISCDI, project number PN-II-ID-PCE-2011-3-0847, PN-II-PT-PCCA-2011-3.2-1290 and PN-III-P2-2.1PTE-2016-0114 to Mihai Moldovan

B04. EFFECT OF LONG TERM If CURRENT BLOCKADE ON THE OCCURANCE OF SPONTANEOUS ATRIAL FIBRILLATION EPISODES FOLLOWING TRANSESOPHAGEAL ATRIAL BURST PACING

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Introduction: Data in the literature regarding the effects of ivabradine, a selective inhibitor of the funny current, on atrial arrhythmogenicity are controversial. Thus, we aimed to assess the effect of pacemaker current blockade the occurrence of spontaneous episodes of atrial fibrillation (AF) following transesophageal atrial burst pacing in rats. Material and Methods: A total of 32 male Wistar rats were randomly assigned into two groups: FA (n = 16) and IVA (n = 16), the latter receiving Ivabradine (10 mg/kg/day) in the drinking water for three weeks prior to and throughout the study. All animals were implanted with radio-telemetry ECG devices and the ECG was recorded for 72-h before, during and one week after transesophageal atrial burst pacing. Transesophageal atrial burst pacing was applied for 10 days to the rats in both groups. Results: The baseline heart rate was significantly lower in the IVA compared with the FA group (302± 40,25 vs. 351± 38,40 bpm, p< 0.001). In the absence of electrical stimulation, rats in the IVA group presented a higher number of AF episodes per 24 hours (p< 0.01) compared to the rats in the FA group. A higher number of AF episodes was also observed after the initiation of the protocol (p< 0.01), as well as one week after its completion (p = 0.02). Conclusions: Our results demonstrate an important in vivo proarrhythmic effect of ivabradine, expressed as an increased number of spontaneous AF episodes. The exact mechanism through which ivabradine increases AF susceptibility needs further investigations.

B05. Electrocorticographic changes induced by deep brain stimulation under anaesthesia in rats

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General anaesthesia is induced for thousands of procedures annually, but the exact mechanism of general anaesthetics is not completely understood. The claustrum is a cerebral structure that, despite its reduced dimensions, has the highest number of connections/volume and it is considered to play a role in the state of consciousness. The aim of this study was to investigate the effects of claustrum electrical stimulation on the anaesthesia depth during ketamine-xylazine anaesthesia in adult rats. In this study, we used ten adult rats. Anaesthesia was induced with a ketamine-xylazine cocktail. Three electrocorticogram electrodes were placed on the left frontal and parietal lobe and right olfactory cortex. A bipolar tungsten electrode was inserted into the left claustrum. The claustrum was electrically stimulated by applying 10 stimuli of 1 second duration each, at interstimulus interval of 5 seconds. Five-second-epochs were selected in the basal period and corresponding to the first three applied stimuli and to the first three interstimuli time intervals. ECoG analysis using fronto-parietal connectivity and median frequency were performed in order to assess the anesthesia depth changes. The results were compared using ANOVA one-way with Dunnet T3 correction. Our results revealed that there were no statistically significant differences in fronto-parietal connectivity (p= 0.835), parietal median frequency (p=0.265) or frontal median frequency (p=0.262) between the basal period, the stimulation period and the period between the stimuli.In conclusion, in this study, we have shown that electrical stimulation of claustrum under ketamine-xylazine anaesthesia induces no changes in the depth of anaesthesia.

B06. Identification of corticotropin releasing hormone projections to the thalamic reticular nucleus

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The thalamic reticular nucleus (TRN) is comprised of GABAergic neurons that ensheathe the thalamus, while receiving collaterals from both thalamic and cortical neurons. Its functions include sensory integration and various modulations of attention, while disfunctions of this area have been associated with afflictions like autism and schizophrenia. The corticotropin releasing hormone (CRH) is mainly associated with its function as the first signaling molecule of the hypothalamus-pituitary-adrenal (HPA) axis and the neuroendocrine response to stressful stimuli. CRH also acts as a neuromodulator in the central nervous system, where it influences behaviors related to anxiety and stress, independent of the HPA axis. Even though TRN is characterized by a high expression level of the CRH receptor 1, the link between CRH and this brain area was not thoroughly investigated. Using transgenic mice which express the Cre recombinase in cells that express CRH and confocal imaging on brain slices, this study identified brain regions that send CRH projections to the TRN. Retrograde labelling using viral vectors identified several candidate regions whose projections may release CRH in the TRN, these being the basolateral amygdala, the supragenicuiate nucleus, the ventral lateral geniculate nucleus and the medial geniculate nucleus. The medial geniculate nucleus and the supragenicuiate nucleus projections have been confirmed with anterograde labelling. Further studies could search for more potential projecting areas, confirm the ones found with retrograde labelling or investigate the functional or behavioral alteration of CRH signaling in the TRN.

Funding: This project has received funding from the European Union Horizon2020 Research and Innovation programme under the Marie Sklodowska-Curie grant agreement No. 813986.

B07. Invasive presurgical exploration of visual system epilepsy

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Epilepsy represents one of the most common neurological chronic diseases worldwide affecting over 50 million people. Although there has been made important progress regarding the pharmacological approach for this disease, over 20% of these pacients have a pharmaco-rezistant form of epilepsy. In this case, the surgical method represents an alternative. We have investigated patients included in the National Pharmacoresistant Epilepsy Programme, hospitalised at the University Hospital in Bucharest. We have analyzed their response when stimulated with electric current provided by intracerebral electrodes and focused on the visual phenomenons, in particular, the visual hallucinations. We have looked at the localisation of the stimulating electrode, the intensity of the electric current, the clinical effect, the color of the hallucination and the initial and final localisation of this visual phenomenon. We have observed a higher number of hallucinations than illusions. Most patients experienced simple hallucinations with "positive" simptomatology. The continuous hallucinations were more frequent than the intermitent ones. When taking into consideration the initial and last position of the hallucination in the visual field, the "static" hallucinations were more common than the "dynamic" ones. The visual elements that have been experienced by the patients were predominantly characterised as "non-color". In terms of secondary symptomatology associated with visual hallucinations, the patients mainly experienced visual illusions.

B08. The impact of general anaesthesia on the developing brain previously exposed to perinatal asphyxia

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Aims: General anaesthesia (A) in paediatric patients is extensively used nowadays, although it still represents a debatable concern, especially in the context of its co-occurrence with other clinical conditions, such as perinatal asphyxia (PA). Our experimental study investigates hippocampal glial activation and inflammation secondary to PA or A alone, and to combined exposure (PAA).
Methods: On postnatal day (PND) 6, we exposed Wistar rats to 90-minute of either asphyxia (PA) or normoxia, and on PND-15 to 180-minute of either sevoflurane anaesthesia (A) or normoxia. Hippocampal tissue was immediately harvested thereafter from each of the 4 groups (control, PA, A, PAA; 15 animals/group), and S-100B and IL-1B were assessed by ELISA.
Results: Our results revealed an increased hippocampal level of S-100B consecutive to PA, A, and combined PAA exposure, showing that both PA and A significantly contribute to glial activation, however with no cumulative effect. The hippocampal level of IL-1B was increased consecutive to PA, was not impacted by A alone when compared to control, and was decreased in PAA group when compared to PA group.
Conclusions: Our study pointed out that PA has a deleterious effect on the immature hippocampus by increasing glial activation and neuroinflammation, while A alone produces only glial activation. When combined, PA and A do not potentiate reciprocally. Further studies are needed to better understand the controversial general anaesthesia impact in pathophysiological conditions like PA, to ultimately increase the patients' safety.
This research was supported by the Romanian Minister of Education, Project No. PN-III-P1-1.2-PD-2019-1219.

B09. siRNA-mediated gene silencing using magnetofection: different perspectives on HMC3 microglia maintained in definedmedium versus standard medium conditions

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Aims: Serum-free microglia culture models supplemented with primary components of astrocyte-derived factors (defined-medium) are required for the cells in vitro to recapitulate the mature, resting microglial phenotype. Here, we characterized the effects of magnetofection to deliver siRNA in HMC3 microglia cultured in defined medium as well as standard medium conditions. Methods: The polarization towards the resting phenotype of HMC3 microglia maintained in defined medium was established by quantifying the degree of cell elongation across the nucleus. The efficacy of magnetofection, a novel transfection method that delivers nucleic acids upon exploitation of magnetic force, was assessed using siRNA molecule labelled with A594. The images were analyzed quantitatively to establish the optimal concentration of siRNA and the ideal ratio between siRNA and the transfection reagent. The efficiency of magnetofection was tested using a customized anti-Iba1 siRNA molecule, by Western blot and LC-MS analysis. Results: The degree of cell elongation, but not the cell area, revealed significant morphological changes in HMC3 microglia cultured in defined-medium as compared to HMC3 cells cultured in serum-supplemented media. The dose-response curve of siRNA-A594 uptake as well as the ratio between siRNA-A594 and the transfection reagent indicate a more effective delivery in serum supplemented cultures as compared to defined-medium conditions. The Western blot data showed a decrease in Iba1 expression after siRNA anti-Iba1 molecule uptake, even though the results were not striking: surprisingly, we confronted a low level of Iba1 protein intrinsically expressed by HMC3 microglia, confirmed by LC-MS analysis. Conclusion: Culture-dependent differences are revealed by magnetofection in HMC3 microglia.

Funding: Unitatea Executiva Pentru Finantarea Invatamantului Superior a Cercetarii Dezvoltarii si Inovarii: PN-IIIP2-2.1-PED-2019-3103

B10. The dose-dependent effects of betacyclodextrin complexed lacosamide on seizure-like events induced by low-magnesium in rat hippocampal slices

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Epilepsy affects around 50 million people worldwide. Drug-resistant epilepsy is frequent, due, in part, to the molecular properties of the available drugs, such as poor solubility and bioavailability. There is evidence that in vitro seizure models can predict the antiepileptic efficacy of standard antiepileptic drugs. The objective of our project was to study the effects of the widely used beta-cyclodextrin (BCD), as excipient for the improvement of bioavailability of several drugs. We also tested the dose-dependent effect of BCD-complexed lacosamide on seizure-like events (SLE) in vitro. We removed the brains of rats (P7-12), obtained 400µm thick slices and placed a microelectrode in the pyramidal layer of CA3 region of the hippocampus to record field potential. Initially an artificial cerebrospinal fluid (nACSF) was applied to record the baseline activity, followed by a seizure-inducing solution (0MgACSF), then 0MgACSF containing BCD either with lacosamide (25µM, 50µM and 100µM) or without and final washout. We observed that the BCD reduced the length of interictal periods significantly: 163±13.26 (mean±SEM) vs 118±12.08. The BCD and 25 µM lacosamide combination significantly decreased both ictal (62.38±3.93 vs 39.18±3.19) and interictal (153.1±8.35 vs 76.72±11.08) periods, so the seizure frequency was increased, but these were shorter. The 50µM concentration lacosamid reduced the ictal length further (39.18±3.19 vs 23.23±2.82), but the interictal period was longer then in 25µM (91.03±9.22), so it resulted even shorter SLE-s and also a lower seizure frequency. We conclude that BCD may preserve the dose-dependent inhibitory effect of lacosamide on the SLE's that warrants its further investigation.

Funding: This work was supported by the University of Medicine, Pharmacy, Science and Technology of Târgu Mureș Research Grant number 615/7, 17.01.2019

B11. The effects of Cornus mas L. extract on cardiovascular modifications in an experimental diabetes mellitus model

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Background. Recent research presents natural extracts as efficient therapies in inflammation, hyperglycaemia and localized pathological processes. Several studies showed the efficiency of gold nanoparticles (AuNPs) in the drug transportation toward target tissues. Aims. Our study investigated, in rats with high fat diet and diabetus mellitus, the cardiovascular effects of the oral administration of Cornus mas, a plant rich in antioxidants, when given as simple extract solution or as a functionalizing agent for AuNPs. Methods. Adult Sprague Dawley female rats, with high fat diet for 8 months that increased their body weight till 600 ± 20g and streptozocin-induced diabetes mellitus, were randomly allocated in: CMC group with carboxymethylcellulose (CMC) administration; Insulin group with Insulin treatment; Pioglitazone group treated with pioglitazone in CMC solution; AuNPsCM group with solution of gold nanoparticles functionalized with Cornus mas L. extract (AuNPsCM) and Cornus mas group treated with extract of Cornus mas L.solution. The treatment was administered for one month. The oxidative stress and inflammatory parameters were evaluated in aorta wall and heart. Results. The administration of Cornus mas L. extract simple solution recorded significant modifications: malondialdehyde and TNF-α were decreased in aorta wall and heart tissue, endothelin-1 was decreased in aorta and GSH/GSSG ratio was increased in heart homogenate. AuNPsCM treatment produced significant effects: TNF-α decreased in aorta and heart, butiNOS increased in the investigated tissues. Conclusions. The aorta and heart were protected by the Cornus mas L. extract simple solution, presenting decreased oxidative stress and inflammation. AuNPsCM treatment presented contradictory effects on inflammation, in aorta and heart tissue.

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B12. The Alteration of Rat Offspring Neurodevelopmental Reflexes after Gestational Gut Microbiome Disturbance and Perinatal Asphyxia

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Introduction: Maternal gut microbiota disturbance has been linked to alterations in the offspring's neurodevelopment. Perinatal asphyxia (PA) can induce altering effects on the immature brain. Our study evaluates the impact of gestational antibiotic administration (GAA) and PA on offspring’s neurodevelopmental reflexes.
Material and methods: We conducted GAA on the 11th gestational day of Wistar rats who were orally administered a cocktail of antibacterial and antifungal medication (ampicillin, vancomycin, neomycin, clindamycin, and amphotericin-B) in the water. After birth, pups were divided into 4 groups: control-normoxia (C-N), antibiotics-normoxia (AB-N), control-perinatal asphyxia (C-PA) and antibiotics-asphyxia (AB-PA). In the 6th postnatal day (PND), we recorded, with a MouseOx monitor, the vital signs of C-PA and AB-PA pups exposed to a 90 min-asphyxia (9% O2, 20% CO2 in N2). In 7-9 PND, we exposed the pups to the following early-life behavioural tests: righting reflex (RR), limbs grasping reflex (LGR), cliff avoidance (CA), negative geotactic reaction (NGR) and grip strength response (GSR).
Results: GAA has led to a high percentage of miscarriage and low offspring birth weight. During PA the oxygen saturation decreased to 45.41%. During RR, pups in AB-PA group showed prolonged time to right. During LGR, we observed a low average of successful limb grasps in C-PA and AB-PA groups. In CA, AB-N and AB-PA groups showed prolonged turning time. The pups in AB-PA group showed the highest latency to turn during NGR. The AB-N group exhibited the weakest paw strength during GSR.
Conclusion: Our preliminary results show that maternal dysbiosis and PA lead to early-onset brain impairment and recommend increased caution when recommending gestational antimicrobials use.

POSTERS

P01. A non-inflammatory soft tissue around implants a key factor for long term success. Clinical cases.

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It is long proven that where we have inflammation there is oxidative stress. The same principle is in the case of dental implants; because between the prosthetic construction and connective tissue (transition zone) that covers the bone next to the implant in most of the cases, patients present signs of inflammation (tumor, pain, and change in color-redness). All of this because the connective soft tissue that surrounds the prosthetic construction in some cases randomly forms a new natural bonding to the prosthesis that similar to the natural Sharpey fibers and in other cases there is no connection. We know that some implantable materials are better than others in terms of plaque adhesion, bacterial biofilm formation, and tissue likeness. Another important criteria for the long term success of the therapy is the general state of health of the patient. As a inclusion criteria for the clinical cases followed was that all the patients to be adults, to have a good state of health, good dental hygiene and proper prosthetic reconstruction. After implantation and reconstruction, we did a 6 month and 1 year follow up. During the healing process we treated our patients with natural local antioxidants. As result we came up with a rate of 3% of implant lost and 97% rate of survival of the implant and prosthetic reconstruction. In our opinion one of the most important is a good healthy and non-inflammatory tissue around dental implants. But we still suggest for making further clinical studies in this direction.

P02. Adiponectin from brain to heart and back

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Adiponectin is the most abundant specific protein secreted and expressed by adipocytes. The different forms of Adiponectin have different biological properties and different tissues targets. To exert its biological effects, Adiponectin must bind to its specific receptors: AdipoR1, AdipoR2 and T-cadherin. The biological actions of Adiponectin are: insulin-sensitizing, anti-inflammatory effect, anti-atherogenic effect, anti-proliferation in cancer, regulation of glucose and lipid metabolism, neuroprotective effects. In conclusion, Adiponectin is gaining attention as a potential therapeutic target.

P03. Anti-inflammatory nanodrugs for stroke treatment

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Despite recent progress, the large majority of ischemic stroke patients still exhibit neurological deficits in the long run, and ischemic stroke continues to be the most frequent cause of long-term disability. Nanosized small extracellular vesicles (sEVs) prepared from mesenchymal stromal cell (MSC) supernatants have previously been shown to promote neurological recovery and brain remodeling in ischemic stroke models. sEV-based therapies are not self-replicating and lack endogenous tumor formation potentials and therefore are rapidly approaching clinical trials in human stroke patients. A major challenge of stroke therapies are vascular risk factors associated with ageing (e.g., hyperlipidemia, diabetes mellitus), which exacerbate inflammatory responses in the brain and compromise recovery. In previous work we have shown that MSC-sEVs efficaciously reversed the post-ischemic responses of polymorphonuclear neutrophils (PMNs), monocytes/macrophages, T cells and B cells in the peripheral blood and/or brain, indicating towards an immunomodulatory effect of MSC-sEVs that might confer their therapeutic activity. The aim of this study is to (a) comprehensively characterize immune signals mediating recovery-promoting effects of MSC-sEVs in the ischemic brain, (b) evaluate consequences of age and age-associated vascular risk factors (i.e., diabetes, hyperlipidemia) for post-ischemic immune responses and the recovery-promoting effects of MSC-sEVs,(c) examine the role of peripheral blood-derived PMNs and microglial cells in MSC-sEV-induced neurological recovery, through nanosizing EVs through colloidal engineering, in depth cell biological characterization, in vitro and in vivo models, confocal and 2-photon microscopy, transcriptomics and behavioral analysis. By providing efficacy data in the aged ischemic brain exhibiting vascular risk factors, we hope to allow an in depth estimate of the therapeutic efficacy of MSC-derived sEVs in human stroke patients.

P04. Blood pressure effects of SGLT-2 inhibitors treatment in patients with type 2 diabetes mellitus

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Introduction. Hypertension is a major cardiovascular risk factor in type 2 diabetes mellitus patients that greatly increases the risk for acute cardiovascular events. The purpose of our study was to evaluate the effects of blood pressure in a real-life study including patients with type 2 diabetes mellitus. Material and methods. 10 patients with type 2 diabetes mellitus evaluated in a private medical clinic in Oradea, Romania were included in the study. Their average age was 57.2 years, 60% were men and 40% women, their average duration of diabetes mellitus was 4.3 years. All of them were on metformin therapy alone. Their average HbA1c was 8,19 ± 0.28%, therefore introduction of another antidiabetic agent was necessary. Dapagliflozin 10mg 1 tablet/ day or empagliflozin 25 mg 1 tablet/day were introduced in their therapy. Blood pressure was measured by auscultatory method using an automated sphygmomanometer according to the ESC 2018 guidelines at treatment initiation and after 2 months. Results. The average systolic blood pressure was 149,6±4,77mmHg while the diastolic blood pressure was 92,1±2.79mmHG. 7 out of 10 patients were treated for blood pressure according to the current guidelines with angiotensin converting enzyme inhibitor with or without calcium channel blockers or beta-blockers. No change in their medication for hypertension was registered during the fallow-up period. After 2 months the average systolic blood pressure 144,1 ± 6,60mmHg (5,5mmHg reduction, $p<0.05$) and average diastolic blood pressure was 88,3 ± 2,67mmHg (3,8mmHg reduction, $p<0,05$). The average HbA1c was 7,03 ± 0,27% which represents a much better glucose control. Conclusion. SGLT-2 inhibitors in addition to improving glucose-control in type 2 diabetes patients they also have a beneficial pleiotropic effect in reducing blood pressure. They act by inhibiting the coupled reabsorption of sodium and glucose from the proximal tubules in the kidney. This way they increase renal glucose and sodium excretion. It is well known that patients from Romania have increased sodium intake therefore this medication can modulate the salt-responsive blood pressure mechanisms.

P05. Changes in aged mice behavior associated with fractalkine receptor

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Aim: Fractalkine is a multi-domain protein found commonly in the brain, particularly in neural cells. Its receptor (CX3CR1) is known to be present on microglial cells; interaction between this protein and its unique receptor induces cell adhesion, chemotaxis, crawling, “accessory cell” activity, and survival. Fractalkine, via signaling through its receptor, may be involved in modulating pathogenesis of several inflammatory neurodegenerative diseases such as multiple sclerosis, amyotrophic lateral sclerosis and Alzheimer disease. Fractalkine mediated neuroprotection was attributed to recruitment of the natural killer cell (subtype, NK1.1) a specific kind of innate immune cell that expresses CX3CR1. Due to those reasons we wanted to identify the behavioral changes produced by fractakine in aged mice. Methods: Aged transgenic TgH(CX3CR1-EGFP) mice (80-96 weeks) were divided into 3 groups: CX3CR1+/+ (n=8), CX3CR1+/- (n=12) and CX3CR1-/- (n=7) were used. We performed several behavioral tests to highlight the motor function (Open field, Cylinder test) and cognitive impairments like social interaction (Social chamber test), short-term memory (Novel object recognition), compulsive, anxiety and depresion-like behaviors (Marble burying, Nesting, Tail suspension, 0-Maze, Hole board, Sucrose preference test). Results: We identified several motor (moving velocity between CX3CR1-/-, CX3CR1+/- compared to CX3CR1+/+) and cognitive (compulsive-like behavior CX3CR1-/-, CX3CR1+/- compared to CX3CR1+/+) behaivour changes.Conclusion: Fractalkine and its specific receptor appear to produce changes in the behavior of aged animals in terms of both cognitive and motor ability.

P06. EEG recordings of sleep/wake dynamics changes in rats

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Funding: Self-funded

P07. Effects of hypothermia as a therapeutic intervention in a model of neonatal cerebral ischemia and hypoxia in rats

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Introduction: The perinatal period is one of the most vulnerable stages in the life of each individual, as the consequences of hypoxic-ischemic damage may be immediate, affecting the successful adaptation to extrauterine life, and long-term, through the disruption of normal brain development. Aims: The main objective of this study was to test the possible protective effect of hypothermia in hypoxic-ischemic encephalopathy at newborn rats. Materials and methods: The experimental study was conducted at the Biobase UMF “Iuliu Haţieganu” and the Biobase of the Department of Physiology of the same University. The material was represented by newborn Wistar rats, males and females, with a weight of 10 g on average, kept in optimal conditions along with their mothers.In the 7th day post birth the hypoxic-ischemic injury is performed, following Levine’s method, modified: under local anesthesia with lidocaine 2%, the common carotid artery ligation was performed. The operation was carried out under the microscope. After ischemia, the animals were subjected to hypoxia, in bariatric chamber with a concentration of oxygen in the air of 8%, for 90 minutes. Subsequently each group of animals was divided into two subgroups, one being cared for under normal temperature and the other in hypothermia with declining central temperature with 40C for 3 hours; then the animals were put to death and the oxidative stress parameters were dosed from brain homogenate. The study was completed by histopathological and imunohistochemical examination, for demonstration of Caspase 3 expression as a marker of apoptosis. Results: In neonatal hypoxic-ischemic encephalopathy hypothermia gives partial neuroprotection by reducing the number of cells expressing apoptosis in hippocampus, thalamus and cerebral cortex. Protein carbonyl level was decreased, and antioxidant enzyme defence increased. Conclusion: The results of this study prove that hypothermia offers neuroprotection in hypoxic ischemic brain injuries.

P08. Expression of sensory neuron-derived CSF1 is spatially correlated with macrophage activation after Spared nerve injury model

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Aims: Growing evidence suggests that macrophage activation at the dorsal root ganglia (DRG) level and neuron-macrophage communication are essential mechanisms underlying the pathogenesis of peripheral neuropathic pain. The aim of this study was to investigate the expression of colony-stimulating factor 1 (CSF1) and its potential role in macrophage accumulation in the DRG after spared nerve injury (SNI) model of neuropathic pain. Methods: CX3CR1-GFP transgenic mice were assigned to 3 groups: Control (animals did not undergo any kind of surgery), Sham (the sciatic nerve was exposed) and SNI (the tibial and common peroneal rami of sciatic nerve were ligated and cut). Seven days after surgery, L3 and L4 DRGs were collected, frozen and cut and DRG sections were double immunostained using antibodies against NF200 or CGRP and against CSF1.Results: CSF1 expression is significantly increased in sensory neurons in both L3/L4 DRGs after SNI, but with a higher expression in L4. This pattern is also observed in the macrophage accumulation, with the highest degree of activation in L4, but still with a significant number of activated cells in L3. Moreover, among CSF1(+) neurons, 40% have peri-neuronal rings of macrophages in L4, while in L3 this percentage decreases to 30%. Lastly, 50% of the CSF1(+) neurons co-express NF200, a marker for large, myelinated neurons, while less than 10% of them are small, peptidergic neurons, co-expressing CGRP.Conclusions: The pattern of CSF1 expression after SNI is spatially correlated with macrophage accumulation, suggesting its role in attracting macrophages in DRGs after peripheral nerve injury.

Funding: This research was funded by UEFISCDI, project no. PED 274/2020 and International Society for Neurochemistry, through Educational grant (CAEN) category 1A.

P09. Frey syndrome following parotid surgery

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Background: Frey syndrome, also known as auriculotemporal syndrome is characterized by localized facial gustatory sweating and flushing and is induced by aberrant reinnervation following injury to the auriculotemporal nerve. Materials and Methods: In our study, we present the implementation of the Minor's starch-iodine test, for confirming the diagnosis in case of clinical suspicion of Frey syndrome following parotid surgery.Results: Using this simple method, we were able to objectify the clinical diagnosis of Frey syndrome, based on patient's reports of symptoms such as facial warmth, flushing, and sweating in the setting of acidic or spicy foods.Conclusion: Frey syndrome can generate a considerable impact on the patients' quality of life. Thus, the clinicians must be aware of this clinical entity which may be frequently encountered as consequence of parotidectomy, in order to take the necessary preventive or therapeutic measures. We can use simple methods to confirm the diagnosis. However, further complex studies that aim to clarify the mechanisms involved at the cellular and molecular level could open new perspectives in nerve regeneration research.

P10. Insights of aromatase immunohistochemistry in invasive breast cancer: importance of menopausal status

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Introduction: Aromatase is key enzyme in local estrogen production by androgen conversion, especially in women post-menopause. There have been controversies concerning aromatase localization in human breast carcinomas. Also, aromatase inhibitors represent important drug class used to manage hormone-sensitive breast cancer cases, but patients that may benefit the treatment are currently selected based on hormone (estrogen, progesterone) receptors statuses, instead of intratumor aromatase immunoreactivity.Patients and methods: Using polyclonal antibody immunohistochemistry technique we assessed (intensity and percentage scores) the localization of aromatase in 70 breast cancer tissue samples in order to assess immunostaining characteristics relative to current histopathological variables of breast carcinomas.Results: Aromatase was found in all tissue compartments: tumor (95.7%), stroma (58.6%) and adipose tissue (94.3%). Aromatase expression in tumor cells inversely correlated with tumor grading (ρ=-0.361, p=0.027), and correlated positively with ER (ρ=0.143, p<0.001). Dividing the study group by age 55, tumor aromatase expression was stronger correlated with ER (ρ=0.410, p<0.001) in women aged <55y (pre- and perimenopause), but not in women aged >55y (post-menopause) (ρ=0.131, p=0.899). Although statistical significance was not reached (p>0.05), negative associations with fibrocystic breast disease (ρ=-0.342), tumor grading (ρ=-0.385), PgR (ρ=-0.224), Ki67 (ρ=-0.222), and a positive association with lymph node invasion (ρ= 0.337) were observed in women aged <55y, while in women >55y this association was present to a lesser extent only with tumor grading (ρ= -0.347) and Ki67 index (ρ= -0.133).Conclusion: Local aromatase was linked to better tumor differentiation and proliferation rate suggesting a potential prognostic role in breast carcinomas.

Funding: This study was financed by internal grant from the "Grigore T. Popa" University of Medicine and Pharmacy Iasi (no. 29024/28.12.2016).

P11. Kv3.3 subunits control presynaptic waveform and improve timing at a central excitatory synapse

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High-voltage activated potassium channels of the Kv3 gene family are key in rapidly repolarizing action potentials (AP), supporting fast spikes and enabling high firing rate. Of the four Kv3 gene family members, Kv3.1 and Kv3.3 are highly expressed throughout the auditory brainstem including the medial nucleus of the trapezoid body (MNTB). It has been shown that MNTB neurons possess functional Kv3 channels that are composed of either Kv3.1 and/or Kv3.3, and the deletion of either subunit caused a small increase in postsynaptic AP duration, consistent with functional redundancy of either subunit in the postsynaptic MNTB cell body. Here we test for Kv3 subunitspecific roles at the presynaptic calyx of Held terminal innervating MNTB neurons using in vivo single unit recordings in Kv3.3 knockout mice. Extracellular recordings from MNTB neurons exhibited a typical complex waveform, comprised of a presynaptic and a postsynaptic component. The time between the peak and trough of extracellular APs are compelling markers for AP half-width and showed that the presynaptic Aps and synaptic delays were significantly longer in Kv3.3 knockouts compared to WT recordings. These results suggest that Kv3.3 is the presynaptic 'delayed rectifier', enabling fast presynaptic APs and precisely timed synaptic delays. The changes in presynaptic AP duration and synaptic delay in the Kv3.3 knockout are likely to affect temporal processing in the MNTB output, such as first spike latency and jitter. However, the longer presynaptic APs will also affect transmitter release and hence spontaneous and sound driven firing rates.

Funding: *Biological Sciences Research Council R001154/1, M016501, H2020 Health ITN LISTEN 722098, DFG SFB870 A-10*

P12. Morphological and histological changes in the developing brain of Rfx4_v3 mutant mice

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Rfx4_v3 is the central nervous system proteoform of Regulatory factor X4 (Rfx4). Interruption of a single Rfx4_v3 allele prevented the formation of the subcommissural organ, resulting in mice with congenital hydrocephalus, whereas disruption of both alleles caused failure of the dorsal midline brain structure formation (Blackshear et al., 2003). Additionally, Rfx4_v3 L298P homozygous mutant mouse embryos (Zarbalis et al., 2004) resemble the Rfx4_v3 null phenotype, being characterised by dorsoventral patterning defects in both telencephalon and spinal cord (Asique et al., 2009). To further explore the involvement of Rfx4_v3 into early brain patterning, we analysed the mesencephalon and rhombencephalon of Rfx4_v3 L298P mouse embryos. Genotyping was performed using variable 3' end method (Mitrecic et al., 2007) and sections of the developing brain were stained by standard hematoxylin-eosin and immunofluorescence techniques. The mutant allele was inherited with a high frequency ($\chi 2 = 2.46$, $P < 0.05$) and was hypomorphic, resulting in heterozygous and mutant embryos with different degrees of phenotypic severity. Collectively, E12.5 mutant embryos presented doming of the skull or hydrocephalus in the telencephalon, which was greatly enlarged at the expense of both mesencephalon and rhombencephalon. Furthermore, these embryos showed a delay in the development of the 4th ventricle choroid plexus and an ectopic expression of the dopaminergic neurons in the ventral hindbrain. A hypoplastic mesencephalon and an abnormal proliferation of both isthmic and rhombomere 1 tissues were noticed at E15.5. Mechanistically, Rfx4 functions as a dimer and structural predictions suggested that P298 mutation would disorganise its regulatory dimerisation domain.

Funding: University of Bucharest, Faculty of Biology

P13. New insights into the ionizing radiation effects at the cerebrovascular endothelium level

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According to WHO, brain tumors represent nowadays the 10th cause of death and researchers consider that one of the most effective treatments is radiotherapy. Brain radiotherapy was proved to induce long term irreversible cognitive impairment. Considering the role of BBB in regulation and protection of the brain microenvironment, a complex characterization of the effects induced by irradiation at therapeutic doses on the brain microvasculature is imposed. We observed the cytotoxic, functional and genotoxic effects after low-energy accelerated proton irradiation upon an in vitro model of murine cerebral microvasculature (bEnd.3 cell line, ATCC). Using the beam line of TR19 cyclotron, we exposed cells to doses in the range 0-10 Gy, (dose rate: 1 Gy/ min). The cells proliferation and surviving rates in stress-induced conditions, the DNA damage, the reactive oxygen species formation, the calcium ions dynamics and the cellular capacity of migration at various time intervals post-irradiation were assayed. For comparison X-ray irradiation was used. As results, we observed an inhibition (~90%) of the cellular proliferation and a strong increase of micronuclei number at doses over 5 Gy, a reduction of the DNA repair capacity by the increased values of the dose (~100%) and the linear energy transfer- LET (~20%) and also a decrease of the cell relative migration rate (~25%). In conclusion, we observed a significant modification of the measured parameters with the dose increase and the LET values. Our study presents preliminary results regarding the BBB endothelial cells behavior in oxidative stress conditions induced by the 2 most used radiotherapy methods, protons and X-ray radiation.

P14. Plasma Biomarkers of Stroke

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Ischemic stroke is an acute disease which often results in severe long-term physical disability, depression, and cognitive decline. To date, patients at risk for these late consequences of stroke are not duly diagnosed and treated due to the lack of reliable biomarkers. Extracellular vesicles derived from neurons (ND-EVs) enter the blood stream and have been shown to reflect neuronal health. Previous work by iBioStroke partners found that miR21 and miR223 are hypoxia inducible and secreted into EVs both in stroke models and stroke patients that were significantly associated with clinical outcome (measured by modified Rankin Scale, mRS) in poststroke patients at 90 days. In addition, two Genome Wide Association studies have found genetic polymorphisms associated with stroke recovery. Our hypothesis is that neuronal-derived EVs (ND-EVs) released into blood and/or CSF can be used as biomarkers for stroke outcome. Our aims are (1) isolating ND-EVs released into blood and CSF in aged mice and rats and patients following ischemic stroke, (2) using proteomics and transcriptomics to identify novel ND-EV-based biomarkers for the prediction of stroke outcome, (3) validate ND-EV-based biomarkers in two highly stratified stroke patient populations, and (4) cross-validate ND-EV-based biomarkers found in aged animal models in a cohort of stroke patients. Thereby novel ND-EV based biomarkers might be able to predict long-term outcome after ischemic.

P15. Post-stroke transcriptomics: lessons from the juvenile brain

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Post-stroke transcriptomics: Lessons from the juvenile brain. A significant number of genes are regulated in order to promote brain repair after a lesion. The kinesin superfamily proteins (KIFs), including KIF1b, KIF4, KIF21b and KIF26b are essential for morphogenesis and functioning of the cell. However, their role in axonal regeneration after injury is still not well understood. Here, we asked if injured young adult brain tissue can re-express developmental genes that were active during early postnatal brain development. By RT-PCR and immunohistochemistry, the brains of 3 days old juvenile rat pups showed high levels of kif1b, kif4, kif21b and kif26b transcripts as well as high levels of KIF4 protein. However, of these only kif1b and kif4 mRNAs and KIF4 were highly re-expressed in the subventricular zone and perilesional cortex of young adult rats. The regenerative capacity was limited to the NPCs in the subventricular zone and endothelial cells of the inflamed blood vessels. Most interesting, KIF4 was also sporadically re-expressed in some surviving neurons in the peri-lesional area, that have been, most likely, contributed by NPCs in the leptomeninges. Conclusion: These results suggest that the young-adult brain has a limited capacity to re-express juvenile genes needed for axonal growth. Indeed, the injured young adult brain recapitulates in part, kinesins gene and protein expression pattern seen during early postnatal brain development.

P16. Reflectance confocal microscopy for in vivo evaluation of Meissner's corpuscles in diabetes mellitus

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Diabetes is a major health care problem and its associated complications, are causes of significant morbidity and mortality. Neuropathy is the most common complication of diabetes and its diagnosis, especially in early stages, is a significant challenge for both research and clinical practice. Meissner corpuscles are complex sensory receptors of the glabrous skin, involved in light touch sensitivity. The density of Meissner corpuscles is a sensitive marker in different types of sensory neuropathies and is correlated with the density of intraepidermal nerve fibers. Reflectance confocal microscopy is a modern imaging technique which allows the micromorphological and functional investigation of skin structures in vivo and in real time, with a similar resolution with histological examination. Here we investigate the changes in density of Meissner corpuscles associated with diabetes mellitus, and evaluate their morphological alterations corelated with diabetic neuropathy. The recent advances in skin imaging and in vivo investigation of cutaneous nerve structures are very promising and could improve the early diagnosis of nerve impairment ensuring timely treatment of the disease. This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CCCDI - UEFISCDI, project number PN-III-P2-2.1-PED-2021-2243, within PNCDI III

Funding: This work was supported by a grant of the Ministry of Research, Innovation and Digitization, CCCDI - UEFISCDI, project number PN-III-P2-2.1-PED-2021-2243, within PNCDI III

P17. The effect of extreme sleep durations on cardiovascular health

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Introduction: Excessive or reduced sleep durations ((≤ 6h/24h or ≥9h/24h) have been associated with an increased incidence of cardiovascular disease (CVD). Several studies propose a diverse array of underlying mechanisms, but only few of them provide a thorough assessment. Materials & Methods: 23 studies were selected following a systematic literature search (PubMed, published in the last 7 years). Articles describing CVD impact on sleep were excluded. Results: Extreme sleep durations have a 35% higher mortality risk of coronary heart disease. Both short and long habitual sleep associate metabolic dysregulation, leading to chronic inflammation and increased pro-atherogenic environment. Observational studies have shown that short sleepers, compared to peers sleeping 7- 8 h, are ≈60% more likely to develop hypertension, have a ≈20% higher risk of myocardial infarction and a ≈30% higher incidence of left ventricular hypertrophy. People with insomnia, a health problem affecting 10-30% of the general population are 45% more likely to develop or die from CVD. The responsible mechanism seems to be increased atherogenesis due to high production of angiotensin II. Atherosclerotic lesions and increased levels of Ly-6C monocytes have been observed in sleep deprived mice as well. Habitual prolonged sleep duration has been associated with CVD risk, although studies examining the underlying mechanisms are rare. Long sleepers often had insulin dysregulation. However, prolonged sleep was linked to decreased HDL levels, an anti-atherogenic biomarker. Besides the biological abnormalities, the lifestyle of long sleepers should be taken into consideration as long sleepers are more prone to engage in CVD-promoting behaviours (insufficient exercise, smoking, increased alcohol intake). It has been shown that the long sleepers' risk of diabetes may ameliorate by adopting a healthier lifestyle (improved diet, increased exercise). Conclusion: Although observational data and biological evidence suggest a relationship between extreme sleep durations and CVD, additional experimental investigation is required to elucidate the mechanistic pathways behind it. Based on the available data, we hypothesise that irregular sleep patterns provoke CVD via metabolic alterations. It should be taken into consideration that the pro-atherogenic environment thus created may be worsened by unhealthy behaviours. As both short and long sleep durations may be risk factors for the emergence of chronic diseases, we recommend assessing sleep length during clinical evaluations.

P18. The impact of Vitis Vinifera L. extract on behavioral changes and redox imbalance in hippocampus and frontal lobe of Wistar rats with experimental menopause

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Background. The decline in estrogen levels in menopause is accompanied by higher risk for cardiovascular and neurodegenerative diseases and changes in physiological processes, including cognitive and motor functions. Menopause-induced alterations in structure and function of hippocampal and cortical circuits could be attenuated by administration of grape extract due to neuroprotective, antioxidant and scavenger properties of grape polyphenols. Aims. Our study aimed to assess the impact of Vitis Vinifera L. (VV) extract on behavioral changes (general locomotion and anxiety like behavior) and oxidative stress in brain in an experimental model of menopause induced by ovariectomy (OV) in Wistar rats. Methods. For each subset of experiments (I and II), 20 male Wistar rats were divided into 4 groups (n=5): animals with sham ovariectomy (SOV) treated with vehicle (SOV+veh), SOV treated with VV extract (SOV+VV), OV treated with vehicle (OV+veh), and OV treated with VV (OV+VV). Vitis Vinifera L. extract (30 mg/kg b.w solved in 0.5 ml water) or vehicle (0.5 ml water) were orally administered for 21 days (subset I) and 42 days (subset II), after the surgery, according to the group protocol. The behavioral tests (open field test – OFT and elevated plus maze - EPM) were conducted after 21 and 42 days, and the malondialdehyde (MDA) and nitrotyrosine (NTZ) levels from frontal lobe and hippocampus were evaluated 24h after the last behavioral test. Results. OV has been shown to increase the level of oxidative stress and have a negative impact on memory, behavior and motor functions of rats. OV reduced, after 21 days, the general locomotion in OFT ($p<0.001$) and motor activity in EPM ($p<0.001$) without significant changes in anxiety-like behavior. After 42 days, the general locomotion and motor activity were kept at low level ($p<0.05$) but the anxiety behavior ($p<0.01$; $p<0.001$) improved significantly. 21 days of VV administration triggered mostly non-significant increases of general locomotion indicators in OFT and EPM and non-significant decreases of the anxiety level in EPM. After 42 days, VV extract improved both general locomotion in OFT and motor activity in EPM ($p<0.05$) and diminished significantly the anxiety ($p<0.05$, $p<0.01$). The MDA levels ($p<0.05$, $p<0.001$) and tyrosine oxidation ($p<0.01$; $p<0.05$) decreased after VV treatment in the frontal lobe, both at 21 days and 42 days, while in hippocampus VV extract had controversial effects, with minimal decreases of MDA and high levels of NTZ ($p<0.05$), especially after 42 days of treatment. Conclusions. Our findings suggest

that Vitis Vinifera L administration for a long period, may have beneficial effects on both locomotion and emotionality and could also have antioxidant properties in menopause, especially in frontal lobe.

P19. The role of music study for a harmonious development of the brain

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Recent research has found that people who study a musical instrument benefit from excellent brain training. Scientists have concluded that simply playing an instrument can actually alter the shape of the brain and its native abilities, including from the perspective of increasing the intelligence quotient, both in children and adults. Studying a musical instrument is, for the brain, the equivalent of an intense fitness training, which works the entire muscles of the body at the same time. Specialists have gathered evidence that the brain regions of musicians are different from those of people who do not practice this art, structurally and functionally. These are the areas of the brain responsible for motor skills, hearing, memory, and hearing information that become more active when a person plays an instrument. This artistic preoccupation can improve important skills in everyday life, such as alertness, action planning or perception of emotions. The entire architecture of the brain changes amid music created with the help of a musical instrument, resulting in a whole series of benefits confirmed by experts. In this study, I would like to present just a few of these benefits: improved memory, training perseverance, improved body coordination, increased ability to focus and stress relief. I will also present some experienced exercises in the class of students.