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28th CONGRESS OF THE POLISH PHYSIOLOGICAL SOCIETY

September 15–17, 2021
(ONLINE)
GDANSK, POLAND

BOOK OF PROGRAMME AND ABSTRACTS

Guest Editors:
Tomasz Wierzba
Pawel Musial
Stanislaw Zajaczkowski

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PREFACE

Dear Friends and Colleagues,

This abstract book published as a supplement of the Journal of Physiology and Pharmacology includes program, schedule and abstracts presented at the 28th Congress of the Polish Physiological Society, September 15 -17, 2021. The Congress is organized by the local Organizing Committee at Medical University of Gdansk and University of Gdansk on behalf of the Council of the Polish Physiological Society and Polish Academy of Sciences. Due to COVID-19 pandemic the Congress is held for the first time in a virtual format.

Since 1937, the meetings of the Polish Physiological Society have become a recognized forum for the presentation of achievements, new scientific and creative concepts, discussions related to the functioning of human and animal body. The scientific program of the 28th Congress of the Polish Physiological Society consists of the plenary state of art lectures by invited top experts, short lectures based on original research studies and e-poster presentations.

Fifteen thematic sessions cover most fields of modern physiology and pathophysiology, from the single molecule level to the whole organism regulatory interactions. The Congress features over 250 lectures and presentations by more than 750 Authors representing 32 countries from five continents.

We would like to thank all Authors for sharing their scientific knowledge and passion, the Scientific Committee of the Congress and the Reviewers for the invaluable feedback they provided in a short time as well as the editorial staff of the Journal Physiology and Pharmacology.

Best regards,

GUEST EDITORS:
Tomasz Wierzba, Pawel Musial, Stanislaw Zajaczkowski

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28th CONGRESS OF THE POLISH PHYSIOLOGICAL SOCIETY
CONGRESS PROGRAMME

Wednesday (September 15, 2021)

9:00 – 9:45 *(virtual stream A)*	Opening ceremony
9:45 – 10:30 *(virtual stream A)*	Opening lecture – **SYMPATHETIC OVERACTIVITY AND CARDIOVASCULAR DISEASE – THE ISSUE IS MORE COMPLEX THAN WE THOUGHT RANSCRIPTOMIC STUDIES FOR MALE INFERTILITY DIAGNOSIS AND THERAPY MONITORING.** Prof. Krzysztof Narkiewicz *(Department of Hypertension and Diabetology, Medical University of Gdansk, Poland).*
10:30 – 11:55 *(virtual stream A)*	Session I – open lectures and oral presentations **MUSCLE FUNCTION/ MUSCLE EXERCISE**
10:50 – 13:20 *(virtual stream B)*	**Session XII** – open lectures and oral presentations **GASTROINTESTINAL AND LIVER PHYSIOLOGY AND PATHOPHYSIOLOGY, PANCREAS AND LIVER.**
12:15 – 15:10 *(virtual stream A)*	**Session IV** – open lectures and oral presentations **FATIGUE. ADAPTATION TO ENVIRONMENT. THERMOREGULATION**
13:20 – 14:05 *(virtual stream B)*	**Special session I** (AnimaLab) **PHYSIOLOGY COMPLEXITY AND ITS TECHNOLOGY. EXAMPLES FROM MOTOR FUNCTION TO CIRCADIAN RHYTHMS BY UGO BASILE, ITALY.**
14:15 – 17:45 *(virtual stream B)*	**Session IX** – open lectures and oral presentations **NEW INSIGHTS INTO CELLULAR FUNCTIONS**
15:30 – 17:50 *(virtual stream A)*	**Session III** – open lectures and oral presentations **BIOLOGICAL RHYTHMS. SLEEP**

Thursday (September 16, 2021)

9:00 – 9:40 *(virtual stream C)*	**Special session II** (AnimaLab) **HEART RATE VARIABILITY, TIME DOMAIN AND FREQUENCY DOMAIN ANALYSIS**
9:00 – 10:10 *(virtual stream A)*	**Session VIII** – open lectures and oral presentations **ENDOCRINE REGULATIONS. CONTROL OF BODY WEIGHT**
9:00 – 13:25 *(virtual stream B)*	**Session XI** – open lectures and oral presentations **PHYSIOLOGY OF REPRODUCTION**
9:10 – 10:05 *(virtual stream D)*	**Session I** – interactive poster presentation **MUSCLE FUNCTION/ MUSCLE EXERCISE**
9:45 – 11:20 *(virtual stream C)*	**Session VI** – interactive poster presentations Part I **HEART. CARDIOVASCULAR AND RESPIRATORY REGULATION**
10:05 – 10:55 *(virtual stream D)*	**Session IV** – interactive poster presentations **FATIGUE. ADAPTATION TO ENVIRONMENT. THERMOREGULATION**
10:15 – 11:20 *(virtual stream A)*	**Session XV** – open lectures and oral presentations **MISCELLANEA**
11:00 – 13:55 *(virtual stream D)*	**Session II** – interactive poster presentations **CENTRAL NERVOUS SYSTEM. NEUROPHYSIOLOGY. PLASTICITY OF NEURAL FUNCTION**

11:30 – 12:15 *(virtual stream C)*	**Session VIII** – interactive poster presentations **ENDOCRINE REGULATIONS. CONTROL OF BODY WEIGHT**
11:30 – 16:15 *(virtual stream A)*	**Session VI** – open lectures and oral presentations **HEART. CARDIOVASCULAR AND RESPIRATORY REGULATION**
12:25 – 13:00 *(virtual stream C)*	**Session III** – interactive poster presentation **BIOLOGICAL RHYTHMS. SLEEP**
13:30 – 15:25 *(virtual stream C)*	**Session XI** – interactive poster presentations **PHYSIOLOGY OF REPRODUCTION**
13:30 – 13:55 *(virtual stream B)*	**Special session III** (AnimaLab) **THE USE OF SMALL ANIMAL TELEMETRY IN PHYSIOLOGY**
13:55 – 14:15 *(virtual stream B)*	**Special session IV** (AnimaLab) **NEW APPROACHES TO TEACHING PHYSIOLOGY**
14:00 – 15:30 *(virtual stream D)*	**Session XII** – interactive poster presentations **GASTROINTESTINAL AND LIVER PHYSIOLOGY AND PATHOPHYSIOLOGY, PANCREAS AND LIVER**
14:20 – 18:05 *(virtual stream B)*	**Session II** – open lectures and oral presentations **CENTRAL NERVOUS SYSTEM. NEUROPHYSIOLOGY. PLASTICITY OF NEURAL FUNCTION**
15:30 – 16:10 *(virtual stream D)*	**Session IX** – interactive poster presentations **NEW INSIGHTS INTO CELLULAR FUNCTIONS**
15:30 – 16:25 *(virtual stream C)*	**Session VII** – interactive poster presentations **FUNCTIONS OF BLOOD. HEMOSTASIS**
16:30 – 18:00 *(virtual stream A)*	**Session VII** – open lectures and oral presentations **FUNCTIONS OF BLOOD. HEMOSTASIS**
16:30 – 17:30 *(virtual stream C)*	**Session VI** – interactive poster presentations Part II **HEART. CARDIOVASCULAR AND RESPIRATORY REGULATION**

Friday (September 17, 2021)

9:00 – 10:45 *(virtual stream A)*	**Session XIV** – open lectures and oral presentations **PHYSIOLOGY MEETS ENGINEERING**
9:00 – 11:30 *(virtual stream B)*	**Session XIII** – open lectures and oral presentations **MULTI-OMICS PROSPECTIVES IN PHYSIOLOGY**
10:00 – 10:45 *(virtual stream C)*	**Session V** – interactive poster presentations **BODY FLUID HOMEOSTASIS. RENAL FUNCTIONS**
10:45 – 11:05 *(virtual stream C)*	**Session X** – interactive poster presentations **AGING**
11:10 – 13:55 *(virtual stream A)*	**Session X** – open lectures and oral presentations **AGING**
11:05 – 11:55 *(virtual stream C)*	**Session XIV** – interactive poster presentations **PHYSIOLOGY MEETS ENGINEERING**
11:45 – 13:35 *(virtual stream B)*	**Session V** – oral presentations **BODY FLUID HOMEOSTASIS. RENAL FUNCTIONS**
12:00 – 13:05 *(virtual stream C)*	**Session XV** – interactive poster presentations **MISCELLANEA**
14:00 – 14:30	**Closing ceremony**

Shaded area – interactive poster sessions

OPENING SESSION

Wednesday (September 15, 2021; 9:00 – 10:30)

Chair:

Prof. STANISLAW OKRASA
President of the Polish Physiological Society
University of Warmia and Mazury in Olsztyn, Olsztyn, Poland

Assoc. Prof. TOMASZ H .WIERZBA
Department of Physiology, Medical University of Gdansk, Poland

DETAILED OPENING SESSION SCHEDULE

Opening ceremony (Wednesday, September 15, 9:00 – 9:45, *virtual stream A*)

Opening lecture (Wednesday, September 15, 9:45 – 10:30; *virtual stream A*)

SYMPATHETIC OVERACTIVITY AND CARDIOVASCULAR DISEASE - THE ISSUE IS MORE COMPLEX THAN WE THOUGHT. RANSCRIPTOMIC STUDIES FOR MALE INFERTILITY DIAGNOSIS AND THERAPY MONITORING - **Krzysztof Narkiewicz** (Department of Hypertension and Diabetology, Medical University of Gdansk, Poland).

S0.L1

SYMPATHETIC OVERACTIVITY AND CARDIOVASCULAR DISEASE - THE ISSUE IS MORE COMPLEX THAN WE THOUGHT. RANSCRIPTOMIC STUDIES FOR MALE INFERTILITY DIAGNOSIS AND THERAPY MONITORING

K. NARKIEWICZ

Department of Hypertension and Diabetology, Medical University of Gdansk, Poland

The sympathetic nervous system plays a central role in cardiovascular regulation in both health and disease. Sympathetic overactivity has been implicated in the pathogenesis of hypertension, coronary artery disease, cardiac arrhythmias and heart failure. Nevertheless, there are several unclear, controversial or unresolved issues prompting further studies in the field. Firstly, despite the mechanistic rationale for the use of beta-blockers in the treatment of hypertension-related tachycardia, their therapeutic impact on patient prognosis in uncomplicated hypertension remains controversial. Secondly, while the ‘‘tracking phenomenon’’ is an important longitudinal characteristic of blood pressure, much less is known about changes in sympathetic nerve activity over time. Thirdly, we should pay more attention to long-term interaction between respiration and sympathetic overactivity. Spontaneous breathing frequency, central sympathetic outflow, and chemoreflex sensitivity exhibit significant interactions in the modulation of neural circulatory control. We need more studies evaluation long-term behavioural interventions directed at altering breathing frequency. Fourthly, microneurography, a gold standard of sympathetic drive assessment, was developed almost 50 years ago. It can be applied only in laboratory conditions. Cardiovascular research is in desperate need of novel broadly applicable tools assessing sympathetic activity also in real life to catch up with the progress in out-of-the office blood pressure and heart rate measurements. Fifthly, MRI-based studies might provide novel insights into relationship between sympathetic overactivity and cardiovascular disease. We have previously shown that compensatory functional reorganization may precede hypertension-related brain damage and cognitive decline. It is unclear how sympathetic overactivity contributes to altered brain mechanisms of higher cognitive processing, and whether these mechanism independently predispose to progression of hypertension or to acceleration in brain aging. Finally, we should better understand the link between sympathetic overactivity, stress and cardiovascular events. This might of particular relevance in the COVID-19 era.

SESSION I

MUSCLE FUNCTION
MUSCLE EXERCISE

Wednesday (September 15, 2021; 10:30 – 11:55)
Thursday (September 16, 2021; 9:00 – 10:05)

Chair:

Prof. Jerzy Zoladz
Department of Muscle Physiology, University School of Physical Education, Krakow, Poland

Prof. Jan Gorski
Department of Physiology, Medical University of Bialystok, Bialystok, Poland

Prof. Adrian Chabowski
Department of Physiology, Medical University of Bialystok, Bialystok, Poland

DETAILED SESSION I SCHEDULE

Opening lecture (Wednesday, September 15, 10:30 – 10:50; *virtual stream A*):

S1.L1 THE FIRST CONCEPT OF FATIGUE THRESHOLD IN HUMANS AS PROPOSED BY HENRY BRIGGS A 100 YEARS AGO. **J.A. Zoladz** (Department of Muscle Physiology, Institute of Basic Sciences, Faculty of Rehabilitation, University School of Physical Education in Krakow, Krakow, Poland).

Oral presentations (Wednesday, September 15, 10:50 – 11:55; *virtual stream A*)

S1.L2 EFFECT OF 8-WEEK SUPPLEMENTATION WITH VITAMIN D3 ON PATIENTS WITH CHRONIC LOW BACK PAIN ELIGIBLE FOR NEUROSURGERY INTERVENTION. **P.A. Chromiec[3], P. Kurlandt[2], M. Czechlowska-Nabozna[3], A. Glinska[3], W.R. Skrobot[1], D. Korewo[1], S. Pietrzak[1], A. Zdun-Ryzewska[3], E. Szurowska[3], W. Kloc[2], J.J. Kaczor[1*]** ([1]Gdansk University of Physical Education and Sport, [2]Department of Neurosurgery Copernicus Healing Entity, Gdansk, [3]Faculty of Health Sciences with the Division of Nursing and Institute of Maritime and Tropical Medicine, Medical University of Gdansk, Poland).

S1.L3 EFFECTS OF A LINEAR BLOCK PROGRESSION STRENGTH TRAINING PROGRAM ON CARDIAC REMODELING PARAMETERS IN RATS. **L. Gomes Dias, M.R. Ramos Paunksnis, A.P. Lima-Leopoldo, A.S. Leopoldo, M.R. Holanda Da Cunha, D.S. Bocalini** (Universiade Federal do Espirito Santo, UFES, Vitoria/ES Brasil).

S1.L4 RELATIONSHIPS BETWEEN PLASMA CONCENTRATIONS OF ANGPTL4 AND OTHER CYTOKINES REGULATING LIPID METABOLISM DURING MARATHON RUNNING IN HEALTHY MEN. **M. Gorecka, K. Krzeminski, M. Buraczewska, A.W. Ziemba** (Department of Applied Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S1.L5 IMPACT OF ENDURANCE TRAINING ON THE NITRIC OXIDE BIOAVAILABILITY IN RAT SKELETAL MUSCLES – RELATIONSHIP TO MUSCLE MITOCHONDRIA BIOGENESIS. **J. Majerczak[1], H. Drzymala-Celichowska[1], A. Kij[2], M. Grandys[3], J. Celichowski[1], S. Chlopicki[2,4], J.A. Zoladz[3]** ([1]Department of Neurobiology, Poznan University of Physical Education, Poznan, Poland, [2]Jagiellonian Centre for Experimental Therapeutics (JCET), Jagiellonian University, Krakow, Poland, [3]Department of Muscle Physiology, Chair of Physiology and Biochemistry, University School of Physical Education, Krakow, Poland, [4]Department of Experimental Pharmacology, Chair of Pharmacology, Jagiellonian University Medical College, Krakow, Poland.)

Session summary

Poster session (September 16, 2021; 9:00 – 10:05, *virtual stream D, interactive*)

S1.P1 THE FACTORS THAT MODULATE GROWTH HORMONE RESPONSES TO A PHYSICAL EFFORT. **B.H. Opaszowski** (Department of Endocrinology, Institute of Sport - National Research Institute, Warsaw, Poland)

S1.P2 EFFECT OF S-EQUOL, SELECTIVE ESTROGEN RECEPTOR β AGONISTS, ON MDX MUSCLE FIBERS. **F. Figueiredo[1], F. Yoshimura[1], J. Suh[1], A. Silva Neto[1], F. Fonseca[2], D. Feder[1], M. Sato[1], T. Hermes[3]** ([1]Department of Morphology and Physiology, Centro Universitario FMABC, Santo Andre, SP, Brazil, [2]Laboratory of Clinical Analysis, Centro Universitario FMABC, Santo Andre, SP, Brazil, [3]Department of Anatomy, Federal University of Alfenas (UNIFAL-MG), Alfenas, MG, Brazil).

S1.P3 FUNCTIONAL OUTCOMES OF DISTAL RADIUS FRACTURES MANAGED WITH VARIOUS METHODS OF FRACTURE STABILIZATION. **J. Olech[1], G. Konieczny[2], P. Morasiewicz[3]** ([1]Orthopedic Surgery Department, Provincial Specialist Hospital in Legnica, Legnica, Poland; [2]Faculty of Health Sciences and Physical Education, The Witelon State University of Applied Sciences in Legnica, Legnica, Poland; [3]Department of Orthopaedic and Trauma Surgery, University Hospital in Opole, Institute of Medical Sciences, University of Opole, Opole, Poland).

S1.P4 CHANGES IN SERUM LIPID PROFILE CAUSED BY FASTING AND PHYSICAL EXERCISE. **K. Pilis, A. Kosior-Lara, K. Leszczynski, A. Pilis** (Department of Health Sciences, Jan Dlugosz University in Czestochowa, Czestochowa, Poland).

S1.P5 RELATION BETWEEN RECTUS FEMORIS AND VASTUS MEDIALIS PASSIVE MECHANICAL PROPERTIES AND BODY MASS INDEX AFTER TOTAL KNEE REPLACEMENT. **D. Lenciauskiene** (Klaipeda State University of Applied Sciences, Klaipeda, Lithuania).

S1.P6 EFFECT OF SODIUM BICARBONATE SUPPLEMENTATION ON MUSCLE PERFORMANCE AND DAMAGE: A DOUBLE BLIND, RANDOMIZED CROSSOVER STUDY. **C. Leite[1], R. Battazza[2], M. Kalytczak[2], M. Lamolha[2], R. Rica[3], J. Baker[4], F. Politti[2], D. Boccalini[1]** ([1]Universidade Federal do Espirito Santo, Vitoria, Espirito Santo, Brazil, [2]Universidade Nove de Julho, Sao Paulo, Brazil, [3]Faculdade Estacio de Sa, Vitoria, Espirito Santo, Brazil, [4]Hong Kong Baptist University Kowloon Tong, Hong Kong, China).

S1.P7 MITOCHONDRIAL ADENOSINE TRIPHOSPHATE-SENSITIVE POTASSIUM CHANNELS OPENING IS CRITICAL FOR ENERGY METABOLISM UNDER PHYSICAL STRESS. **O. Akopova, I. Mankovska, V. Nosar, L. Kolichynskaya, V. Sagach.** (A. Bogomoletz Institute of Physiology, NAS of Ukraine, Kiev, Ukraine).

S1.P8 EFFECT OF LOSS OF MIR-23-27-24 CLUSTER MICRO-RNAS ON MUSCLE REGENERATION. **T. Kato[1], S. Oikawa[2], M. Lee[2], T. Akimoto[2]** ([1]Graduate School of Sport Sciences, Tokorozawa, Japan; [2]Faculty of Sport Sciences, Waseda University, Tokorozawa, Japan)

S1.L2

EFFECT OF 8-WEEK SUPPLEMENTATION WITH VITAMIN D3 ON PATIENTS WITH CHRONIC LOW BACK PAIN ELIGIBLE FOR NEUROSURGERY INTERVENTION

P.A. CHROMIEC[3], P. KURLANDT[2], M. CZECHLOWSKA-NABOZNA[3], A. GLINSKA[3], W.R. SKROBOT[1], D. KOREWO[1], S. PIETRZAK[1], A. ZDUN-RYZEWSKA[3], E. SZUROWSKA[3], W. KLOC[2], J.J. KACZOR[1]

[1]Gdansk University of Physical Education and Sport, Gdansk, Poland, [2]Department of Neurosurgery Copernicus Healing Entity, Gdansk, Poland, [3]Faculty of Health Sciences with the Division of Nursing and Institute of Maritime and Tropical Medicine, Medical University of Gdansk, Poland.

Chronic pain in the lumbar spine (CLBP) is the second most common complaint in adults. The complex function of paraspinal muscles in CLBP leads to macroscopic degeneration of the multifidus muscles. Numerous studies have shown a decreased cross-sectional area of this muscle in patients with CLBP compared to healthy muscles. Also, it has been proven that vitamin D deficiency is correlated with chronic pain in the lumbar region of the spine. In addition, as a result of vitamin D deficiency, mitochondrial dysfunction and paraspinal muscle atrophy occur. The study aimed to evaluate the effects of 8-week supplementation with vitamin D3 with an average dose of 6 000 IU/day in patients with CLBP before surgery and 8-week physical activity after neurosurgery intervention. Patients depending on the BMI were supplemented with vitamin D3 (19–25/4000; 25–29.9/6000; and >30/8000 IU; SUPD) or placebo (vegetable oil; PLG). Each patient has been done three times MRI scan of the lumbar spine, first before supplementation, second 2 weeks after end supplementation, and about 6–8 weeks after surgery. Patients performed functional tests, and blood was collected for later analysis at every examination. We found an increase in serum of vitamin D3 concentration in the SUPD as compared to the PLG. There was an improvement in two of the three functional tests in the SUPD. Data indicate that supplementation with vitamin D had a positive response in well-being and pain sensations. Even in one case, there was a reversal of morphological changes, confirmed by MRI.

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S1.L3

EFFECTS OF A LINEAR BLOCK PROGRESSION STRENGTH TRAINING PROGRAM ON CARDIAC REMODELING PARAMETERS IN RATS

L. GOMES DIAS, M.R. RAMOS PAUNKSNIS, A.P. LIMA-LEOPOLDO, A.S. LEOPOLDO, M.R. HOLANDA DA CUNHA, D.S. BOCALINI

Universiade Federal do Espirito Santo, UFES, Vitoria/ES Brasil

Strength training (ST) is an effective strategy for increasing muscle strength, inducing important changes in both performance and health parameters. However, even though many studies show positive responses with the practice of TF in skeletal muscle parameters, the effects on cardiac remodeling still remain inconclusive. Thus, the aim of the study was to evaluate the effects of strength training program with linear progression in block on parameters of cardiac remodeling in rats. Methods: Twenty rats were distributed in two groups: control (C, n:10) and trained (T, n:10). The training protocol (12 climbs with 90 seconds of interval) was organized in three mesocycles of four weeks, with load increment in a linear way (60%, 65%, 70% and 75%) at each block, considering the established weight in the test of maximum strength. The parameters evaluated: muscle strength, ventricular function by echocardiogram, ventricular hemodynamics and changes in cardiac mass. The Student t test was used with a significance level of $p < 0.05$ with values presented as mean ± standard error of the mean. Training induced a 45 ± 4% increase in muscle strength. There were no significant changes ($p > 0.05$) in ventricular function by FEAT (C: 61 ± 3, T: 63 ± 5; %) and diastolic areas (C: 2.83 ± 0.01, T: 2, 94 ± 0.07; mm) and systolic (C: 1.07 ± 0.07, T: 1.07 ± 0.01) between groups. Regarding hemodynamic parameters, no differences were found ($p > 0.05$) in LVSP (C: 122 ± 5, T: 119 ± 4; mmHg), PD2LV (C: 5.1 ± 0.3, T: 5 .3 ± 0.3; mmHg), +dP/dt (C: 11800 ± 1200, T: 14416 ± 1120; mmHg/s) and –dP/dt (C: 8523 ± 493, T: 8415 ± 499; mmHg /s). As well as in the atrial mass (C: 0.17 ± 0.02, T: 0.15 ± 0.02; mg/g), RV (C: 0.56 ± 0.01, T: 0.59 ± 0.03; mg/g), LV (C: 2.27 ± 0.06, T: 2.22 ± 0.03, mg/g) and cardiac mass (C: 3.06 ± 0.05; T: 3.01 ± 0.09 mg/g). In conclusion the realization of a linear strength training program in block for 12 weeks promoted an increase in muscle strength, without promoting significant changes in cardiac morphofunctional parameters.

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S1.L4

RELATIONSHIPS BETWEEN PLASMA CONCENTRATIONS OF ANGPTL4 AND OTHER CYTOKINES REGULATING LIPID METABOLISM DURING MARATHON RUNNING IN HEALTHY MEN

M. GORECKA, K. KRZEMINSKI, M. BURACZEWSKA, A.W. ZIEMBA

Department of Applied Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland

Angiopoietin-like protein 4 (ANGPTL4), tumour necrosis factor-α (TNF-α) interleukin 6 (IL-6) and interleukin 10 (IL-10) regulates lipid metabolism and inflammation. The aim of this study was to find out whether the marathon running influences plasma ANGPTL4 and whether it is related to plasma changes of IL-6, IL-10, TNF-α and lipids. Ten healthy men (age 33.7 ± 1.2 years) completed a marathon running. Plasma ANGPTL4, IL-6, IL-10, TNF-α, free fatty acids (FFA), triacylglycerols (TG), glycerol (Gly), total cholesterol (TC), low (LDL-C) and high (HDL-C) density lipoprotein-cholesterol were determined before, immediately after the run and after 90 min of recovery. Plasma ANGPTL4 increased during exercise from 55.5 ± 13.4 to 78.1 ± 15.0 ng/ml ($p < 0.001$). This was accompanied by significant increases in plasma concentrations of IL-6, TNF-α, IL-10, FFA, Gly and decreases in plasma TG ($p < 0.01$). After 90 min of recovery, plasma ANGPTL4 and TG did not differ significantly from the exercise values, while plasma IL-6, TNF-α, IL-10, FFA and Gly were significantly lower than immediately after the run, but still higher than at baseline. TC, TC/HDL-C and TG/HDL-C molar ratios after the recovery were significantly lower than before the run. Positive correlations were found between exercise-induced increases in plasma ANGPTL4 and those of TNF-α ($r = 0.83$; $p < 0.01$), IL-6 ($r = 0.71$; $p < 0.02$) and FFA ($r = 0.71$; $p < 0.02$). Increases in plasma ANGPTL4, IL-6 and TNF-α correlated positively with those of Gly ($r = 0.78$, $r = 0.75$ and $r = 0.81$; $p < 0.01$; respectively). After 90 min of recovery plasma concentrations of IL-6 and TNF-α correlated positively with plasma FFA ($r = 0.74$, $p < 0.01$; $r = 0.61$, $p < 0.05$; respectively) and Gly ($r = 0.60$, $r = 0.61$; $p < 0.05$; respectively). The present data suggest that the exercise-induced increases in plasma FFA, IL-6 and TNF-α during marathon running may be involved in plasma ANGPTL4 release and that increase in ANGPTL4 secretion may be a compensatory mechanism against fatty acid induced oxidative stress. The data also suggest that ANGPTL4, IL-6, TNF-α can stimulate adipose tissue lipolysis during marathon run. Additionally, the exercise-induced significant increases in plasma IL-6, TNF-α and IL-10 may reflect both immunological changes in skeletal muscle and exercise-induced endotoxemia.

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S1.L5

IMPACT OF ENURANCE TRAINING ON THE NITRIC OXIDE BIOAVAILABILITY IN RAT SKELETAL MUSCLES - RELATIONSHIP TO MUSCLE MITOCHONDRIA BIOGENESIS

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Nitric oxide ($NO^{\bullet}$) is considered to be a multifunctional signalling molecule that is found in almost all living cells. It is postulated that $NO^{\bullet}$ is involved among others in the training-induced intensification of mitochondrial biogenesis. Skeletal muscles has been found to be a reservoir of the $NO^{\bullet}$ in the form of nitrate and nitrite. The aim of the present study was to determine the changes in the nitrite and nitrate concentration in soleus muscle in relation to the changes of mitochondrial electron transport chain (ETC) proteins after 1, 2, 4 and 8 weeks of endurance training. The ETC proteins were determined using Western immunoblotting. Muscle nitrate and nitrite has been evaluated using HPLC. We have found that the endurance training as soon as after 1 week decreased muscle nitrite concentration ($p < 0.05$), which remained attenuated until the 8th week of training. On the other hand the level of muscle nitrate concentration was less sensitive to endurance training and remained unchanged until the 8th week of training, with the exception of its temporal attenuation ($p = 0.05$) found after the 2nd week of training. Moreover, an increase ($p < 0.05$) in the ETC proteins content has been found not sooner than at the 8th week of the training. Endurance training rapidly diminishes muscle nitrite concentration but its effect on muscle nitrate concentration is less evident. The training-induced decrease in the muscle nitrite concentration is a much faster muscle adaptive response than the training-induced increase of the ETC proteins content.

Acknowledgements: This study was supported by the funds from the National Science Centre (NCN) 2017/27/B/NZ7/01976.

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S1.P1

THE FACTORS THAT MODULATE GROWTH HORMONE RESPONSES TO A PHYSICAL EFFORT

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Exercise is a strong stimulator of growth hormone secretion (GH). Its increase release takes place during increased anaerobic processes, large O_2 deficit and oxygen debt. The GH response mechanism is complex. Data indicate, that a crucial contribution to exercise response of GH have the adrenergic and cholinergic systems. This research aimed to assess an impact of 'warm up' and cholinergic preparation on the GH response to exercise. Eight students of age 22–25 and VO_{2max} 5.019 ± 0.301 l O_2/min volunteered in this study. They performed 3 separated supra-maximal runs on a treadmill (22 km/h) until exhaustion, without information about the time completing of the effort. On the first visit the effort was preceded by 10-min warm-up. On the two next visits prior to the efforts without warm-up, placebo or cholinergic preparation (DMAE) were administered in a randomized order. Physiological parameters, such as: like heart rate (HR), oxygen uptake (VO_2), O_2 deficit and oxygen debt were recorded. Pre- and post-effort capillary blood were sampled for determination of lactate and GH levels. Run 'ad maximum' lasted on average 132 s with placebo, 146 s with cholinergic preparation and 149 s with warm-up. It was found, that the longer the time, the higher contribution the aerobic processes. The effort with warm up was characterized by the lower O_2 deficit as compared to two other runs. The highest lactate peak 14.8 mm was recorded after run with cholinergic preparation, followed by placebo 13.7 mM and with warm up 12.6 mM. GH_{max} concentration after the 'ad maximum' run without warm-up was 63.4 μU/ml, with cholinergic preparation 47.4 μU/ml and with the warm-up 32 μU/ml and appropriate areas under curves (AUCs) were 2462, 2055 and 1597 μU × min × ml^{-1}. GH correlated with O_2 deficit (r = 0.656), with LA (r = 0.866) and GH_{max} with time of run. (r = –0.880). Warm-up and DMAE reduce the exercise response of growth hormone after supramaximal exertion. Sub-maximal warm-up performed prior to supra-maximal effort increases oxygen availability, activates oxidative processes and cholinergic system, thus in turn moderates GH response to supra-maximal effort and protects the 'secretory reserve' of the pituitary gland.

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S1.P2

EFFECT OF S-EQUOL, SELECTIVE ESTROGEN RECEPTOR B AGONISTS ON MDX MICE MUSCLE FIBERS

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Duchenne muscular dystrophy (DMD) is the most prevalent human dystrophinopathy. It is a recessive disease characterized by progressive and irreversible degeneration of the skeletal striated musculature. As a X chromosome-linked disease, it is more common in males, affecting approximately 1 in every 3500–6000 live births. We investigated the effects of S-equol, a selective ligand for estrogen receptor (ER)-β, on muscle fibers of mdx mice. Mdx mice (14-days-old) were randomly divided in groups: treated with S-equol (20 mg/kg dissolved in DMSO, i.p.), DMSO (vehicle, i.p.), and control group (without drug treatment). After 14 days of daily treatment, the animals were euthanized for morphological analyzes of different skeletal muscles. We obtained different results depending on the muscle studied. The group treated with S-equol showed an increase in cells with central nucleus in the *quadriceps* and *biceps brachii* muscles compared to the other experimental groups. The vehicle treated group (DMSO) demonstrated a statistically significant reduction in the total number of cells with a central nucleus of the *quadriceps* muscle in comparison to the control and S-equol groups. No significant difference was observed in the percentage of central nucleus for the *tibialis anterior* muscle, however we observed an increase in the inflammatory area of the control group. In the *extensor digitorum longus* and *sternomastoid* muscles, a reduction in the percentage of cells with central nucleus in the group treated with S-equol was observed. *Extensor digitorum longus* muscle also showed a decrease in the inflammatory area in the vehicle treated group (DMSO). No significant changes were observed in the *diaphragm* muscle comparing the different groups. Conclusions: Both S-equol and DMSO treatments reduced muscle fiber degeneration. Although the positive results were not observed in all skeletal muscle studied, either S-equol or DMSO can be promising in the treatment of DMD, suggesting a possible novel therapeutic approach, given the current lack of satisfactory treatments and its several adverse effects.

Acknowledgments: NEPAS.

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S1.P3

FUNCTIONAL OUTCOMES OF DISTAL RADIUS FRACTURES MANAGED WITH VARIOUS METHODS OF FRACTURE STABILIZATION

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The purpose of our study was to assess the functional parameters following distal radius fractures (DRF) treatment with three different fracture stabilization methods. Fifty patients (33 women and 17 men), the mean age at the beginning of treatment was 56.5years. The mean duration of follow-up was 2 years and 8 months. The first subgroup (n = 14) were the patients treated with volar plating, another subgroup (n = 23) were the patients with cast immobilization and the third subgroup (n = 13) were the patients treated with closed reduction and K-wire fixation. We assessed: 1) muscle strength, 2) range of motion, 3) pain severity. The mean relative grip power values in the volar-plate, cast and K-wire subgroups were 56%, 79% and 56% respectively. These differences were statistically significant ($p = 0.0028$). The best range of flexion (75.7°) was achieved in the cast subgroup and the most limited flexion (59.9°) was observed in the volar-plate subgroup. By far the lowest pain severity was reported by patients in the volar-plate subgroup (VAS score of 1.9). The most severe pain was reported by patients from the K-wire group (score 4.1), whereas the patients from the cast subgroup rated their pain severity as 3. The greatest muscle strength in the affected limb, similar to that in the uninjured limb and the greatest mean range of wrist flexion was achieved in the cast subgroup. The lowest pain severity was reported in the volar-plate subgroup. The best functional outcomes were achieved in the cast subgroup.

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S1.P4

CHANGES IN SERUM LIPID PROFILE CAUSED BY FASTING AND PHYSICAL EXERCISE

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Fasting causes specific adaptive changes in the body. Therefore, it was decided to investigate what changes occur in the serum lipid profile after 8-days of fasting in middle-aged men under conditions of rest and exercise. To this end, 13 volunteered for 8-days of total fasting, during which the subjects drank only any amount of moderately mineralized water. Before and after the fasting intervention, venous blood was collected from men under resting conditions and immediately after the exercise test, in which the concentration of β-hydroxybutyrate (β-HB), total cholesterol (Ch-T), high-density lipoprotein cholesterol (Ch-HDL), low-density lipoprotein cholesterol (Ch-LDL), and triglycerides (TG) was determined. The mutual relations of the individual plasma lipid fractions were also calculated, that is: R_1 = Ch-T/Ch-HDL, R_2 = Ch-LDL/Ch-HDL, R_3 = TG/Ch-HDL. The applied fasting together with exercise resulted in significant changes in the concentration of the following variables: β-HB ($p < 0.001$), Ch-T ($p < 0.001$), Ch-HDL ($p < 0.001$), Ch-LDL ($p = 0.018$), TG ($p < 0.001$), and R_3 coefficient ($p = 0.036$), with the upper limits of the reference values being exceeded for Ch-T, Ch-LDL and the R_1 coefficient. Post hoc analysis showed that the applied fasting increased only the concentration of β-HB, both at rest and under the conditions of the ergocycle test ($p < 0.001$). Serum concentration of Ch-T ($p = 0.009$), Ch-HDL ($p = 0.004$), Ch-LDL ($p = 0.038$) obtained after exercise under the conditions of a standard diet, as well as post-exercise Ch-HDL concentrations ($p = 0.011$) and TG ($p = 0.038$) measured after the applied fasting was significantly higher than the values obtained, respectively, under resting conditions. In conclusion, it was found that the 8-day fasting coupled with exercise changed the serum lipid profile, with physical exercise playing a more important role in this change than the fasting intervention.

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S1.P5

RELATION BETWEEN RECTUS FEMORIS AND VASTUS MEDIALIS PASSIVE MECHANICAL PROPERTIES AND BODY MASS INDEX AFTER TOTAL KNEE REPLACEMENT

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More than 50 percent patients undergoing total knee arthroplasty are obese. Obesity has influence on healing process complications after surgery of tendons. There is deficit of studies justifying correlation between body mass index (BMI) and rectus femoris (RF) and vastus medialis (VM) muscles passive mechanical properties after knee arthroplasty. Aim of the study was to determine the relation between RF and VM muscles passive mechanical properties and BMI after total knee arthroplasty. Calculation of BMI was used to classify the patient weight status and to assign to one of the experimental group, miotonometry of RF and VM was used to assess stiffness, elasticity, tone. Statistical data analysis was carried out using SPSS 25.0 statistical analysis package. Data compliance with the normal distribution was verified using Kolmogorov-Smirnov test. Regularity of data differences was checked by non-parametric analysis tests: Mann-Whitney, Kruskall-Wallis. Non-parametric Spearmen correlation coefficient *r* was used to determine relation between parameters. Level of significance was determined as $p < 0.05$. The sample consisted of n = 21 patients after total knee arthroplasty. Patients were divided into three groups according BMI: overweight group (BMI 25.0–29.9 kg/m^2, n = 7), obesity class I group (BMI 30–34.9 kg/m^2, n = 7), obesity class II group (BMI 35.0–39.9 kg/m^2, n = 7). Examination was carried out 1 weak after knee arthroplasty. The results of present study has revealed that overweight was strongly inversely related to RF muscle tone ($r = –0.82$ $p < 0.05$), elasticity ($r = –0.75$ $p < 0.05$). Obesity class I was strongly inversely related to RF muscle stiffness ($r = –0.75$ $p < 0.05$). We have not detected relation between obesity class II and RF and VM muscles passive mechanical properties ($p > 0.05$). BMI was strongly inversely related to RF muscle stiffness ($r = –0.79$ $p < 0.01$), moderately related to RF muscle tone ($r = –0.66$ $p < 0.01$), elasticity ($r = –0.50$ $p < 0.05$), VM muscle tone ($r = –0.48$ $p < 0.05$), stiffness ($r = –0.56$ $p < 0.05$). BMI statistically significantly was inversely related to RF, VM muscles tone, stiffness and RF elasticity after total knee arthroplasty, therefore the relation between obesity class and passive mechanical RF and VM muscles mechanical properties should be further investigated involving larger sample size.

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S1.P6

EFFECT OF SODIUM BICARBONATE SUPPLEMENTATION ON MUSCLE PERFORMANCE AND DAMAGE: A DOUBLE BLIND, RANDOMIZED CROSSOVER STUDY

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This study investigated the effects of sodium bicarbonate ($NaHCO_3$) supplementation on parameters related to the external and internal exercise load in trained individuals submitted to fatigue induction using an isokinetic dynamometer. Ten subjects were tested on two occasions: after ingesting 0.3 g.kg^{-1} of body mass of $NaHCO_3$ or placebo. Maximum voluntary isometric contraction tests were performed before and after a dynamic protocol consisted of 10 series of 10 movements of unilateral extension (concentric phase) and flexion (eccentric phase) of the knee extensors at 120° s-1 at an interval of 60 seconds between series. Performance was assessed using peak torque values. Muscle damage was assessed prior and 24 hours post exercise. The subjective perceptions of effort, pain and recovery were assessed at different times and the internal load of the session was assessed 30 minutes post-effort. Although significant ($p < 0.05$) reductions in peak torque were noted both in isometric ($NaHCO_3$: –20.5 ± 4.1%; Placebo: –17.9 ± 3.0%) and isokinetic strength (NaHCO3: –23.0 ± 13.9%; Placebo: –19.6 ± 9.1%), there was no effect of supplementation on performance ($p > 0.05$). There were no significant differences ($p > 0.05$) between conditions in blood creatine kinase concentrations ($NaHCO_3$ - pre: 225.3 ± 135.9 U/L, post: 418.4 ± 318.4 U/L; Placebo - pre: 238 ± 94.03 U/L, post: 486 ± 336.6 U/L). Curiously, only perception of recovery enhanced ($p < 0.05$) after supplementation. The findings indicate that $NaHCO_3$ supplementation did not attribute benefits in performance or in parameters related to the internal load of the exercise.

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S1.P7

MITOCHONDRIAL ADENOSINE TRIPHOSPHATE-SENSITIVE POTASSIUM CHANNELS OPENING IS CRITICAL FOR ENERGY METABOLISM UNDER PHYSICAL STRESS

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The modulation of mitochondrial ATP-sensitive potassium (mKATP) channel activity by pharmacological means is known to have a great impact on energy metabolism in a living organism. In multiple studies it was shown that mKATP channels openers were effective for the recovery of cardiac and neuronal tissues from ischemia and the risks of oxidative damage after reperfusion. The aim of this work was to examine the impact of endogenous activity of mKATP channel on physical endurance of the rats subject to compulsory swimming. Male Wistar rats were separated in two groups exhibiting high and low resistance to physical stress and subject to compulsory swimming with a load. Swimming time (ST) was monitored till the fatigue, and KATP channel activity was determined *ex vivo* in liver mitochondria. ST was higher in high resistance group, which reliably coincided with higher endogenous mKATP channels activity. Administration of mKATP channels blockers, glibenclamide and 5-hydroxydecanoate, dramatically reduced ST in both high- and low-resistant groups, and completely blocked mKATP channel *in vivo*, which indicated the dependence of physical endurance on mKATP channel activity. To find a mechanistic basis for observed dependence, we studied the direct effects of mKATP channel opening by diazoxide and blocking by glibenclamide on mitochondrial functions *in vitro*. Diazoxide stimulated state 4 respiration, reduced RCR and the rate of phosphorylation, but increased phosphorylation efficiency (P/O). Glibenclamide reduced the rates of state 3 and 4 respiration, and dramatically suppressed phosphorylation, which was exhibited by reduced P/O and the rate of phosphorylation. Based on the experiments, we came to the conclusion of the correlation between the physical endurance and P/O ratio, both dependent on mKATP channels activity. Thus, mKATP channels blocker dramatically reduced P/O and increased oxygen consumption by mitochondria as well as energy expense for ATP synthesis. Unlike this, mKATP channels opener increased phosphorylation efficiency and reduced oxygen consumption by oxphos system, which helped to avoid oxygen depletion under the conditions of oxygen shortage during exercise training. *In vivo* this resulted in the reduction of fatigue and improvement of the endurance in the animals with elevated endogenous mKATP channel activity.

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S1.P8

EFFECT OF LOSS OF MIR-23-27-24 CLUSTER MICRO-RNAS ON MUSCLE REGENERATION

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Recent studies have revealed that microRNAs (miRNAs) inhibited translation and/or promoted degradation of their target mRNAs, which in turn regulated various biological processes. It was shown that specific interactions between muscle-specific transcriptional factors and miRNAs controlled muscle development. Previous studies have reported several miRNAs in miR-23-27-24 cluster regulated myogenic differentiation *in vitro*. However, function of miR-23-27-24 cluster miRNAs *in vivo* has not been elucidated. We conducted a functional analysis of miR-23-27-24 cluster miRNAs in muscle regeneration process. We generated mice lacking miR-23-27-24 cluster miRNAs in a muscle-specific manner using MyoD promoter. Mice were dissected to harvest muscles. Tibilias anterior (TA) muscle was injured using cardiotoxin and harvested 7 days after the injection to evaluate regeneration ability. Primary myoblasts were isolated from muscles and differentiated for 5 days to analyze differentation capacity. We found that significant decreases in body weight, muscle weights as well as muscle cross sectional area from knockout mice. We also confirmed that a decreased cross sectional area of myofibers with centralized nuclei in TA from knockout mice. In addition, myoblast from the knockout mice showed a decrease in fusion index, suggesting inhibited differentiation capacity. These results suggest that miR-23-27-24 cluster miRNAs play an important role in muscle regeneration.

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SESSION II

CENTRAL NERVOUS SYSTEM NEUROPHYSIOLOGY PLASTICITY OF NEURAL FUNCTION

Thursday (September 16, 2021; 11:00 – 13:55)
Thursday (September 16, 2021; 14:20 – 18:05)

Chair:

Prof. JOANNA LEWIN-KOWALIK,
Department of Physiology, Medical University of Silesia, Katowice, Poland

Dr. hab. ADRIAN SMEDOWSKI
Department of Physiology, Medical University of Silesia, Katowice, Poland

DETAILED SESSION II SCHEDULE

Opening lectures (Thursday, September 16; 14:20 – 16:50; *virtual stream B*)

S2.L1 ELECTRICAL COUPLING OF OPTIC NERVE AXONS - A NOVEL MODEL OF GAP JUNCTIONS' INVOLVEMENT IN OPTIC NERVE FUNCTION. **A. Smedowski** (Department of Physiology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland).

S2.L2 BETWEEN RETINA AND BRAIN: PATTERN ELECTRORETINOGRAPHY. **D. Pojda-Wilczek[1], K. Gibinski[2]** ([1]Department of Ophthalmology, Faculty of Medical Sciences in Katowice, Poland, [2]University Clinical Centre, Medical University of Silesia in Katowice, Poland).

S2.L3 THE ROLE OF HUMAN ANTIGEN R (HuR)/ABNORMAL VISUAL SYSTEM-LIKE 1 (ELAVL1) IN AGE-RELATED OCULAR PATHOLOGIES – UPDATING THE PUZZLE. **M. Amadio** (Department of Drug Sciences, Section of Pharmacology, University of Pavia, Pavia, Italy).

S2.L4 NEUROVASCULAR CROSS-TALK IN RETINAL DISEASES – MODELS OF DIABETIC RETINOPATHY. **M. Pietrucha-Dutczak** (Department of Physiology, Faculty of Medical Sciences in Katowice, Medical University of Silesia, Katowice, Poland).

S2.L5 CAN WE REGULATE PERINEURONAL NETS AFTER SPINAL CORD INJURY? AN INSIGHT FROM GENE, PROTEIN EXPRESSION AND WFA LABELING. **M. Skup, K. Grycz, A. Glowacka, B. Ji, O. Gajewska-Wozniak** (Group of Restorative Neurobiology, Nencki Institute of Experimental Biology PAS, Warszaw, Poland).

Oral presentations (Thursday, September 16; 16:55 – 18:05; *virtual stream B*)

S2.L6 MECHANISMS OF OXIDATIVE STRESS IN THE RAT HEART IN A ROTENONE MODEL OF PARKINSON'S DISEASE. **O. Gonchar, O. Klymenko, T. Drevytska, V. Nosar, L. Bratus, I. Mankovska** (Bogomoletz Institute of Physiology, National Academy of Science of Ukraine, Kiev, Ukraine).

S2.L7 INFLUENCE OF BONE MARROW-DERIVED MESENCHYMAL STEM CELL THERAPY ON CCL2, CCL19 AND CCL20 LEVELS IN MINIMALLY CONSCIOUS STATE PATIENTS. **W. Czelejewska, E. Sinderewicz, W. Maksymowicz, K. Jezierska-Wozniak** (Department of Neurosurgery, Laboratory of Regenerative Medicine, School of Medicine, Collegium Medicum, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland).

S2.L8 DROSOPHILA BRAIN REWARD SYSTEM AND POSSIBLE CONSEQUENCES FOR UNDERSTANDING THE HUMAN PLEASURE. **J. Dvoracek[1,3], D. Kodrik[1,2]** ([1]University of South Bohemia, Ceske Budejovice, Czech Republic, [2]Institute of Entomology, Biology Centre, CAS, Ceske Budejovice, Czech Republic; [3]Psychiatric Hospital Cerveny Dvur, Czech Republic).

S2.L9 PHYCHOPHYSIOLOGICAL, HORMONAL, AND RECEPTOR CORRELATIONS OF GENDER AND INDIVIDUAL DIFFERENCES IN PAIN SENSATION. **I. Kvachadze[1], M. Apkhazava[1], M. Tsagareli[1,2]** ([1]Tbilisi State Medical University, Tbilisi, Georgia; [2]Beritashvili Center for Experimental Biomedicine, Tbilisi, Georgia).

Session summary

Poster session (Thursday, September 16; 11:00 – 13:55; *virtual stream D, interactive*)

S2.P1 A NEW LOOK AT THE EXISTENCE OF THE INTERACTION OF THE AMYGDALA WITH THE VISUAL SYSTEM. **K.H. Miryusifova[1], A. Allahverdiyeva[1], N. Huseynova[1], E. Panachova[1]** (Institute of Physiology, Baku, Azerbaijan).

S2.P2 INHIBITION OR STIMULATION OF SHELL NUCLEUS ACCUMBENS CHANGES INTRAVESICAL PRESSURE AND CARDIOVASCULAR PARAMETERS IN WISTAR RATS. **R. De Carvalho[1], B. Antonio[1], N. Dsouki[1], B. Do Vale[1], P. Aronsson[2], L. De Luca Jr[3]., M. Sato[1]** ([1]Department of Morphology and Physiology, Centro Universitario FMABC, Santo Andre, SP, Brazil, [2]Department of Pharmacology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden, [3]Department of Pathology and Physiology, Dentistry School, Sao Paulo State University (UNESP), Araraquara, SP, Brazil).

S2.P3 BIDIRECTIONAL EFFECT OF THE EXTREMELY LOW-FREQUENCY ELECTROMAGNETIC FIELD (50 HZ) ON BDNF LEVEL. **A. Klimek, H. Kletkiewicz, A. Siejka, M. Klimiuk, J. Maliszewska, M. Jankowska, A. Nowakowska, J. Wyszkowska, M. Stankiewicz, J. Rogalska** (Department of Animal Physiology and Neurobiology, Faculty of Biological and Veterinary Sciences, Nicolaus Copernicus University in Torun, Poland).

S2.P4 EARLY-LIFE STRESS AFFECTS PERIPHERAL AND BRAIN RESPONSE TO IMMUNE CHALLENGE IN FEMALE RATS. **A. Solarz, I. Majcher-Maslanka, J. Kryst, A. Chocyk** (Maj Institute of Pharmacology, Polish Academy of Sciences, Department of Pharmacology, Laboratory of Pharmacology and Brain Biostructure, Krakow, Poland).

S2.P5 COMPARATIVE ANALYSIS OF THE INFLUENCE OF EPIPHYSIS AND SUPRACHIASMATIC NUCLEUS OF HYPOTHALAMUS ON VISION FUNCTION. **U. Hashimova, E. Panahova, X. Miryusifova, A. Alahverdiyeva, N. Huseynova** (Institute of Physiology named after A.I. Garayev of ANAS, Baku, Azerbaijan).

S2.P6 CONFIRMATION OF THE INFLUENCE OF AMIGDALA ON THE FUNCTIONS OF THE VISUAL ANALYZER STRUCTURES IN AMIGDALAR EPILEPSY. **A. Alahverdiyeva, U. Hashimova, E. Panahova, X. Miryusifova, N. Huseynova** (Institute of Physiology named after A.I. Garayev of ANAS, Baku, Azerbaijan).

S2.P7 THE ACTIVATED MICROGLIA IN HIPOCCAMPUS AS A CHARACTERISTIC OF STREPTOZOTOCIN INDUCED MODEL OF ALZHEIMER DISEASE IN RATS. **J. Dunacka, G. Swiatek, I. Majkutewicz, P. Matulewicz, B. Grembecka, W. Glac, D. Wrona** (Department of Animal and Human Physiology, University of Gdansk, Faculty of Biology, Gdansk, Poland).

S2.P8 EFFECT OF SEROTONIN, ADRENALINE AND DOPAMINE ON THE FUNCTION OF THE VISUAL SYSTEM STRUCTURES. **N. Huseynova, U. Hashimova, E. Panahova, X. Miryusifova, A. Alahverdiyeva** (Institute of Physiology of ANAS A.I. Garayeva, Baku, Azerbaijan).

S2.P9 INFLUENCE OF CAFFEINE ON THE GENE EXPRESSION OF PROINFLAMMATORY CYTOKINES AND THEIR RECEPTORS IN THE HYPOTHALAMIC-PITUITARY UNIT. **M. Wojcik[1], M. Tomczyk[1], J. Bochenek[1], D. Tomaszewska-Zaremba[1], A. Antushevich[1], A. Krawczynska, A. Herman[2], A.P. Herman[1]** ([1]The Kielanowski Institute of Animal Physiology and Nutrition Polish Academy of Sciences, Poland, [2]Faculty of Health Sciences, Warsaw School of Engineering and Health, Warsaw, Poland).

S2.P10 THE CB_1 RECEPTOR ANTAGONIST REDUCES THE PRESSOR RESPONSE OF ANGIOTENSIN II AND ANGIOTENSIN 1-7 INJECTED INTO PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS (PVN) IN CONSCIOUS NORMOTENSIVE AND HYPERTENSIVE RATS. **K. Minczuk, B. Malinowska** (Medical University of Bialystok, Bialystok, Poland).

S2.P11 THE EFFECT OF NIACIN, VITAMIN B3, ON THE β-AMYLOID-ASSOCIATED PROCESS OF NEURODEGENERATION. **A. Litwiniuk[1], M. Kalisz[1], L. Martynska[1], M. Chmielowska[1], A. Domanska[1,2], W. Bik[1]** ([1]Department of Neuroendocrinology, Centre of Postgraduate Medical Education, Warsaw, Poland, [2]Department of Physiological Sciences, Warsaw University of Life Sciences (SGGW), Warsaw, Poland).

S2.P12 SWIM TRAINING AMELIORATES OXIDATIVE STRESS IN THE SPINAL CORD OF ALS MICE. **K.P. Dzik[1], D.J. Flis[1,2], Z.K. Bytowska[2], M.J. Karnia[1], W. Ziolkowski[2], J.J. Kaczor[1]** ([1]Gdansk University of Physical Education and Sport, Gdansk, Poland, [2]Medical University of Gdansk, Gdansk, Poland).

S2.P13 THE EFFECT OF BENZO[A]PYRENE ON OXIDATIVE STRESS IN CHICKEN EMBRYOS BRAIN. **R. Muchacka, L. Kolodziejczyk, G. Formicki, A. Gren** (Institute of Biology, Pedagogical University of Krakow, Krakow, Poland).

S2.P14 NEUROPHYSIOLOGICAL STUDY OF DISORDER AND RECOVERY OF SPATIAL MEMORY IN AN EXPERIMENTAL MODEL OF ALZHEIMER'S DISEASE. **E. Panakhova, U. Hashimova, K. Javadova, I. Galandarli, Kh. Miryusifova** (Institute of Physiology, Baku, Azerbaijan).

S2.P15 EFFECT OF DIMETHYL FUMARATE ON DISORDERS OF THE OLFACTORY BULB NEUROGENESIS IN THE STREPTOZOTOCIN-INDUCED RAT MODEL OF ALZHEIMER'S DISEASE. **E. Kurowska, I. Majkutewicz, J. Rucinski, D. Myslinska, K. Sawicka, N. Piekarczyk** (University of Gdansk, Department of Animal and Human Physiology, Gdansk, Poland).

S2.P16 EFFECT OF PREBIOTICS SUPPLEMENTATION ON SOCIAL BEHAVIOUR AND PLASMA TUMOR NECROSIS FACTOR-α LEVEL DISTURBANCES IN HIGH- AND LOW-RESPONDERS RATS WITH CENTRAL AMYGDALA HYPERACTIVATION. **J. Rucinski, E. Kurowska, N. Piekarczyk, D. Myslinska, I. Majkutewicz** (University of Gdansk, Department of Animal and Human Physiology, Gdansk, Poland).

S2.P17 IMPROVED MOTOR FUNCTION AS A RESULT OF THE INFLUENCE OF MINOCYCLINE ON MOTOR CORTEX NEURONS IN CORTICAL MODEL OF PHOTOTHROMBOTIC ISCHEMIC STROKE IN RATS. **K. Pawletko[1], A. Grajoszek[1,2], H. Jedrzejowska-Szypulka[1]** ([1]Department of Physiology, School of Medicine in Katowice, Medical University of Silesia, Katowice, Poland, [2]Department of Experimental Medicine Medical University of Silesia, Katowice, Poland).

S2.P18 CHANGES IN THE RESPONSIVENESS OF THE RAT DORSOMEDIAL HYPOTHALAMUS TO DIFFERENT METABOLIC CONDITIONS UNDER HIGH-FAT DIET. **A.M. Sanetra, K. Palus-Chramiec, L. Chrobok, J.S. Jeczmien-Lazur, J.D. Klich, M.H. Lewandowski** (Jagiellonian University in Krakow, Krakow, Poland).

S2.P19 MODULATION OF PAIN IN BRAIN LIMBIC AREAS: ROLE OF OPIOID AND CANNABINOID SYSTEMS. **N. Tsiklauri[1], N. Tsagareli[1,2], I. Kvachadze[2], M. Tsagareli[1,2]** ([1]Beritashvili Center for Experimental Biomedicine, Tbilisi, Georgia; [2]Tbilisi State Medical University, Tbilisi, Georgia).

S2.P20 MINOCYCLINE AFFECTS SPLEEN T AND B LYMPHOCYTES PERCENTAGE IN STREPTOZOTOCIN-INDUCED MODEL OF ALZHEIMER'S DISEASE IN RATS. **G. Swiatek, J. Dunacka, W. Glac, B. Grembecka, I. Majkutewicz, D. Wrona** (Departament of Animal and Human Physiology, Faculty of Biology, University of Gdansk, Gdansk, Poland).

S2.P21 EFFECT OF KETOGENIC DIET ON NEURODEVELOPMENTAL REFLEXES. **W. Kosiek, Z. Rauk, Z. Setkowicz-Janeczko** (Jagiellonian University, Krakow, Poland).

S2.P22 ARCHITECTURE OF A FUNCTIONAL SYSTEM OF THE SAGITTAL BALANCE MAINTAINING. **A. Goncharova** (Kharkiv National Medical University, Kharkiv, Ukraine).

S2.P23 EFFECT OF PROCAINE BLOCKADE OF THE VENTRAL TEGMENTAL AREA ON THETA RHYTHM INDUCED BY PHARMACOLOGICAL ACTIVATION OF THE PEDUNCULOPONTINE NUCLEUS. **A. Piwka, J. Orzel-Gryglewska, A. Walczek** (University of Gdansk, Department of Animal and Human Physiology, Gdansk, Poland).

S2.P24 MET-ENKEPHALIN INVOLVEMENT IN THE PROTECTION OF CEREBELLAR AND FRONTAL CORTEX IN VAGOTOMIZED RAT. **K. Pierzchala-Koziec[1], M. Wieczorek[2], A. Kobrzycka[2], P. Napora[2]** ([1]Department of Animal Physiology and Endocrinology, University of Agriculture in Krakow, Poland, [2]Department of Neurobiology, University of Lodz, Lodz, Poland).

S2.P25 FREQUENCY-DEPENDENT PLASTICITY OF SPONTANEOUS ACTION POTENTIALS WITHIN IDENTIFIED LYMNAEA'S NEURONS. **Z. Seval, A.V. Sidorov** (Belarusian State University, Minsk, Belarus).

S2.L1

ELECTRICAL COUPLING OF OPTIC NERVE AXONS – A NOVEL MODEL OF GAP JUNCTIONS' INVOLVEMENT IN OPTIC NERVE FUNCTION

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Retinal neurons are considered to be part of the central nervous system, resulting in lack of their spontaneous regeneration in response to damage. Glaucoma, a progressive optic neuropathy, is thought to be the main cause of severe visual impairment or permanent vision loss. Connexins are important channel proteins that form gap junctions connecting neighbor cells, including neurons. Despite of their undoubted importance in cell homeostasis, in neurons they may promote spreading of apoptotic insult, leading to secondary neurodegeneration. The presence of previously unknown GJs (electrical synapses) between optic nerve (ON) axons, which directly connect axons within bundles in the ON head potentially accelerates signal transduction along the ON and allows modulation of the signal passage from the retina to the brain. By creating crosswise conduction within bundles of the ON, it could possibly allow bypass of local damage within axons. We hypothesize that density and conductivity of these synapses may be crucial with respect to the susceptibility of the ON to having different impairments develop into symptomatic pathologies. We showed that transient chemical blocking of ON electrical synapses slows down visual signal conduction. In the case of axonal structural or functional impairment, the signal could possibly be passed crosswise *via* GJs to the neighboring axon; thus, the preservation of the syncytial structure of the ON can prevent the blockage of visual information propagation. This finding could have substantial implications for understanding of the pathogenesis of various optic neuropathies and identifies a new potential target for a therapeutic approach.

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S2.L2

BETWEEN RETINA AND BRAIN: PATTERN ELECTRORETINOGRAPHY

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Visual pathways start off with a retina. Retinal ganglion cells (RGC) are the last level of retinal cells. T heirs neurits form long optic nerves and transmit action potential from the eyes to the next station, lateral geniculate nucleus. Pattern electroretinography (PERG) is unique examination of RGC function. Two main waves P50 (positive) and N95 (negative) of PERG reflect function of central and pericentral RGC, respectively. In this way early localization of visual disturbances origin is possible. Abnormalities of P50 wave are attributed to macular diseases while incorrect N95 wave points diagnostic procedures at optic neuropathy. Unfortunately, the procedure is not simple. It requires not only expensive equipment and single use electrodes but also patient's good cooperation and experienced staff. Much easier is to get photopic negative response (PhNR ERG), the new modification of full field flash electroretinography. Abnormal PhNR indicates optic neuropathy but the clinical use of this response is still under consideration.

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S2.L3

THE ROLE OF HUMAN ANTIGEN R (HUR)/EMBRYONIC LETHAL, ABNORMAL VISUAL SYSTEM-LIKE 1 (ELAVL1) IN AGE-RELATED OCULAR PATHOLOGIES - UPDATING THE PUZZLE

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Increasing evidence suggests that loss of RNA homeostasis is a central feature in many pathological states, including eye diseases. Gene expression is controlled at post-transcriptional level by several factors (e.g. RNA-binding proteins, coding and non-coding RNAs) playing in concert to determine the fate of a given transcript. Among mammalian RNA-binding proteins, the ELAVL (embryonic lethal, abnormal visual system-like) family is a masterpiece of gene expression regulation by affecting RNA metabolism from splicing to translation. The ubiquitous member of this family, HuR/ELAVL1, controls the expression of genes with a key function in physio and pathological contexts. Alterations in HuR/ELAVL1 levels and/or function have been found in some cellular and animal models of age-related ocular diseases. Although the picture is far to be completed, intriguing findings suggest HuR/ELAVL1 involvement in the aetiopathology and its potentiality as a therapeutic target in eye diseases.

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S2.L4

NEUROVASCULAR CROSS-TALK IN RETINAL DISEASES – MODELS OF DIABETIC RETINOPATHY

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Diabetic retinopathy (DR) is one of the most common complications of diabetes leading to vision impairment. Among patients with diabetes, the prevalence of DR is 35.4% and is higher in those with type 1, compared with type 2 diabetes. A high glucose level alters several cellular functions, such as intracellular calcium level, NADPH oxidase activity and the signalling of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). Hyperglycaemia stimulates the production of free radicals and reactive oxygen species (ROS) which are the main cause of oxidative stress leading to retinal vasculature damage. Vascular pathology in DR is characterised by alterations in the integrity of retinal capillaries and their occlusion, vascular leakage, subsequent neovascularization, and retinal haemorrhages. Diabetes in a rodent model is associated with an elevated apoptosis ratio in the retina, decreased numbers of ganglion cells (RGC) and a reduction in retinal nerve fiber layer thickness. Furthermore, the expression of intermediate filament glial fibrillary acid protein (GFAP) increases in Muller cells, which is a common marker for neural degeneration. It is very difficult to point out only one factor causing RGC death in DR. Many related mechanisms correspond to RGC loss, such as glutamate accumulation and toxicity, reduced expression of neurotrophic factors, signalling pathway impairment and increased production of proinflammatory cytokines. There is currently a growing body of evidence indicating that the damage of RGC appears before vascular changes and clinical signs of DR. Moreover, RGC apoptosis is preceded by synaptic neurodegeneration and dendritic retraction of these cells. Because dendritic abnormalities occur prior to RGC loss, identifying dendrite pathology can be treated as an early sign of neurodegeneration. Various animal models of diabetes have been established to improve understanding of the pathophysiology in diabetes and its complications such as nephropathy, retinopathy and neuropathy. Zucker diabetic fatty rats, BioBreeding Diabetes-Prone rat, streptozotocin rats/mouse or nonobese diabetic mouse are commonly used diabetic animal models. These animal models are of great importance in basic as well as in preclinical research. It is not only helping in understanding the disease mechanism of diabetes but also in evaluating new therapies with curative potential.

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S2.L5

CAN WE REGULATE PERINEURONAL NETS AFTER SPINAL CORD INJURY? AN INSIGHT FROM GENE, PROTEIN EXPRESSION AND WISTERIA FLORIBUNDA AGGLUTININ (WFA) LABELING

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In the adult nervous system, extracellular matrix (ECM) may be both dispersed in the neuropil and well-organized in a form of lattice-like neuronal envelopes, called perineuronal nets (PNNs). PNNs are composed of hyaluronan which creates a scaffold and of aggregating chondroitin sulfate proteoglycans (CSPGs) which are essential for formation and stabilization of PNN structures. In the spinal cord the most elaborated PNNs encapsulate motoneurons (MNs) by unsheathing soma and proximal parts of dendrites, forming a "perisynaptic barrier" controlling neural communication. The peri-motoneuronal net may be of essential importance for stabilization of neuronal connections in conditions of prolonged, self-sustained activity, characterizing α-MNs. Injury to the spinal cord reveals the other face of CSPGs: their overexpression in the scar contributes to pathology, by limiting fiber regrowth from the site of injury and impeding recovery of motor functions. The attempts to stimulate neuronal circuits to grow fibers and reorganize them assume processes loosening or decomposing the expanded web. We shall review our studies which demonstrated that moderate, long-term locomotor training that activates the entire spinal network is capable to enrich MN innervation, and improve locomotor function after spinal cord transection (SCT) (Macias *et al*., 2009, Skup *et al*., 2012; Gajewska-Wozniak *et al*., in prep.). In search for the molecular underpinnings of those effects we asked whether locomotor training can influence CSPGs metabolism at the protein level, and the structure and distribution of the PNNs around MNs after SCT. We shall demonstrate that SCT at the thoracic level leads to (1) a significant increase of mRNA levels and to a lesser extent protein levels of neurocan, phosphacan, brevican, aggrecan, and NG2 but not Hapln1 protein linking the net, in thoracic and to a lesser extent in lumbar segments of the spinal cord at subacute (2-nd week) and chronic (5 weeks) postinjury; (2) a decrease in their transcripts in MNs located in the lower lumbar segments, at 2 weeks post-injury. Surprisingly, in MNs, a denervation-elicited suppression of transcription was not reflected by the levels of CSPGs proteins, which were maintained at control level around these cells. We shall show also that locomotor training, which was not effective in modulating CSPGs central core protein levels around MNs, was a stimulus to down-regulate markedly a density of PNNs which was significantly increased after SCT. These results point to the possibility that training applied to spinal animals leads to modification of PNNs density through modifying chondroitin sulfate glycosaminoglycan side chains of central domains. To verify this possibility studies on enzymes catalyzing glycosamino-glycan assembly are needed.

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S2.L6

MECHANISMS OF OXIDATIVE STRESS IN THE RAT HEART IN A ROTENONE MODEL OF PARKINSON'S DISEASE

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Oxidative stress (OS) is caused by an imbalance in the redox state of the cell either by overproduction of reactive oxygen species (ROS), predominantly in dysfunctional mitochondria, or by impairment of the antioxidant systems. Accumulating evidence suggest that OS may play a significant role in pathogenesis of neurodegenerative diseases including Parkinson's disease (PD). In rodents, rotenone administration reproduces several features of PD, including nigrostriatal dopaminergic degeneration and typical alpha-synuclein-positive intracytoplasmic inclusions in the brain. Whereas evidence for increased ROS production and impaired antioxidant defenses in PD brain is reasonably strong, relatively few studies to date have established the mechanisms of OS in other organs and tissues, in particular, in PD heart. At the same time, PD is a well-recognized risk factor for developing heart failure, and cardiovascular complications are the important cause of PD-related morbidity and mortality. The identification of a number of PD-related genes that are strongly associated with mitochondrial function (*PINK 1, DJ-1, Parkin*) further adds weight that mitochondrial dysfunction with resultant OS is a primary event in PD pathogenesis. This study was therefore designed to investigate the biochemical and genetic mechanisms of OS developing in the rat heart in a rotenone model of PD. It was found that prolonged systemic subcutaneously rotenone administration significantly increased the H_2O_2 production, protein oxidative modification and the intensity of lipid peroxidation in rat heart mitochondria. Rotenone administration caused a significant increase in the MnSOD activity with concomitant decrease in the activity of GPx ($P < 0.05$). Simultaneously, we have found an increase in GSSG level, a decrease in GSH content, and at that the ratio of reduced to oxidized form was 2 times less than the control value ($P < 0.05$). These changes were accompanied by an increase in MnSOD and a decrease in DJ-1 protein synthesis. It was also established *DJ-1* gene deficiency, whereas the level of *PARK2* mRNA was increased ($P < 0.05$). In addition, we studied the hypoxia inducible factor (HIF) gene expression, which regulates transcriptional activation of several genes responsive for oxygen transport, glycolytic metabolism, angiogenesis, and apoptosis. Therefore, HIF activation can serve as an indicator of mitochondrial homeostasis. It was found that the *HIF* (subunits 1;2;3-α) mRNA levels in the rat heart were reduced compared to the control value ($P < 0.05$). So, increased ROS production and impaired antioxidant defenses in the heart under rotenone administration could result from the established *DJ-1* gene and DJ-1 protein deficiency. Moreover, we can assume that a decrease in HIFs gene activation may have an effect on mitochondrial functional state as well.

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S2.L7

INFLUENCE OF BONE MARROW-DERIVED MESENCHYMAL STEM CELL THERAPY ON CCL2, CCL19 AND CCL20 LEVELS IN MINIMALLY CONSCIOUS STATE PATIENTS

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Minimally conscious state (MCS) is a severe disturbance of consciousness, in which minimal behavioral evidence of self or environmental awareness is demonstrated. MCS may arise from traumatic brain injury or structural brain lesions, which are often accompanied by an excessive release of inflammatory factors by activated microglia and astrocytes, leading to neuroinflammation. Lack of the effective therapy of MCS has highlighted the need to look for alternative treatment methods, such as mesenchymal stem cells (MSC) therapy. These cells display high secretory activity and have been shown to possess immunomodulatory properties which can modify neuroinflammation. Therefore, the aim of the study was to assess the impact of bone marrow-derived mesenchymal stem cell (BM-MSC) administration on chosen chemokines - CCL2, CCL19 and CCL20 - levels in CSF and plasma of MCS patients. Nine patients aged 19–45 years, remaining in MCS for 3–14 months, were given BM-MSC three times at two-month intervals. The samples of CSF and plasma were collected before the treatment (control) and after the first and second BM-MSC administration. Relative expression levels of selected chemokines were determined by dot-blot method using Human XL Cytokine Array Kit. Obtained data revealed alterations in chemokine contents both in plasma and CSF after BM-MSC administration. The increased level of CCL2 and decreased levels of CCL19 and CCL20 were observed in CSF after cell administration, compared to the control values. In plasma, only CCL19 level was lower after the therapy. Our data suggest that BM-MSC treatment may be involved in the modulation of chemokine signaling in MCS patients.

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S2.L8

DROSOPHILA BRAIN REWARD SYSTEM AND POSSIBLE CONSEQUENCES FOR UNDERSTANDING THE HUMAN PLEASURE

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Disorders of the brain pleasure system are one of the promising topics of interdisciplinary study. The core problem of the disorder (dysregulation of the brain reward system) is being investigated by neuroscience in various animal models. The fly *Drosophila melanogaster* is a common laboratory model for studying the principles of neural network functioning. When studying the brain reward system, Drosophila is very attractive model because its relatively well-arranged brain and precisely described genome. Moreover, it can be beneficial that using Drosophila brain we do not encounter so many complex concepts with unlimited meanings (e.g. emotions, feelings, consciousness). The main problem in interpreting the study of the human brain is the complexity and ambiguity of concepts and functions. Until recently, 'pleasure' was perceived as a function of the brain of mammals and was seen as a manifestation of higher brain functions (as part of emotional circuits) or as a manifestation of complicated neural networks. In our contribution, we first clarify the current knowledge of the Drosophila reward system, emphasizing that 1) the brain regions involved in associative learning and reward functions are surprisingly complex, although the fly is a relatively simple and short-lived organism, 2) its brain almost certainly has a system that creates motivational drive (similar to the 'wanting'component of reward function in higher animals), 3) there are indications of the possible presence of the hedonic component of reward or its evolutionary precursor. Further, we mention several possible inspiring moments for understanding the human brain system, and possibly for general modeling of the reward function. Reward brain function appears to be 1) based hierarchically; 2) not organized, but operating rather with functions distributed among other brain networks; 3) its individual parts can be independent of each other and work in parallel; 4) reinforcement processing of a specific stimulus with the desired behavior can be rather multilevel. This way of understanding the pleasure system would also result in another comprehension of its disorders: e.g. 'addiction' could not be perceived only as a distortion of the mesolimbic dopaminergic system or hedonic systems of endogenous opioids/endocannabinoids, but also as a generalized disorder from cortical to cellular level, with the need for corresponding generalized interventions.

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S2.L9

PHYCHOPHYSIOLOGICAL, HORMONAL, AND RECEPTOR CORRELATIONS OF GENDER AND INDIVIDUAL DIFFERENCES IN PAIN SENSATION

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Most psychophysiological studies of experimentally induced pain revealed increase pain sensation in females compared with males, as well as variations in pain sensation over different phases of the ovarian-menstrual cycle (OMC) in females. The largest group of receptor proteins that deal with thermal and mechanical pain sensation is the subfamily of the transient receptor potential (TRP) channels and its most studied representative TRPV1 - polymodal sensory transducer activated by a diverse variety of stimuli, including heat (>40°C), mechanical pressure, acids, vanilloids (e.g., capsaicin), gingerol and endo-cannabinoids. Among the structures of the endogenous opioid system, a major player is the mu-opioid receptor (MOR), activated in the process of interaction with endogenous or exogenous opiates. Our results revealed that males show significantly higher heat pain threshold and mechanical pain tolerance than females in both phases of the OMC. Mechanical pain threshold, mechanical pressure threshold, cold pain threshold, and heat sensation threshold are insignificantly higher in males than in females in both the follicular phase and luteal phase of the OMC. The luteal phase of the OMC compared with follicular, females revealed significantly lower degrees of heat and mechanical pain thresholds, also mechanical pain tolerance, as well as nonsignificant lower degrees of cold pain and heat sensation thresholds. In males, degrees of heat, cold, mechanical pain thresholds, mechanical pain tolerance significantly positively correlate with free testosterone and MOR levels, significantly negatively - with TRPV1 levels. In females significantly positive correlation revealed between degrees of mechanical pressure, pain thresholds and tolerance and the follicular stimulating hormone (FSH) level in follicular phase of the OMC, as well as progesterone level in the luteal phase of the OMC; significantly positive correlation revealed between cold pain threshold degree and MOR level in both phases of the OMC; also a significant positive correlation between heat pain interphase decrease degree and TRPV1 interphase increase degree, as well as progesterone level in the luteal phase of the OMC. Thus, there is a significant correlation between the threshold of thermal and mechanical pain in men with psychological indicators, and the absence of such correlation in women is important for the development of gender and personalized methods of pain relief and the role of individual psychophysiological characteristics for perception and assessment of pain.

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S2.P1

A NEW LOOK AT THE EXISTENCE OF THE INTERACTION OF THE AMYGDALA WITH THE VISUAL SYSTEM

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We showed it for the first time in electrophysiological experiments that amygdala has a regulatory effect on the perceptive function of the visual system. Amygdala takes part in the regulation of visually controlled behavior and carries out the identification and discrimination of the visual image. The amygdala is known to be involved in identifying not only anxiety and fear, but also pleasure. It has been established that amygdala multidirectional effect on the visual system structures along the parvo- and magnocellular pathways are reconsidered. Reliable data obtained are a prerequisite for revising existing views of ‘independence’ and ‘parallelism’ of these pathways and is a new approach to understanding visual perception. These pathways are opposite and reciprocal to each other. These findings regarding the important regulatory multidirectional role of Amygdala in brain cognitive function have been confirmed in many papers by other scientists. The interneurons in the lateral amygdala and basal amygdala are physiologically distinct populations and suggest they may have differing roles during associative learning: basolateral amygdala contributes to a variety of behavioral patterns. Jhaveri *et al*. established the evidence for newly generated interneurons in the basolateral amygdala of adult mice 2020. It was found that the amygdala has a control effect on the visual system function.

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S2.P2

INHIBITION OR STIMULATION OF SHELL NUCLEUS ACCUMBENS CHANGES INTRAVESICAL PRESSURE AND CARDIOVASCULAR PARAMETERS IN WISTAR RATS

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Neuroanatomical studies have shown that rostral regions of the dorsomedial shell nucleus accumbens (NAcc) project to the lateral preoptic area (LPA). Injections of angiotensin-(1-7) into the LPA evokes a huge increase in intravesical pressure (IP). It is still unknown whether the shell NAcc has any role in micturition control or not. This study focused to investigate the possible involvement of shell NAcc in the micturition control. Adult male Wistar rats (~450 g) with stainless steel guide cannulas implanted bilaterally in the shell NAcc 7 days prior to the experiments were anesthetized with 2% isoflurane in 100% O_2 and subjected to cannulation of the femoral artery and vein for mean arterial pressure (MAP) and heart rate recordings (HR) and infusion of drugs, respectively. The urinary bladder was cannulated for IP measurement. A miniaturized Doppler flow probe was placed around the left renal arterial for renal blood flow (RBF) recordings. After the baseline MAP, HR, IP and RBF recordings for 15 min, GABA (50 mM, 1 µL) or L-glutamate (50 mM, 1 µL) or saline (vehicle, 1 µL) injections were made bilaterally into the shell NAcc and the variables were measured for additional 30 min. Data are as mean ± SEM and submitted to Student's t test ($P < 0.05$). Bilateral injections of GABA into the shell NAcc (bilateral) significantly increased IP (168 ± 11% vs. 5 ± 3%, saline) and renal conductance (RC, 124.67 ± 23.51% vs. 5.45 ± 0.90%, saline), whilst a significant fall in MAP (–64 ± 2 mmHg vs. –2 ± 2 mmHg, saline) and HR (–92 ± 14 bpm vs. 1 ± 2 bpm, saline) were observed compared to saline injections. Bilateral injections of L-glutamate into the shell NAcc significantly increased IP (132 ± 18% vs. 5 ± 3%, saline), and MAP (13 ± 3 mmHg vs. –2 ± 2 mmHg, saline), whereas a significant decrease in RC (–7.39 ± 0.58% vs. 5.45 ± 0.90%, saline) and no changes in HR (13 ± 6 bpm vs. 1 ± 2 bpm, saline) were observed compared to saline injections. Conclusion: The shell NAcc participates in the neural circuitry involved in micturition control and plays a possible tonic role in the arterial pressure regulation.

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S2.P3

BIDIRECTIONAL EFFECT OF THE EXTREMELY LOW-FREQUENCY ELECTROMAGNETIC FIELD (50 HZ) ON BRAIN-DERIVED NEUROTROPHIC FACTOR LEVEL

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The impact of the extremely low-frequency electromagnetic field (ELF-EMF) on living organisms is still intensively and widely evaluated. Previous reports paid attention to its harmful effects such as sleep and mental disorders. However, ELF-EMFs are increasingly used in therapy of e.g. brain injuries. Some authors described ELF-EMF as a mild stress factor. Depending on the value of magnetic induction, the repeated ELF-EMF exposure 'turns on' different intracellular mechanisms: compensatory or deleterious ones. As the stress hormones (mainly corticosterone and noradrenaline) are known to modulate hippocampal function and may modify the plasticity processes in this area, we decided to determine the ELF-EMF-induced changes in BDNF (brain derived neurotrophic factor) level in hippocampus. Wistar rats were divided into three groups: control and exposed to 1 or 7 mT ELF-EMF. Rats were exposed to ELF-EMF 1 hour a day for 7 days. Control animals were subjected to the same experimental procedure as the exposed groups, except ELF-EMF exposure. The procedure was repeated three times with three week interval between exposures. After the end of each exposure the part of rats was sacrificed and brains were collected. The level of BDNF in hippocampus was determined. Our results showed that low-dose (1 mT) ELF-EMF increased the expression of BDNF, while the high dose (7 mT) ELF-MF reduced the expression of mRNA of the protein. Thus we concluded that the ELF-EMF effect on brain plasticity is bidirectional and depends on the value of magnetic induction of the field.

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S2.P4

EARLY-LIFE STRESS AFFECTS PERIPHERAL AND BRAIN RESPONSE TO IMMUNE CHALLENGE IN FEMALE RATS

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Early-life stress (ELS) is considered as a risk factor for mental and neurodegenerative disorders. Nowadays coexistence of blood-brain barrier (BBB) disturbances and inflammation appears to play an important role in the etiology, development and progression of those diseases. Data on females are still insufficient in this regard, so in our study, we focused on the consequences of ELS in female rats during preadolescence and adulthood periods. Specifically, we examined whether ELS, based on the maternal separation (MS) paradigm, can condition female subjects to other environmental factors later in life, such as an infection. To mimic this state, a single administration of bacterial lipopolysaccharide (LPS) was used. 24 h later, BBB permeability in the medial prefrontal cortex (mPFC) and hippocampus (Hp) was evaluated using fluorescent tracer and mRNA expression of tight junctions proteins (TJPs) and adhesion molecules representatives, *Cldn5*,*Ocld* and *Icam-1 was* measured, respectively. Moreover, serum levels of proinflammatory cytokines were studied and also their mRNA expression in the mPFC and Hp together with microglia markers (such as: *Aif1* and *Itgam*) and toll-like receptor 4 (*Tlr4*), representing the first line of defense against infections. Administration of LPS induced proinflammatory response on the periphery and in consequence increased BBB permeability, TJPs and *Icam-1* expression in the mPFC and Hp. Moreover, LPS enhanced mRNA expression of *Tlr4*, microglial markers and proinflammatory cytokines. Interestingly, the magnitude of LPS-induced effects was blunted in females previously subjected to MS. Within the studied brain regions, this was manifested mainly through suppressed mRNA expression of Icam-1, Tlr4, microglial markers and proinflammatory cytokines. However, those changes were more pronounced in adulthood than in preadolescence period. Particularly, tumor necrosis factor-α serum levels and the mRNA level of *Tlr4* and *Aif1* in the Hp were significantly lower in MS adult females. Concurrently, MS enhanced LPS-induced upregulation of *TJPs* expression in the Hp. These findings indicate that previous ELS experience may trigger adaptive response counteracting the impact of acute immune challenge in females.

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S2.P5

COMPARATIVE ANALYSIS OF THE INFLUENCE OF EPIPHYSIS AND SUPRACHIASMATIC NUCLEUS OF HYPOTHALAMUS ON VISION FUNCTION

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The main goal of the study was comparative analysis of the influence interaction suprachiasmatic nucleus of the hypothalamus and the pineal gland on the function of the structures of the visual analyzer. The experiments were carried out of rabbits. The electrophysiological parameters of the evoked potentials in the studied structures of the visual analyzer (retina, colliculus superior, visual cortex) were comparatively analyzed against the background of stimulation of the suprachiasmatic nucleus of the hypothalamus and pineal gland. On the basis of the obtained experimental results, it was effects influences of the suprachiasmatic nucleus and the pineal gland on the electrophysiological parameters of the evoked potentials of the structures of thge visual analyzer are opposite to each other.

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S2.P6

CONFIRMATION OF THE INFLUENCE OF AMIGDALA ON THE FUNCTIONS OF THE VISUAL ANALYZER STRUCTURES IN AMIGDALAR EPILEPSY

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As a result of the studies, it was found that the introduction of a solution of penicillin into the amygdala led to the development of prolonged convulsive activity. Ten minutes after the vision in elektroensofaloqramma shows epileptiform discharces. Epileptiform activity encompassed all structures of the brain. Such elektroensofaloqramma changes were recorded within 3–4 hours. The seizures reached a peak point within an hour, followed by a definite dynamics of epileptiform waves. Penicillin caused the appearance of generalized peaks in all structures of the visual analyzer. Sometimes were observed myoclonic seizures, rapidly developing into an epileptic seizure. elektroensofaloqramma analysis showed that epileptic activity first manifests itself in the amygdala, then in the visual cortex, the upper tubercles of the quadruple. Probably, the manifestation of such a sequence is associated with morphofunctional connections between these structures.

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S2.P7

THE ACTIVATED MICROGLIA IN HIPOCCAMPUS AS A CHARACTERISTIC OF STREPTOZOTOCIN-INDUCED MODEL OF ALZHEIMER DISEASE IN RATS

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Streptozotocin (STZ) induced model of Alzheimer disease (sAD) in rats is an equivalent of sporadic AD in humans. In the course of this disease appears many pathological features for example neurodegeneration of hippocampus. This pathology may be caused by neuroinflammation. In turn, it is effects activation of microglia. Wistar rats (N = 5) induced sporadic form of Alzheimer disease by intracerebroventricular (i.c.v.) microinjection of STZ (3 mg/kg) to check the level of microglia activation in this model 90 days after induction of sAD. The rats (N = 6) from control group (VEH) received a citrate buffer. Activation of microglia was checked using primary antibodies anti-macrophages/monocytes bound by secondary antibodies with fluorescent marker. Next using fluorescence microscope and a computer program Axio Vision photographed parts of hippocampus and counted number of activated cells with the use of calibrated frame. Analysis (Mann-Whitney test) of activation microglia in different parts of the hippocampus shows statistically significant differences in CA1 ($p < 0.01$; STZ $6.8 \pm 3.27/0.1$ mm^2; VEH $0 \pm 0/0$, 1 mm^2), CA2 ($p < 0.05$; STZ $4.8 \pm 1.92/0.1$ mm^2; VEH $0 \pm 0/0.1$ mm^2), CA3 ($p < 0.01$; STZ $4 \pm 1.73/0.1$ mm^2; VEH $0 \pm 0/0.1$ mm^2), DG ($p < 0.05$; STZ $7.25 \pm 3.6/0.1$ mm^2; VEH $0 \pm 0/0.1$ mm^2) parts of hippocampus. Activation of microglia was observed only in rats with sAD. All date are presented as mean ± SD. Conclusion: Activation of microglia in hippocampus only in animals with sporadic Alzheimer disease, suggest the increased neuroinflammatory response is presence even 3 months after induction of AD and may be the reason of behavioural disturbances.

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S2.P8

EFFECT OF SEROTONIN, ADRENALINE AND DOPAMINE ON THE FUNCTION OF THE VISUAL SYSTEM STRUCTURES

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It was revealed that the influence of the components of the monoaminergic system on the function of the structures of the visual analyzer is different. Thus, serotonin and dopamine have a positive effect on retinal function. However, the effect of dopamine was reflected in the 'a' wave of the electroretinogram, but did not affect the 'b' wave. The effect of adrenaline on the electrical activity of the investigated structures was negative. The effects of serotonin, adrenaline, and dopamine on electrical activity in the visual cortex similarly affect on the retina. All three components negatively influence the function of the superior colliculus.

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S2.P9

INFLUENCE OF CAFFEINE ON THE GENE EXPRESSION OF PROINFLAMMATORY CYTOKINES AND THEIR RECEPTORS IN THE HYPOTHALAMIC-PITUITARY UNIT

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Inflammatory cytokines are considered to be important mediators modulating neuroendocrine system at the level of the brain. The origin of these cytokines are differentiated. Some of them reach the brain parenchyma from periphery or are produced in the cells of choroid plexus; however these cytokines and their corresponding receptors are also expressed in the hypothalamic and pituitary cells both during homeostasis milieu and inflammation. Caffeine is one of the most widely consumed pharmacologically active substances which receptors are also widespread in the hypothalamic-pituitary unit. There are reports suggesting that caffeine may influence secretion of pituitary hormones however, this mechanism is not fully elucidated. The aim of the study was to determine the influence of caffeine on the expression of proinflammatory cytokines and their receptors in the hypothalamus and pituitary. The study was performed on sheep model. The experiment was carried out on 12 ewes intravenously injected with caffeine at the dose of 40 mg/kg (n = 6) or saline (n = 6). Animals were euthanized 3 hours after caffeine or saline injection. Hypothalamic tissue and anterior pituitary (AP) was dissected. The gene expression of cytokines such as: interleukin (IL)-1, IL-6 and tumor necrosis factor alpha (TNF-α) and their receptors IL-1R1, IL-1R2, IL-6R, gp-130, TNFR1, TNFR2 was determined. It was found that caffeine stimulated the gene expression of IL-6 both in the hypothalamus and pituitary, on the other hand caffeine suppressed the amount of TNF mRNA in these tissues. The effect of caffeine on IL-1β mRNA expression was differentiated, caffeine lowered the level of IL-1β in the AP, whereas it did not influence this mRNA level in the hypothalamus. Caffeine reduced the gene expression of TNFR1 and TNFR2 both in the hypothalamus and AP, but increased the amount of IL-1R2 mRNA in these tissues. Our study showed that caffeine exerted both stimulatory and suppressory effect on the gene expression of proinflammatory cytokines and some of these cytokines receptors in the hypothalamic-pituitary unit. This suggests that one of the mechanisms *via* caffeine influence the secretory activity of the hypothalamic-pituitary unit may be modulation of proinflammatory cytokines synthesis in this brain tissues.

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S2.P10

THE CB1 RECEPTOR ANTAGONIST REDUCES THE PRESSOR RESPONSE OF ANGIOTENSIN II AND ANGIOTENSIN 1-7 INJECTED INTO PARAVENTRICULAR NUCLEUS OF THE HYPOTHALAMUS IN CONSCIOUS NORMOTENSIVE RATS

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Previous experiments on anesthetized normotensive rats, have shown that intravenous injection of angiotensin II (Ang II) AT1 receptor antagonist losartan reverses the pressor response resulting from stimulation of cannabinoid CB_1 receptors (CB_1-R) in the paraventricular nucleus of the hypothalamus (PVN). The aim of this study was to determine the interaction between CB1-R and Ang II as well as Ang 1-7 in the regulation of blood pressure in conscious rats with spontaneous hypertension (SHR) and their normotensive control - Wistar Kyoto (WKY). All compounds were administered into the PVN through a stainless steel cannula and blood pressure was measured using noninvasive tail-cuff method (for a verification of normo- and hypertensive rats) and from the carotid artery (main experiments). Basal systolic (SBP), diastolic (DBP) and mean (MAP) pressure were approximately 60% lower in WKY compared to SHR. Angiotensin II (0.3 nmol/rat) and angiotensin 1-7 (0.3 nmol/rat) increased blood pressure both in WKY and SHR. The pressor effects of both compounds were stronger in SHR than in WKY. The increases in blood pressure stimulated by Ang II were inhibited by the antagonists of AT1 and AT2 receptors (losartan (8 nmol/rat) and PD123319 (10 nmol/rat), respectively) and those induced by Ang 1-7 were reduced by A779 (3 nmol/rat; the antagonist of Mas receptors) both in WKY and SHR. The CB_1-R antagonist AM251 (0.03 μmol/rat) significantly inhibited the effect of Ang II, and reversed the pressure response of Ang 1-7 in SHR and WKY. None of the solvents (DMSO, NaCl) nor antagonists caused a significant effect on blood pressure on its own. In conclusion, the CB_1 receptors in the PVN reduce the pressor response of Ang II and Ang 1-7 (elicited by the activation of AT1, AT2 and Mas receptors, respectively) in conscious normotensive and hypertensive rats.

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S2.P11

THE EFFECT OF NIACIN, VITAMIN B3, ON THE BETA-AMYLOID-ASSOCIATED PROCESS OF NEURODEGENERATION

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Alzheimer's disease (AD) is the most common form of dementia. Mechanisms of synaptic damage in AD are related to the neurotoxic effects of soluble forms of β-amyloid oligomers (AβO). AβOs attach to the synapses, inhibit synaptic plasticity, damage synaptic cytoskeletal proteins, and ultimately leads to synapse loss. The current direction of research is focused on identifying factors that protect neurons from the toxic effects of AβO. Because niacin is associated with energy metabolism, mitochondrial function, cell death, and aging, it could affect Aβ-dependent neurodegeneration. We aimed to assess the effect of two different forms of niacin: nicotinic acid (NA) and nicotinamide (N) on the Aβ-dependent neurodegeneration process. The second aim was to investigate whether NA and N could stimulate the neuroprotective effects of astrocytes. Experiments were performed on human cell lines: SH-SY5Y (neuroblastoma) and NHA astrocytes. The SH-SY5Y cells were differentiated for 10 days. 24 hours before the end of the experiment, the SH-SY5Y cells were incubated with CM (conditioned medium) derived from NHA astrocyte cultures: the control (CM), and treated with NA (CM-NA) or N (CM-N). After 1 h preincubation with CM, CM-NA or CM-N differentiated SH-SY5Y cells were incubated for another 24 h with Aβ (5 μM). The MTT test was used to assess the cytotoxicity of the tested factors. The expression level of *PSD95* (postsynaptic density protein 95, which plays an important role in synaptic plasticity) mRNA in neurons was assessed by qRT-PCR. Microscopic observation of autophagolysosomes (acidic vesicular organelles, AVO) in neurons was also performed. 24 hours incubation with Aβ decreased the viability of SH-SY5Y cells ($p < 0.001$). Incubation of SH-SY5Y cells with CM reduced the cytotoxicity of Aβ relative to control ($p < 0.02$). This effect increased significantly after the addition of CM-NA or CM-N ($p < 0.05$). We also observed that Aβ decreased the expression level of *PSD95* mRNA ($p < 0.01$) compared to the control, thus reducing the synaptic activity of differentiated SH-SY5Y cells. Concomitant use of Aβ with NA abrogated the synaptotoxicity of Aβ ($p < 0.01$). Microscopic examination showed that AVO formation was increased in Aβ treated SH-SY5Y cells ($p < 0.01$). AVO formation was antagonized by adding CM-NA CM-N ($p < 0.05$). CM from astrocyte cultures protects neurons from the toxic effects of Aβ. The use of two different forms of niacin: CM-NA or CM-N enhances this effect.

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S2.P12

SWIM TRAINING AMELIORATES OXIDATIVE STRESS IN THE SPINAL CORD OF AMYOTROPHIC LATERAL SCLEROSIS MICE

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Amyotrophic lateral sclerosis (ALS) is an incurable, neurodegenerative disease causing muscle atrophy. In some cases, ALS causes behavioral disturbances and cognitive dysfunction. Swimming has revealed a neuroprotective influence on the motor neurons in the SOD1-G93A mice model of ALS. In the present study, transgenic male mice overexpressing human SOD1 with G93A substitution, with wild-type B6SJL mice as controls were used. ALS mice were analyzed before ALS onset (10th week of life), at ALS 1 onset (first symptoms of the disease, ALS 1 onset and ALS 1 onset SWIM), and at terminal ALS (last stage of the disease, ALS TER, and ALS TER SWIM), and compared with wild-type mice. Swim training was applied 5 times per week for 30 minutes. The spinal cord was analyzed for the enzymes activities and oxidative stress markers. The present study identified the metabolic changes in the spinal cord already at the pre-symptomatic stage of the disease with the shift towards glycolytic processes at the terminal stage of ALS. Moreover, in the current study, we recognized the pathophysiological alteration resulting in a higher glutathione peroxidase activity in the terminal stage of ALS after swim training. Only slight modifications of oxidative stress markers were found. Nevertheless, they favor swim training as the protection against oxidative stress. Our results are relevant for therapeutic aquatic activity in ALS patients where physical activity recommendations still remain controversial.

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S2.P13

THE EFFECT OF BENZO[A]PYRENE ON OXIDATIVE STRESS IN CHICKEN EMBRYOS BRAIN

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Benzo[a]pyrene belongs to a large group of polycyclic aromatic hydrocarbons (PAHs). It is one of the most dangerous to health components of tobacco smoke with proven carcinogenic activity. Benzo[a]pyrene is also an important air pollutant and some food pollutants. The aim of the study was to show whether early exposure to benzo[a]pyrene affects the antioxidant system in the brain during the embryonic development of the bird. For this purpose, 100 fertile eggs of Ross 308 broiler parent stock were used. The eggs were divided into 5 groups as control, vehicle control, 0.1, 0.5, and 1 mg BaP/kg of egg weight. The eggs were injected to the yolk on day 6 of incubation. At day 14 of incubation, eggs were opened until 6 living embryos were obtained from each group. The activity of catalase, glutathione peroxidase (GPx), superoxide dismutase (SOD) and the level of glutathione (GSH) and malondialdehyde (MDA) were determined in the collected tissues. It was observed that, in benzo[a]pyrene-treated groups, the activity of SOD and GPx was increased. It was also indicated that the level of GSH was significantly decreased and the level of MDA - significantly increased. The greatest changes in the examined parameters were observed in the group of eggs injected with the dose of 1 mg BaP/kg of egg weight. These results indicate that *in ovo* administration of benzo[a]pyrene causes oxidative stress in the brains of chicken embryos.

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S2.P14

NEUROPHYSIOLOGICAL STUDY OF DISORDER AND RECOVERY OF SPATIAL MEMORY IN AN EXPERIMENTAL MODEL OF ALZHEIMER'S DISEASE

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The cluster the amygdala - the visual system - the olfactory analyzer normally jointly carry out the formation of behavior and spatial memory in the Morris water maze. Impaired memory and cognitive functions during the creation of an analogue of Alzheimer's disease in old albino rats was observed after bilateral surgical bulbectomy. Administration of curcuma solution after total memory loss in animals was accompanied by restoration of spatial memory. This was evidenced by the reduction in the latent time for searching for an invisible platform. The result of the effect of curcuma is the expression of neurotrophic factor and neurogenesis in the amygdala. This phenomenon can be explained by the effect of curcumins (active substances in curcuma) as a trigger for neurogenesis in the basolateral amygdala. This phase leads to the rehabilitation of cognitive function in the spatial disturbance of the connection between the amygdala and the olfactory receptor was possibly accompanied by structural rearrangements and increased interconnection and the development of new contacts between the amygdala and the visual system. The amygdala contains glutamatergic pyramidal neurons and GABA-ergic interneurons It became known that the amygdala, like the hippocampus and the bulb, is capable of neurogenesis in adult animals.

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S2.P15

EFFECT OF DIMETHYL FUMARATE ON DISORDERS OF THE OLFACTORY BULB NEUROGENESIS IN THE STREPTOZOTOCIN-INDUCED RAT MODEL OF ALZHEIMER'S DISEASE

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The sporadic late-onset form of Alzheimer's disease (sAD) affects 90% of AD patients and it is associated mainly with environmental factors. The intracerebroventricular injection of streptozotocin (STZ-icv) rat model of the sAD is widely used in basic research for understanding of the sAD pathophysiology and testing new therapeutic methods. One of the mechanisms contributing to memory impairment in AD is disruption of the postnatal neurogenesis in both the hippocampus and the olfactory bulb (OB). New neurons in OB determine the proper functioning of perceptual and memory processes related to smell, which in adults may be associated with adaptive mechanisms in response to environmental changes. It has been shown that patients with mild cognitive impairment and olfactory deficits are at higher risk of developing AD. Methods: young (n = 20) and old (n = 20) male Wistar rats were randomly divided into four groups (in each young n = 5 and old n = 5): 1) STZ+DMF with STZ-icv injection (3 mg/kg) and fed with chow containing DMF (0.4% by weight), 2) STZ with STZ-icv injection and fed with standard chow, 3) Sham+DMF with icv injection of vehicle (citrate buffer) and fed with DMF chow, 4) Sham – vehicle-icv and fed with standard chow. One week after STZ or vehicle icv rats were subjected to intraperitoneal injection of 5-bromo-2'deoksyurydine (BrdU) (50 mg/kg, once daily for three days) - a marker of cells undergoing cell division. Rats were sacrificed 9 days after the third BrdU injection and brain were subjected to immunofluorescent BrdU and doublecortin (DCX, marker of immature neurons) labelling. Data were analyzed using three-way ANOVA and Tukey's post-hoc test. Results and conclusion: both young and aged STZ rats were characterized by the lowest number of new immature neurons (BrdU+DCX containing cells) in the olfactory bulb ($p < 0.001$; STZ vs. other groups). STZ+DMF young and aged rats showed higher density of newly born neurons in the OB ($p < 0.001$) compared to STZ group. The highest percentage of immature neurons was observed in the OB of Sham+DMF rats in both age groups compared to the other experimental groups. STZ-icv causes significant disorders of neurogenesis in the OB. DMF therapy improved the disruption of adult neurogenesis in the OB induced by STZ-icv treatment.

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S2.P16

EFFECT OF PREBIOTICS SUPPLEMENTATION ON SOCIAL BEHAVIOUR AND PLASMA TNF-ALPHA LEVEL DISTURBANCES IN HIGH- AND LOW-RESPONDERS RATS WITH CENTRAL AMYGDALA HYPERACTIVATION

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Amygdala (Amg) hyperactivity as well as higher TNF-α plasma concentration occurs in patients with PTSD, anxiety disorders or depression. Long-term electrical stimulation (ES) induces abnormal hyperactivation of the Amg and can be used as an animal model of mentioned disorders. The central nucleus of the Amg (CeA) contribute to neural and endocrine responses to stress and it's functioning is associated with anxiety and social behaviour. Moreover Amg is considered to have a crucial role in the microbiota signals processing and integration. Between the gut microbiota and central nervous system exists a functional bidirectional communication. Manipulating the gut microbiome may improve host mental health and reduce inflammatory processes. Galactooligosaccharides (GOS) are prebiotics - non-digestable polysaccharides that increase the growth and activity of health-promoting microorganisms. Individual differences in the neuronal, endocrine and immune responses to stress may result in different susceptibility to the development of anxiety disorders in humans. The rat model in which male rats are divided into high responders (HRs) and low responders (LRs) - based on their locomotor activity during exposure to the novel environment - is well-described and reflects differences observed in humans. Twenty eight male Wistar rats categorized as HRs or LRs in the novelty test were subjected to 14-day electrical stimulation of the CeA and 21-day supplementation with GOS. Three chamber sociability test was used to assess social behaviour. One hour after the test blood samples were collected and centrifuged to obtain plasma. TNF-α plasma concentration was determined by ELISA test. Data were analyzed using three-way ANOVA and Tukey's post-hoc test. The long-term ES of the CeA caused deficits in social behaviour (avoiding interaction with a non-familiar rat and spending more time with the familiar rat; $p < 0.01$). It also led to a significant increase in plasma TNF-α level ($p < 0.001$). In HRs rats these effects were enhanced. GOS supplementation improved disturbances induced by the ES of the CeA as stimulated and supplemented rats exhibited more prosocial behaviour and lower TNF-α plasma concentration ($p < 0.05$). GOS therapeutic effects were more pronounced in LRs rats.

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S2.P17

IMPROVED MOTOR FUNCTION AS A RESULT OF THE INFLUENCE OF MINOCYCLINE ON MOTOR CORTEX NEURONS IN CORTICAL MODEL OF PHOTOTHROMBOTIC ISCHEMIC STROKE IN RATS

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Cerebrovascular diseases are the principal causes of mortality and disability worldwide. In survivors, strokes can result in long-term disability. Ischemic strokes constantly pose for great amount of mortality worldwide. Minocycline, by launching plethora of neuroprotective mechanisms may be beneficial as the treatment which has been confirmed in many research models of acute brain damage. Therefore, it is important to search for neuroprotection mechanisms that would allow to extend the therapeutic window and develop new strategies for treating ischemic strokes. The first goal in our research was to develop experimental models of cerebral ischemia that mimic human stroke. The second aim was to investigate the effect of minocycline on penumbra and functional outcomes after ischemic stroke. Photothrombotic ischemia of motor cortex was produced in 72 male Long-Evans rats. We tested different time windows: 24 h, 48 h and 7 days after stroke induction. Half of the experimental groups received an intravenous dose of minocycline (1 mg/1 kg b.w/1ml solution, 10 minutes after stroke). CatWalk XT, Grip Strength-test and elevated runway-tests were performed. These functional tests were applied before and after ischemic stroke. In groups with minocycline we observed statistically significant improvement of speed of walking, correctness of the stepping pattern and increase of grip strength. Penumbra and necrosis were localized by immunohistochemical techniques and we measured its size and quality. Conclusion: minocycline improves motor function in ischemic rats. Minocycline action also correlates with size of necrosis and penumbra but determining the exact relationship between them requires in-depth studies.

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S2.P18

CHANGES IN THE RESPONSIVENESS OF THE RAT DORSOMEDIAL HYPOTHALAMUS TO DIFFERENT METABOLIC CONDITIONS UNDER HIGH-FAT DIET

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Food intake and metabolism are controlled by a network of brain structures, most of which are located within the hypothalamus. Feeding behaviour undergoes regulation by homeostatic signals incoming from the digestive system (*via* the hunger and satiety signalling peptides), as well as by the circadian clock, driving an increased food intake during the active, and reduced during the behaviourally quiescent phase. Therefore most animals display a natural preference or restriction of feeding to a particular part of the day. The brain structure especially responsive to restricted feeding is the dorsomedial hypothalamus (DMH). In this study we aimed at verifying how the DMH responds to different metabolic states in both *ad libitum* and restricted-fed rats. Moreover, we checked whether these responses change under 4-week-long high-fat diet (HFD). For this we performed immunohistochemical staining for the cFOS protein, an early response gene reflecting changes in the neuronal activity. In the first protocol, rats which had been fed *ad libitum*, were then food deprived for 48 h (hunger). Following, one group was refed for 2 h (full satiety). In the restricted-feeding (RF) protocol, rats had a limited access to food to 6h every day during the night (active phase) for a period of two weeks. Separate groups of animals were then culled either 0.5 h before, or 1.5 h and 3.5 h after the scheduled meal. The experiment revealed that in both protocols and for both diets, the number of cFOS positive cells in the DMH is the lowest during hunger and the highest after feeding. However, HFD-fed animals showed a higher increase in cFOS immunoreactivity after a refeed following food deprivation. On the other hand, in HFD restricted-fed animals, the increase in cFOS after a scheduled meal was lower than in the control group. These results highlight the involvement of DMH in the processing of the information about the metabolic states of an organism and present ways in which HFD disrupts its responsiveness to satiety, which differ depending on the feeding schedule.

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S2.P19

MODULATION OF PAIN IN BRAIN LIMBIC AREAS: ROLE OF OPIOID AND CANNABINOID SYSTEMS

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The development of pain as a common experience and its treatment is very important, not only where it is caused by injury or inflammation, but also in chronic states where the nerves themselves are damaged. Non-steroidal anti-inflammatory drugs (NSAIDs) are the most widely used analgesics. However, a few recent studies have demonstrated that these non-opioid drugs in the case of their prolonged use, elicit the opioid-like effect, tolerance may entail serious adverse effects. The brain limbic system is involved in affective-emotional aspects of pain and this study has shown brain mechanisms of non-opioid induced antinociceptive tolerance to NSAIDs in the 'formalin test'. Opioids remain the drug of choice for the clinical management of moderate to severe pain and play a large role in the pain modulatory system. Studies over the past decade have shed light on the influence of endocannabinoids on the opioid system. Evidence from both animal and clinical researches point toward an interaction between these two opioid and cannabinoid systems, and suggest that targeting the endocannabinoid system may provide novel interventions for managing morphine addiction, opiate dependence and tolerance, and of withdrawal reactions. In this study, we present new experimental data indicating that microinjections of widely used non-opioid, in particular, NSAIDs diclofenac, ketoprofen, ketorolac, and lornoxicam into pain matrix key structures of brain limbic areas, such as the rostral part of the anterior cingulate cortex, agranular insular cortex and central nucleus of amygdala (CeA) of rats, - induce antinociception. When administered repeatedly, tolerance developed to the antinociceptive effects of these drugs. Pre- or post-treatment with opioid receptor antagonists, naloxone and CTOP as well as cannabinoid CB1 receptor antagonist AM-251, separately or in combination in the CeA, prevented or abolished antinociceptive effects of these non-opioid analgesics. These new findings confirmed the concept that antinociception and the development of tolerance to NSAIDs are mediated *via* endogenous opioid and cannabinoid systems involving the descending pain modulatory circuits attenuating pain behavior in rats - defensive withdrawal reflexes at the spinal cord level. The crucial structures of this descending pain modulatory system are midbrain periaqueductal grey matter and rostral ventro-medial medulla. These findings, thus, emphasized the important role of these limbic regions, the rostral anterior cingulate cortex, agranular insular cortex, and central amygdala in rats' pain behavior.

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S2.P20

MINOCYCLINE AFFECTS SPLEEN T AND B LYMPHOCYTES PERCENTAGE IN STREPTOZOTOCIN-INDUCED MODEL OF ALZHEIMER'S DISEASE IN RATS

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Minocycline was shown to have anti-inflammatory and neuroprotective effect in neurodegenerative diseases. Here, we investigated immunomodulatory properties of minocycline (MINO) at a dose of 35 mg/kg b.w., administered intraperitoneally (i.p.) for 7 consecutive days, on immune system in rats with STZ-induced model of sporadic form of Alzheimer's disease (sAD). Thirty male Wistar rats were divided into groups: STZMINO (intracerebroventricular, i.c.v., streptozotocine (STZ) and i.p MINO injections), VEHMINO (i.c.v. vehicle and i.p minocycline injections), STZ (i.c.v. STZ injection), VEH (i.c.v. vehicle injection). Spleens were collected and homogenized. Flow cytometry with a three-color combination of fluorescent monoclonal antibodies was used to identify T (CD3+), B (CD45RA+), NK (CD161a+) lymphocytes and T lymphocyte subsets of CD4+ and CD8+ lymphocyte percentages in spleen supernatants, according to the method that we previously described. Statistical significance was ascertained by U Mann-Whitney test and the results were considered significant at $p \leq 0.05$. Data is presented as mean percentage (%) of cells ± SD. As a result significantly ($p < 0.05$) increased T lymphocytes (STZMINO: 40.82 ± 9.61; VEHMINO: 42.13 ± 3.71) and B lymphocytes (STZMINO: 17.05 ± 2.64; VEHMINO: 24.2 ± 8.29) percentages were observed in minocycline-treated groups relative to corresponding T lymphocytes (STZ: 20.4 ± 1.16, VEH: 17.75 ± 3.65) and B lymphocytes (STZ: 7.35 ± 1.71, VEH: 11.87 ± 1.97) percentages in non-treated animal groups. Moreover, percentages of T lymphocytes subsets TCD4+ (39.5 ± 7.18) and TCD8+ (16.09 ± 3.16) in STZMINO group were significantly ($p < 0.05$) increased as compared to corresponding STZ (TCD4+: 15.58 ± 3.4; TCD8+: 9.09 ± 1.45) groups. The results indicate that minocycline changes spleen lymphocyte distribution, including $TCD4^{+}/TCD8^{+}$cell ratio in the sAD model.

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S2.P21

EFFECT OF KETOGENIC DIET ON NEURODEVELOPMENTAL REFLEXES

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The ketogenic diet is a type of nutritional system based on deriving energy from fats while minimising carbohydrate intake while maintaining an adequate amount of protein in the diet. It is currently used for the treatment of drug-resistant epilepsy with very good results. There are many studies showing the positive effect of diet on the nervous system in the case of neurodegenerative disorders, endocrine immune disorders, obesity, diabetes and certain types of cancer, while there is a lack of data on the effect of diet on the development of the nervous system. It is important from the point of view of the use of diet by pregnant women. In order to test the effect of diet on neurodevelopment, a series of experiments were carried out on Wistar rats. These tests aimed to check reflexes such as forelimb grasp, hindlimb grasp, righting, hindlimb placing, cliff avoidance, gait, auditory startle, posture, eye openings and accelerated righting. The rats were divided into three study groups: a control group on a normal diet (ND) , rats on a prenatal ketogenic diet (KD/ND) and a group on a ketogenic diet until P21. The first conclusion is a significant difference in weight and weight gain between the groups and in body hair. Rats on ketosis are smaller and less hairy. My research shows that there is a trend when pregnant female Wistar rats are on a diet that indicates a difference in reflexes often to the disadvantage of rats on a ketogenic diet. The longer a group was on the ketogenic diet the later they developed reflexes.

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S2.P22

ARCHITECTURE OF A FUNCTIONAL SYSTEM OF THE SAGITTAL BALANCE MAINTAINING

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Body balance is required for a static position and locomotor function. Its maintaining means alignment of the different levels structures of the body in space with respect to each other for organizing the skeleton geometry and locomotor apparatus structure so as to ensure their correspondence to gravity. In the form of mechanical stress this environmental factor affects the processes of adaptive remodeling of bone tissue, and a number of other structures with it. The state of the bone tissue is even considered as a reflection of the effects of gravity on the body in the evolution. The balance of the body in space can be characterized by such an integrative indicator as the sagittal balance of the spine - the vertical alignment of the trunk above the pelvis. Its quantitative characteristic is the horizontal distance between the centers of the body of the 7th cervical vertebra (C7) and the posterosuperior border of the sacrum on lateral radiographs of the spine in full growth. To understand the mechanisms of maintaining the sagittal balance within physiological borders, it is important to consider it within the P.K. Anokhin's concept of functional system. In this case, the sagittal balance should take a central place forming the functional system, being the final adaptive result of functioning, that is, one of the parameters of homeostasis, for the maintenance of which all functional systems of the body are formed. In the architecture of such a functional system, it is necessary to distinguish functional blocks - structures that interact with each other to maintain this parameter and perform a certain role, for further multilateral study of such systems. The receptors that determine homeostasis parameter (sagittal balance) deviations and trigger the functional system are vestibuloreceptors, proprioceptors, and the visual sensory system. In the physiological center, which includes a number of central nervous system structures, the resulting afferentation is integrated in the creation of motor programs. At each current moment, there are changes in the state of the body's executive structures involved in maintaining the sagittal balance. Such efferent structures are not only skeletal and muscle macrostructures, but also elements of bone microarchitecture. They undergo changes in a shorter time interval during remodeling, ensuring the body adaptation with the external environment at higher levels of interaction. Consideration of the structures involved in maintaining the sagittal balance from this point of view will allow us to determine the possible causes of its displacement and methods of its correction.

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S2.P23

EFFECT OF PROCAINE BLOCKADE OF THE VENTRAL TEGMENTAL AREA ON THETA RHYTHM INDUCED BY PHARMACOLOGICAL ACTIVATION OF THE PEDUNCULOPONTINE NUCLEUS

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The ventral tegmental area (VTA) and the pedunculopontine nucleus (PPN) are structures that have important influence on the induction and regulation of hippocampal theta rhythm, which plays a key role in important processes such as memory and REM sleep. PPN is one of the initial structures of an extensive theta rhythm induction network, additionally - one of the nuclei that sends cholinergic projections to the VTA. Recent studies has also shown that VTA stimulation is accompanied by the theta rhythm in the hippocampus. However, the functional relationships between these structures and hippocampal theta rhythm is still not fully understood. The aim of the experiment was to investigate the effect of pharmacological cholinergic activation (carbachol) of PPN and inactivation (procaine) of VTA on the formation and regulation of hippocampal theta rhythm. The surgery was performed under urethane anesthesia (maintained at such a level that theta rhythm does not appear spontaneously). Rats were implanted with the use of stereotaxic frame with bilateral hippocampal recording electrodes and bilaterally with standard pedestal guides for infusions to the VTA and PPN. Local field potential (LFP) was recorded from the hippocampal electrodes during the whole experiment with the use of Spike-2 softwere. Total power in the hippocampal signal was analyzed. Theta and delta bands peak power (P_{max}) was extracted. P_{max} value in the theta frequency band (3–4 Hz and 4–5 Hz) temporarily decreased after intra-VTA injection of procaine during carbachol - induced theta episode in comparison to control group. P_{max} value in the delta frequency band (1–2 Hz and 2–3 Hz) temporarily increased after intra-VTA injection of procaine during carbachol-induced theta episode in comparison to control group. In control group - water injection to VTA during carbachol - induced theta rhythm episode had no effect in the signal power (P_{max}) in both theta and delta bands. The results suggest that the VTA probably might be a part of the broad network involved in theta rhythm induction.

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S2.P24

MET-ENKEPHALIN INVOLVEMENT IN THE PROTECTION OF CEREBELLAR AND FRONTAL CORTEX IN VAGOTOMIZED RATS

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Met -enkephalin, one of the opioids peptide, exerts protective effects on the pain sensation, mood, modulation of all endocrines axis and dopamine activity in the brain. Dopamine and other monoamines are involved in depressive disorders in parkinsonians and epileptic patients. Moreover, evidences were found, that vagus nerve which is connected with the gastrointestinal system, is affected very early in the parkinson disease. Recently, it was also postulated that opioids and cholinergic systems interacts (*via* vagus nerve) at the level of brain - gastrointestinal axis. The question arises about the role of opioids in the regulation of vagus nerve effect on the brain structures connected with movement and mental disorders. Thus, the aim of this study was to examine the effect of vagotomy on the activity of Met-enkephalin in the cerebellar cortex (CBR) and frontal cortex (Fctx) in rats during control and inflammation conditions. Experiment was performed on adult, male Wistar rats divided into seven groups (8 rats/group): 1) control without treatment (CNT); 2) NaCl (injection of NaCl); 3) Sham surgery and injection with NaCl (Sham); 4) Subdiaphragmatic vagotomy (Vgax); 5) NaCl treated with lipopolysaccharide (LPS) (NaCl+LPS); 6) Sham +LPS; 7) Vags+LPS. Following surgeries, animals recovered for 30 days, then were injected i.p. with NaCl or LPS (10 μg/rat *E.coli* 026:B6). Two hours later, animals were euthanized and cerebellar cortex and frontal cortex were isolated, weighed and stored at –80°C. Native Met- enkephalin concentration in the brain structures was estimated by radioimmunoassay method. Vagotomy increased the level of Met-enkephalin in the CBR by 86% ($P < 0.01$), LPS also caused higher level of opioid (by 68%, $P < 0.05$). Unexpectedly, LPS did not potentiated the vagotomy effect on Met-enkephalin concentration (increase only by 14%). Fctx Met-enkephalin level was increased by 4.4 times compared to CNT group; LPS caused increase of opioid by 140%. In contrast to CBR, LPS potentiated the opioid response to vagotomy and induced 335% increase compared to CNT group. In conclusions: 1) CBR and Fctx opioid system similarly responded to vagotomy (increase) but showed different sensitivity to inflammation; 2) Met-enkephalin protective effect on cholinergic system under inflammation condition in vagotomized rats was significantly higher in frontal cortex than in cerebellar cortex.

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S2.P25

FREQUENCY-DEPENDENT PLASTICITY OF SPONTANEOUS ACTION POTENTIALS WITHIN IDENTIFIED *LYMNAEA'S* NEURONS

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Action potential (AP or spike) is a key reaction of neuronal membrane underlying the responses of the nervous cells on any type of irritation. Some neurons are able to generate spontaneous AP independently from external impact (pacemaker neurons and pacemaker potentials). There is no doubt that AP duration can determine the total excitability of the neuronal membrane due to ability to regulate a time course of it refractory period, i.e. defines a firing rate of the neurons which is critically important for correct operation of neuronal networks. In our days, an initial point of view on AP as 'all-or-none', permanent-type event is considerably revised. The plastic nature of AP has been described in various neuronal types both in vertebrates and invertebrates. As a rule it is talking about frequency-dependent broadening of neuron soma spikes, evoked by intracellular current injection. From the other hand, AP variability during spontaneous activity is less described. We report about frequency-dependent changes in the duration of various AP phases: depolarization (DP), repolarization (RP) and undershoot (US) in identified central neurons of mollusk *Lymnaea stagnalis*. Glass microelectrodes were used for a 10 min record both for giant dopamine- (RPeD1, $n = 6$) and serotonin- (LPeD1, $n = 4$) containing cells in isolated CNS preparations. Based on initial data distribution of frequencies, all spikes in a record were combine in 3 groups - low (first quartile or less), base (between first and third quartiles), high (third quartile or more) and then analyzed by conventional electrophysiological (InputWin) and statistical (Statistica 6.0) tools. For RPeD1 we were able to observe a slight AP broadening both for DP and RP phases at high frequencies, while for LPeD1 about two-time decrease of duration in all AP phases under the study was determined, meaning compression of the signal. AP amplitude is also varied in frequency-dependent manner in RPeD1 and LPeD1 - both a positive (an area above) and a negative (an area below rest potential value) phases of AP decline with spike frequency rise. However, total time of neuronal membrane depolarization and hyperpolarization state was significantly increased at high frequencies in both cells. We hypothesize that mentioned above differences in AP frequency-dependent plasticity can underlie variations in the efficiency of interneuronic communication in dopamine- and serotoninergic networks of molluscan brain.

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SESSION III

BIOLOGICAL RHYTHMS
SLEEP

Wednesday (September 15, 2021; 15:30 – 17:50)
Thursday (September 16, 2021; 12:25 – 13:00)

Chair:

Dr. hab. Jolanta Orzel-Gryglewska
Department of Animal and Human Physiology, University of Gdansk Poland

DETAILED SESSION III SCHEDULE

Opening lectures (Wednesday, September 15, 2021; 15:45 – 16:55; *virtual stream A*)

S3.L1 SLEEP FOR MENTAL HEALTH. **G. Lipinska[1], R. Lewis[1], L.C. Roden[7,8], K. Scheuermaier[5], F.X. Gomez-Olive[4], D.E. Rae[7], S. Iacovides[5], A. Bentley[2], J.P. Davy[3], C.J. Christie[3], S. Zschernack[3], J. Roche[5], K.G.F. Thomas[1]** ([1]UCT Sleep Sciences and Applied Cognitive Science and Experimental Neuropsychology Team (ACSENT), Department of Psychology, University of Cape Town, Cape Town, South Africa, [2]Department of Family Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [3]Department of Human Kinetics and Ergonomics, Rhodes University, Grahamstown, Makhanda, South Africa, [4]MRC/Wits Rural Public Health and Health Transitions Research Unit (Agincourt), School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; [5]Brain Function Research Group, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [7]Division of Exercise Science and Sports Medicine, Department of Human Biology, Faculty of Health Sciences, University of Cape Town, Cape Town, South Africa, [8]Faculty Research Centre for Sport, Exercise and Life Sciences, School of Life Sciences, Faculty of Health and Life Sciences, Coventry University, Coventry, United Kingdom).

S3.L2 WHAT DOES THE SLEEPING BRAIN KNOW ABOUT ITS SURROUNDING? **M. Wislowska** University of Salzburg, Centre for Cognitive Neuroscience, Laboratory for Sleep and Consciousness Research, Salzburg, Austria).

Oral presentations (Wednesday, September 15, 2021; 16:55 – 18:05; *virtual stream A*)

S3.L3 REPETITIVE ACTIVATIONS OF POSTERIOR AND/OR PERIFORNICAL HYPOTHALAMIC REGIONS ELEVATE CSF OREXIN-A CONTENT AND FASTEN RECOVERY OF NORMAL SLEEP CYCLE FROM DEEP ANESTHESIA INDUCED ARTIFICIAL SLEEP. **Kh. Bezhanishvili, E. Chkhartishvili, N. Maglakelidze, M. Babilodze, O. Mchedlidze, N. Nachkebia** (I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

S3.L4 THE CIRCADIAN AND ANNUAL RHYTHM OF OREXIN A SECRETION INTO BLOOD PLASMA IN EWES. **K. Kirsz[1], K. Lukowicz[1], M. Szczesna[1], D. Zieba-Przybylska[1]** ([1]Agricultural University in Krakow, Animal Science Faculty, Department of Animal Nutrition, Biotechnology and Fisheries, Krakow, Poland).

S3.L5 LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM AND ITS' SUPER-SENSITIVITY IN ADULT AGE – CHARACTER OF SLEEP DISORDERS AND BEHAVIORAL DISTURBANCES. **N. Nachkebia, E. Chkhartishvili, O. Mchedlidze, N. Maglakelidze, M. Babilodze, E. Chijavadze** (I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

S3.L6 OREXIN-A INJECTED IN LATERAL VENTRICLE AMELIORATES LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM ON SLEEP-WAKEFULNESS CYCLE. **N. Maglakelidze, O. Mchedlidze, E. Chkhartishvili, M. Babilodze, Kh. Bejanishvili, E. Chijavadze, N. Nachkebia** (I. Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

Session summary

Poster session (September 16, 2021; 12:25 – 13:00; *virtual stream C, interactive*)

S3.P1 THE SLOW OSCILLATION (<1 HZ) BEFORE SLEEP IN THALAMO-CORTICAL NEURONS. **V. Tsomaia, N. Nachkebia** (Ivane Beritashvili Center of Experimental Biomedicine, Tbilisi, Georgia).

S3.P2 ANTIBACTERIAL ACTIVITY OF ANTIDEPRESSANTS, INHIBITORS OF MONOAMINE'S REUPTAKE, DEPENDS FROM THEIR ANTIDEPRESSIVE EFICACY ON SLEEP DISORDERS. **N. Rogava[1,2], Z. Lomtatidze[2], N. Maglakelidze[1], Kh. Bejanishvili[1], N. Nachkebia[1]** ([1]I. Beritashvili Center of Experimental Biomedicine,[2]Sokhumi State University, Tbilisi, Georgia).

S3.P3 BLOOD LEUKOCYTES IN YOUNG AND OLD RATS UNDER DESYNCHRONOSIS INITIATION ON THE BACKGROUND OF WHOLE BODY CRYOSTIMULATION. **V.V. Lomako, O.V. Shylo** (Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine, Department of Cryophysiology, Kharkiv, Ukraine).

S3.P4 PITUITARY-THYROID SYSTEM IN YOUNG AND OLD RATS UNDER PREVENTIVE WHOLE-BODY CRYOSTIMULATION AND CIRCADIAN DISRUPTION. **O. Shylo[1], V. Lomako[1], D. Lutsenko[1], L. Samokhina[2]** ([1]Institute for Problems of Cryobiology and Cryomedicine, NAS of Ukraine, Kharkiv, Ukraine, [2]G.D. L.T. Malaya National Institute of Therapy of National Academy of Medical Sciences of Ukraine, Kharkiv, Ukraine).

S3.L1

SLEEP FOR MENTAL HEALTH

G. LIPINSKA[1], R. LEWIS[1], L.C. RODEN[7,8], K. SCHEUERMAIER[5], F.X. GOMEZ-OLIVE[4], D.E. RAE[7], S. IACOVIDES[5], A. BENTLEY[2], J.P. DAVY[3], C.J. CHRISTIE[3], S. ZSCHERNACK[3], J. ROCHE[5], K.G.F. THOMAS[1]

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Sleep is critical physiological state that has emerged as an important regulator of multiple biological systems. For decades, researchers have understood that sleep difficulties are pervasively reported in individuals with psychiatric disturbances, but more recently findings have described how sleep disturbance may help drive psychopathology or interact with other biological and psychological states to exacerbate symptoms. For example, findings from our own laboratory show that sleep difficulties are related to the presence of cognitive disturbances in individuals diagnosed with posttraumatic stress disorder. Another study we conducted showed that emotional dysregulation characteristic of depressive and posttraumatic symptoms had an influence on symptom severity, but primarily *via* sleep disturbance. We showed *via* structural equation modeling that individuals who tended to struggle with emotion regulation strategies had poor sleep quality and these sleep disturbances were strongly predictive of increased depressive and posttraumatic symptom severity, with little direct influence of emotion regulation strategies on symptoms. In a recent study conducted during the COVID pandemic we broadened our understanding of how sleep interacts with lifestyle factors such as exercise and sedentary behaviour including time spent on screens. We showed that spending more time on screens and sitting, and less time being active, increased insomnia symptoms and in turn depressive and anxiety-related symptoms. These findings highlight the importance of sleep, not as an isolated physiological function, but nested in a greater biological and psychological milieu.

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S3.L2

WHAT DOES THE SLEEPING BRAIN KNOW ABOUT ITS SURROUNDING?

M. WISLOWSKA

University of Salzburg, Centre for Cognitive Neuroscience, Laboratory for Sleep and Consciousness Research, Salzburg, Austria

During sleep, the brain turns "inward", and engages in processes like regeneration or memory consolidation. At the same, it needs to continue monitoring the environment for potential threats. If a lion appears in the vicinity, arousal and awareness need to be fully regained at once, to allow the organism to undertake an appropriate action. Nowadays, we rarely expect to find a lion in our bedroom - nevertheless, we take an advantage of the sleeping brain's watchfulness, when for example setting up our alarm clocks. However, if one of the main functions of sleep is to consolidate new memories, these processes should be protected from unnecessary interference. It would therefore make sense to filter out all of the environmental noise, like sounds for example, and prevent them from reaching the sleeping brain. Nevertheless, our own experience, along with the scientific evidence, shows that this is not the case. How does the sleeping brain achieve the balance between internal processing and external monitoring, is not a trivial question. During this lecture, we will look into the results of recent empirical studies investigating information processing during sleep. Presentation of (usually acoustic) stimuli to sleeping participants induces patterns of the brain activity that can be very similar to, or very different from those observed during wakefulness, depending on the sleep stage, stimulus material, or even analytical strategy. After the lecture, we shall be left with an impression, that the sleeping brain is complex, magnificent, and anything but trivial. It holds the key to our wellbeing, success in university exams, and even our survival.

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S3.L3

REPETITIVE ACTIVATIONS OF POSTERIOR AND/OR PERIFORNICAL HYPOTHALAMIC REGIONS ELEVATE CEREBROSPINAL FLUID (CSF) OREXIN-A CONTENT AND FASTEN RECOVERY OF NORMAL SLEEP CYCLE FROM DEEP ANESTHESIA INDUCED ARTIFICIAL SLEEP

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Consideration of the hypothalamic orexinergic system as the neurophysiological substrate or cellular target necessary for the acceleration of coming out from barbiturate anesthesia-induced artificial sleep is the main goal of the present investigation. For this aim the effects of repetitive electrical stimulations of posterior (PH) and perifornical hypothalamus (PfH) on the recovery of normal sleep-wakefulness cycle from barbiturate anesthesia-induced artificial sleep was studied by us for the first time. For the assessment whether this methodical approach can indeed elevate the level of endogenous orexins in cerebrospinal fluid (CSF), we have also studied for the first time the changes in the level of CSF orexin-A in different stages of barbiturate anesthesia, under the impact of repetitive electrical stimulations of PH and PfH orexin-producing neuronal regions. In white wild rats (n = 9), after surgical implantation of recording/stimulating electrodes and postoperative recovery, deep anesthesia was induced by intraperitoneal injection of different doses of sodium ethaminal. EEG registration was started immediately and lasted continuously for 48 hours (control, group I). In experimental rats, 10 min after anesthesia to be started, electrical stimulations (8–12v, 200c/s, 0.1 ms) of PH (group II) and PfH (group III) were begun. Stimulations lasted for 1 hour with 5 min intervals between subsequent ones. CSF orexin-content was measured by ELISA. It appears that repetitive activations of PH and PfH orexin neurons significantly accelerate (by 30–40%) wakefulness recovery from anesthesia-induced sleep. The first fragments of wakefulness were soon followed by normal deep slow wave sleep (DSWS) episodes. Normal DSWS recovery was accelerated in post-stimulation period by 1.5 h then during spontaneous recovery in un-stimulated controls. The latency of the first episode of REM sleep decreased significantly, from 23–24 h in un-stimulated controls to 11–12 h in experimental animals. REM sleep latency diminished much more, to 10 ± 0.5 h, after repetitive electrical stimulation of PfH orexin-producing neurons. Significant elevation of CSF orexinA content was noted in stimulated animals from both experiments. Therefore elevation of the content of endogenous orexin-A in CSF, in response to the repetitive electrical stimulations of PH and PfH orexin-producing neuronal regions, significantly shortens anesthesia time and accelerate coming out from barbiturate anesthesia-induced artificial sleep, through the acceleration of normal sleep-wakefulness cycle recovery.

Acknowledgements: Supported by SRNSFG, Grant #11/04

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S3.L4

THE CIRCADIAN AND ANNUAL RHYTHM OF OREXIN-A SECRETION INTO BLOOD PLASMA IN EWES

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Orexin-A (OXA) is a hypothalamic neuropeptide, which has been mainly recognized as a regulator of sleep/arousal state, energy homeostasis and feeding behaviour. In our earlier studies on seasonally breeding sheep, we demonstrated involvement of OXA in the regulation of annual rhythm of secretory activity of the pineal and the pituitary glands. Studies mostly on nocturnal and nonseasonal rodents have shown that extracellular levels of orexin vary in a circadian pattern, with high levels during the waking period. However, it is difficult to relate this results directly to diurnal, seasonal sheep, in which OXA activity occurs in an annual cycle. Therefore, the purpose of this study was to investigate the circadian and annual rhythm of OXA secretion into blood plasma in ewes. Experiments were conducted separately for June (non-breeding, long-day season, LD) and December (breeding, short-day season, SD). During the LD, ewes were anovulatory and expressed no signs of estrus (progesterone concentration was 0.41 ± 0.03 ng/ ml). Whereas during the SD, estrous cycles of ewes were synchronized by the Chronogest® CR (Merck Animal Health, Boxmeer, The Netherlands). Experiments were performed when ewes were in the midluteal phase (days 8–10) of the estrous cycle. In the morning on the day of each experiment, 5 ewes were fitted with jugular catheters (Careflow, Argon, Billmed Sp. z o.o., Warsaw, Poland) for intensive blood sampling for 24 hours. Blood samples (3 ml) were collected at 15-min intervals beginning 2 hours after fitting catheters. The plasma was separated by centrifugation at 3000×g at 4°C for 10 min and stored at –80°C until the measurement of OXA by enzyme-linked immunosorbent assay (Sheep ELISA kit, Phoenix Pharmaceuticals, Inc., USA). The mean concentrations of OXA was higher ($P < 0.01$) during the LD compared to the SD. In both seasons, we observed the day-night differences in OXA secretion. In the LD, OXA circulating concentrations increased ($P < 0.05$) during the night compare with day. The mean concentration of OXA during the dark phase was 0.92 ± 0.14 ng/ml and during the light phase it was 0.6 ± 0.06 ng/ml. In contrast, OXA secretion decreased ($P < 0.05$) in the dark phase compare to the light phase during the SD. The mean concentration of OXA in the night was 0.7 ± 0.03 ng/ml and in the day it was 0.6 ± 0.05 ng/ml. Our results indicate that there are differences in OXA circulating concentrations depending on the season and the phase of the day in sheep.

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S3.L5

LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM AND ITS' SUPER-SENSITIVITY IN ADULT AGE - CHARACTER OF SLEEP DISORDERS AND BEHAVIORAL DISTURBANCES

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The question about the involvement of brain muscarinic cholinergic system (MChS) in the mood disorders, and in the major depressive disorder (MDD) among them, has a long history. However, the effects of early postnatal dysfunctioning of this system were not studied at all. We decided to investigate lasting effects of this procedure on the sleep-wakefulness cycle, open field behavior, forced swim test, sucrose preference and the density of M2/M4 muscarinic cholinoreceptors in neocortex and hippocampus. We performed a comparative analysis of the results, obtained by us, with the disorders of the same parameters during MDD for the aim of revealing possible linkage between them and early postnatal dysfunctioning of MChS. Rat pups received subcutaneously atropine (Atr, n=10) and/or scopolamine (Scop, n=10) 30 mg/kg two times daily from postnatal day 7 (P7) until P28. Afterwards rat pups were maintained in home cages under special care. Control rat pups (n=10) receiving distilled water with the same volume and procedure. Surgery and implantation of stainless screws was made in adult age 8–12 weeks after drugs discontinuation. EEG registration of sleep-wakefulness cycle was started 5–7 days after surgery and continued for 10 h daily during 7 consecutive days, in control and experimental animals. Density of M2/M4 muscarinic cholinoreceptors in hippocampus and neocortex was measured by Western blotting by means of specific antibodies. Statistical processing was made by Students' t-test. Adult rats exposed postnatally to anticholinergic drugs showed motor retardation in open field, increased immobilization and "behavioral despair" in forced swim condition, signs of anhedonia assessed by sucrose preference. Incidence of delta waves at the frequencies of 1–1.5 c/s became very low. Slow wave sleep became fragmented and superficial; number of awakenings was raised considerably. REM latency appeared three times shorter, REM incidence was significantly frequent and REM total time increased for two times. Adult hippocampal neurogenesis was significantly reduced. The density of M2/M4 muscarinic cholinoreceptors appeared significantly higher in neocortical and hippocampal plasma membranes. These disturbances are very similar to the disorders characteristic for MDD. We can conclude, that early postnatal dysfunctioning of MChS can be the one of factors contributing depression-like state in adult age.

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S3.L6

OREXIN-A INJECTED IN LATERAL VENTRICLE AMELIORATES LASTING EFFECTS OF EARLY POSTNATAL DYSFUNCTIONING OF BRAIN MUSCARINIC CHOLINERGIC SYSTEM ON SLEEP-WAKEFULNESS CYCLE

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Orexin/hypocretin-producing neurons are involved in the consolidation of arousal/wakefulness that becomes unstable if orexins are deficient in the brain. On the other hand, suppression of wakefulness can be of the main reasons for the development of sleep disorders and depression. Therefore, it is believed that the hypothalamic orexinergic system may also be involved in the pathophysiology of depression. The aim of the present investigation was to study the effects of intravenously (icv) administered orexin-A on sleep disturbances produced by early postnatal exposure of rat pups to the dysfunction of muscarinic cholinergic system (MChS). Dysfunctioning of MChS was produced by subcutaneous injection of scopolamine (30 mg/kg) in rat pups (n=10), twice daily, from postnatal days 7 to 28. Control rat pups (n=5) received the same volume of saline. Experiments were started 2–3 months after discontinuation of the drug. Implantations of stainless steel screws, for epidural EEG registration, and microinjection cannulas (plastics ones) were made under general anesthesia. Two doses of orexin-A (10 µg/µl and/or 25µg/µl) were injected in lateral ventricle. Experiments with EEG registration of the sleep-wakefulness cycle lasted continuously for 5 hours daily for three consecutive days on each animal, have been started immediately after icv microinjection of orexin-A, after the post-surgery recovery period. It was found that animals exposed in the early postnatal period to the MChS dysfunctioning were characterized in adult age by significant disturbances of the sleep-wakefulness cycle. These changes were very similar to sleep disorders, characteristic of major depressive disorder. ICV microinjection of orexin-A dose-dependently ameliorated disturbances in sleep-wakefulness stages. The elevation of the level of orexin-A in cerebrospinal fluid has an anti-depressive effect in animals subjected in early ontogenesis to the dysfunctioning of muscarinic cholinergic system. It was manifested in the enhancement and stabilization of wakefulness, in an increase of the latency of REM sleep, which was sharply reduced in these animals, and decrease in the incidence of REM sleep that develops as frequently as during depression and requires to be partially deprived.

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S3.P1

THE SLOW OSCILLATION (<1 HZ) BEFORE SLEEP IN THALAMO-CORTICAL NEURONS

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The slow oscillation (<1 Hz) is an EEG hallmark of the resting state. The thalamus is involved in several types of oscillatory activity including slow (<1 Hz) rhythms that are considered as the forerunner of the deeper stages of sleep during the transition from wakefulness to sleep as well as the faster activity that occurs during awakening. In order to examine the involvement of muscarinic acetylcholine receptors in slow oscillatory activities, it was interesting for us to investigate the effects of muscarinic combined agonist, carbochol, on the extracellular unitary and field activities and intracellular discharges in brain slice preparations of the rat and cat lateral geniculate nucleus and ventrobasal thalamus. We suggest that the presence of an low-threshold Ca^{2+} potential (LTCP)-mediated burst at the commencement of each UP state may be a mechanism whereby the thalamus is sending a specific priming signal to the cortex that the 'activated' or 'processing' phase of the slow oscillation is about to begin. Of course, the idea that the LTCP-mediated bursts of the slow oscillation signal the upcoming transmission of high-priority information is essentially equivalent to that which has been suggested for the role of LTCP-mediated bursts in TC neurons during wakefulness. Indeed, we have recently postulated that similar cellular mechanisms may underlie both the slow oscillation and the ability to generate LTCP-mediated bursts from depolarized membrane potentials during the wake state. Thus these results suggest that whilst moderate activation of muscarinic acetylcholine receptors on thalamo-cortical neurons mediates a natural change from sleep to wake-related electrical activity.

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S3.P2

ANTIBACTERIAL ACTIVITY OF ANTIDEPRESSANTS, INHIBITORS OF MONOAMINE'S REUPTAKE, DEPENDS FROM THEIR ANTIDEPRESSIVE EFICACY ON SLEEP DISORDERS

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Unlimited uses of antimicrobial agents, frequently applied arbitrarily, contributed to the development of „antibiotic resistance" and new infectious diseases. Therefore searching for non-antibiotic agents with antimicrobial activity, antidepressants among them, is very topical. No less important is the question of whether the antimicrobial activity of antidepressants can be dependent on their effectiveness in restoring sleep disturbances in animal models of depression. Problem is important because antidepressants are supposed to restore disturbances characteristic for major depressive disorder (MDD) - sleep disorders among them, and effective drugs mustn't additionally worsen sleep and general condition of depressive patients. Study was aimed to investigate the antibacterial action of tricyclic, non-selective (melipramin, Group I) and selective (fluoxetine, Group II), antidepressants and the possible dependence of antimicrobial activity on their anti-depressive efficacy to sleep disturbances in animal models of depression. Wild white rat pups (n=5 in each group) received a subcutaneous injection of antidepressants, 30 mg/kg, two times daily, from postnatal day 7 to 28. Control rat pups received saline. Sleep EEG registration have been started 8–12 weeks after the drug discontinuation. Continuous sleep registration in each control rat was made for three consecutive days, 10.00 a.m. – 20.00 p.m. In experimental groups, EEG registration of sleep-wake cycling (SWC), with the same duration, was started after intraperitoneal injection of melipramin and /or fluoxetine (10 mg/kg and/or 15 mg/kg). *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus* and *Mycobacterium phlei* were used as test cultures. Melipramin, (0.01, 0.1 and 1 g/L) and fluoxetine (0.01, 0.1 and 1 g/L) were used for the studying of antibacterial spectrum. In adult rats, with postnatal exposure to melipramin and/or fluoxetine, sleep was disturbed significantly. Single-dose of melipramin produced worsening of sleep quality and whole inhibition of REM sleep during 4–5 h after drug injection. Sleep disorders like depression were developed in the recovery period (24 h after drug injection) - sleep quality becomes deteriorated, sleep interruptions increases, REM sleep latency diminishes, but its incidence rise. The influence of fluoxetine on SWC was relatively weaker and short-term indicating to higher anti-depressive efficacy of the drug. Antimicrobial activity of melipramin and/or fluoxetine on growth-development of *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus* and *Mycobacterium phlei* was dependent on their anti-depressive efficacy on sleep disturbances which has been only revealed by the selective inhibitor of serotonin reuptake, fluoxetine.

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S3.P3

BLOOD LEUKOCYTES IN YOUNG AND OLD RATS UNDER DESYNCHRONOSIS INITIATION ON THE BACKGROUND OF WHOLE BODY CRYOSTIMULATION

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The aim of the work was to study the effect of whole body cryostimulation (WBC) on leukocyte blood parameters in rats of different ages with a model of circadian desynchronosis (CD). The work was carried out on young and old (6 and 18 months) male outbred white rats according to biotic requirements. CD was initiated by single prolongation the light period by 12 h. One WBC (–120°C, 90 s) session was applied the day before CD initiation. Quantitative and qualitative assessment of leukocyte types were performed in blood smears after treated with fixative and stained with hematological dye, and integral leukocyte indices (ILI,), allowing to assess the state of certain links of immune system and body resistance without using special methods, were calculated. CD increased the band neutrophils number as well as cause leukocytosis and leukopenia in young and old rats correspondingly. Segmental neutrophils decreased in young animals and increased in old animals, but the change in lymphocyte number had the opposite direction. Eosinophils decreased only in young animals. Changes in ILI indicate an increase in young neutrophils, activation of cells of specific protection and hypersensitivity of the immediate type, strengthening of humoral immunity, intoxication, lack of inflammation and impaired immunoreactivity, and also increase adaptation ability in young animals. In old rats, immunoreactivity was impaired, inflammation and non-specific defence cells increased. CD initiation on the background of WBC caused to an increase in the total number of leukocytes and monocytes in young animals, and to decrease in old rats; segmental neutrophils, on the contrary. The lymphocytes and eosinophils decreased only in old rats. Band neutrophils increased, more significantly in young animals. ILI revealed a predominance of young neutrophils, macrophages and effector immune system activity, decreased immunoreactivity in young rats. The predominance of cellular immunity, increased intoxication, activation of inflammation and impaired immunoreactivity, predominance of nonspecific defence cells, microphages and allergy reduction were noted in old rats.

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S3.P4

PITUITARY-THYROID SYSTEM IN YOUNG AND OLD RATS UNDER PREVENTIVE WHOLE-BODY CRYOSTIMULATION AND CIRCADIAN DISRUPTION

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Perturbation of fluctuation of the endocrine system that occurs due to chronic circadian disruption (CD), resulted from shift-work, jet lag or irregular sleep-wake cycle, is recognized as the main mechanism of increasing the risk of cardiovascular, autoimmune and metabolic disorders as well as a number of psychological disorders. Thyroid hormones (TH) are necessary for normal differentiation and growth of the body, metabolism and thermoregulation, etc. Their synthesis and secretions from thyroid follicular cells are controlled by the thyroid-stimulating hormone (TSH), which level depends on the TH concentration in the blood. The main circadian pacemaker of the body located in the suprachiasmatic nuclei (SCN) of the anterior hypothalamus affects the TSH level as well, which is manifested in its daily fluctuations in the blood. Moreover, TSH amount is modulated by the sleep-wake cycle, the quality of which is altered to some extent under the whole-body cryostimulation (WBC). We aimed to study the preventive effect of WBC on activity of the pituitary-thyroid system in rats with the model of circadian disruption (CD). In young and old (6 and 18 months) males of white outbred rats, CD was modelled by a 12 h single prolongation of the light period. One WBC session was performed in a cryochamber (at a temperature of –120°C, 90 s) the day before the initiation of CD. The content of total (T4) and free thyroxine (T4f), total (T3) and free triiodothyronine (T3f) as well as TSH in blood serum (BS) was determined by enzyme-linked immunosorbent assay. The data were statistically processed by the Kruskal-Wallis method. Initiation of CD led to a decrease in TSH in BS in both young (5.35 ± 0.66 vs. 1.47 ± 0.07 nM/L, $p < 0.05$) and old rats (3.38 ± 1.42 vs. 0.81 ± 0.01 nM/L, $p < 0.05$). The preventive WBC application before CD initiation helped to maintain the level of TSH in the BS at the level of control values (4.64 ± 1.8 and 1.91 ± 0.11 nM/L, in young and old animals, respectively). No significant differences in the levels of total or free T3 and T4 in BS after CD and preventive WBC application were found (with exception for a decrease in T3f in old rats with WBC). Thus, the preventive WBC application stabilizes the response of the pituitary-thyroid system of young and old rats to the CD initiation.

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SESSION IV

FATIGUE
ADAPTATION TO ENVIRONMENT
THERMOREGULATION

Wednesday (September 15, 2021; 12:05 – 15:40)
Thursday (September 16, 2021; 10:05 – 10:55)

Chair:

Prof. Pawel Zalewski
Department of Physiology and Functional Anatomy, Collegium Medicum, Bydgoszcz

Prof. Malgorzata Tafil-Klawe
Department of Human Physiology, Collegium Medicum, Bydgoszcz

Prof. Justyna Rogalska
Department of Animal Physiology and neurobiology, The Nicolaus Copernicus University, Torun

DETAILED SESSION IV SCHEDULE

Part I - **FATIGUE**

Opening lectures (Wednesday, September 15, 2021; 12:05 – 13:25; *virtual stream A*)

S4.L1 STANDING UP FOR FATIGUE. **J. Newton** (Newcastle University - Consultant Physician, Newcastle Hospitals - Medical Director - Academic Health Science Network for North East and North Cumbria, United Kingdom).

S4.L2 FATIGUE AND NEUROLOGICAL IMPAIRMENT IN LONG-HAUL COVID-19. **M. Murovska** (Institute of Microbiology and Virology, Riga Stradins University, Riga, Latvia).

S4.L3 THE ROLE OF THE MICROBIOME IN FATIGUE: DOES SEX MAKE A DIFFERENCE? **K. Morten[1], I. Williams[1], J. Maclennan[2] J. Kenyon[4]** (Nuffield Department of Women's and Reproductive Health, University of Oxford, UK, [2]SoftCell Biological Research Soft Cell Biological Research, St. George, USA, [3]The Doveclinic, Hampshire, United Kingdom).

S4.L4 CARDIOPULMONARY AND AUTONOMIC CHARACTERISTIC OF FATIGUE. **S. Kujawski** (Nicolaus Copernicus University in Torun, Torun, Poland).

Oral presentations (Wednesday, September 15, 2021; 13:25 – 13:40; *virtual stream A*)

S4.L5 EFFECT OF FATIGUE GENERATED BY EFFORT ON REACTION TIME. **A. Jastrzebska, E. Bakonska-Pacon, I. Wierzbicka-Damska** (Department of Physiology and Biochemistry, University of Physical Education, Wroclaw, Poland).

Questions and answers

Part II – ADAPTATION TO ENVIRONMENT. THERMOREGULATION

Opening lectures (Wednesday, September 15, 2021; 13:45 – 15:05; *virtual stream A*)

S4.L6 PHYSIOLOGICAL ADAPTATIONS TO HEAT STRESS AND EXERCISE IN CELL CULTURE MODELS AND HUMANS. **K. Dokladny, P. Moseley** (University of New Mexico, Department of Internal Medicine, Division of Gastroenterology, Albuquerque, New Mexico, USA).

S4.L7 NEW VIEW ON THE IMPACT OF THE LOW FREQUENCY ELECTROMAGNETIC FIELD (50 HZ) ON STRESS RESPONSES - IS THE ADAPTATION POSSIBLE? **M. Stankiewicz, A Klimek, H. Kletkiewicz, A. Siejka, M. Klimiuk, J. Maliszewska, M. Jankowska, A. Nowakowska, J. Wyszkowska, J. Rogalska** (Department of Animal Physiology and Neurobiology, Faculty of Biological and Veterinary Sciences, Nicolaus Copernicus University in Torun, Torun, Poland).

S4.L8 FREEZE TO SURVIVE: ROLE OF MICROBIOM **A. Nowakowska, P. Idczak** (Nicolaus Copernicus University in Torun, Faculty of Biological and Veterinary Sciences, Department of Animal Physiology and Neurobiology, Torun, Poland).

Oral presentations (Wednesday, September 15, 2021; 15:05 – 15: 40; *virtual stream A*)

S4.L9 CAPSAICIN AND THERMOREGULATORY RESPONSES IN THE AMERICAN COCKROACH. THE INVOLVEMENT OF TRP RECEPTORS. **J. Maliszewska, M. Jankowska, H. Kletkiewicz, M. Stankiewicz, J. Rogalska** (Department of Animal Physiology and Neurobiology, Faculty of Biological and Veterinary Sciences, Nicolaus Copernicus University, Torun, Torun, Poland).

S4.L10 SOME FEATURES OF COLD ADAPTATION IN MEN DURING OVERWINTERING IN ANTARCTICA **D. Lutsenko[1], O. Shylo[1], K. Danylenko[2,3]** ([1]Institute for Problems of Cryobiology and Cryomedicine, Kharkiv, Ukraine, [2]National Antarctic Scientific Center, Kyiv, Ukraine, [3]Kharkiv National Medical University, Kharkiv, Ukraine).

Session summary

Poster session (Thursday; September 16, 2021; 10:05 – 10:55; *virtual stream D, interactive*)

S4.P1 DO ELITE ATHLETES HAVE DIFFERENT LEVELS OF A PHYSIOLOGICAL STRAIN (PSI) IN RESPONSE TO A SIMILAR SUBMAXIMAL EXERCISE PERFORMED UNDER TEMPERATE CONDITIONS AFTER A MEDIUM-TERM ACCLIMATION TO WHOLE BODY HYPERTHERMIA (MWBH) AND WHOLE BODY CRYOSTIMULATION (MWBC)? **I. Pokora[1], L. Wolowski[2], P. Wyderka[2]** ([1]The Jerzy Kukuczka Academy of Physical Education in Katowice, Institute of Sport Sciences, Department of Physiological-Medical Sciences, Katowice, Poland; [2]The Jerzy Kukuczka Academy of Physical Education in Katowice, Doctoral Studies, Katowice, Poland).

S4.P2 THE INFLUENCE OF REGULAR PROFESSIONA TRAINING ON THE RESTING TEMPERATURE DISTRIBUTION OF THE BODY SKIN. **M. Binek[1,2], I. Pokora[1], Z. Drzazga[2]** ([1]Academy of Physical Education in Katowice, Katowice, Poland, [2]University of Silesia in Katowice, Katowice, Poland).

S4.P3 EFFECT OF ANTI-INFLAMMATORY EXTRACTS ON COELOMOCYTES OF THE EARTHWORM LUMBRICUS TERRESTRIS. **A. Gren[1], G. Formicki[1], P. Massanyi[1,2], M. Halo[2], M. Massanyi[2]** ([1]Department of Animal Physiology, Institute of Biology, Pedagogical University of Krakow, Poland; [2]Department of Animal Physiology, Faculty of Biotechnology and Food Sciences, Slovak University of Agriculture, Nitra, Slovak Republic).

S4.P4 GEOGRAPHICAL ORIGIN REFLECTED IN PHYSIOLOGY - DIFFERENCES IN THERMAL BEHAVIOUR OF THREE HONEYBEE *APIS MELLIFERA* SUBSPECIES. **J. Bacia, P. Grodzicki** ([1]Nicolaus Copernicus University, Faculty of Biological and Veterinary Sciences, Department of Animal Physiology and Neurobiology, Torun, Poland).

S4.P5 BIORITHMOGENIC PROBLEMS OF HUMAN ADAPTATION TO ANTARCTIC CONDITIONS OF ACTIVITY. **Y. Moiseyenko, N. Vaschenko, E. Rozova** (Bogomoletz Institute of Physiology of the National Science Academy of Ukraine, Kyiv, Ukraine).

S4.P6 A NEW VIEW ON OVERWINTERING IN SNAILS: THE ROLE OF MICROBIOTA IN FREEZE TOLERANCE. **P. Idczak[1], A. Nowakowska[1], A. Kalwasinska[2]** ([1]Department of Animal Physiology and Neurobiology, [2]Department of Environmental Microbiology and Biotechnology, Nicolaus Copernicus University in Torun, Torun, Poland).

S4.L1

STANDING UP FOR FATIGUE

J. NEWTON

Newcastle University; Academic Health Science Network for North East and North Cumbria;
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Fatigue is a common symptom experienced by people with a range of chronic conditions. Its cause is unknown but its presence and severity associate with the presence of autonomic nervous system dysfunction. Abnormalities in autonomic function can be subjectively and objectively assessed and evidence is emerging that an individualized approach to management can lead to improvements in some patients. Innovative approaches to management such whole body cryotherapy might offer those with fatigue new treatments.

S4.L2

FATIGUE AND NEUROLOGICAL IMPAIRMENT IN LONG HAUL COVID-19

M. MUROVSKA

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Emerging aspects of the COVID-19 clinical presentation are its long-term effects, which are characteristic of the so-called “long-haul COVID”. Long-haul COVID-19 was defined as symptoms persisting for more than 6 weeks, with the consensus that most patients fully recover from COVID-19 in 4 to 6 weeks. Many COVID-19 „long haulers“ experience at least four lingering neurological symptoms, such as brain fog, headache and the loss of sense of smell or taste, even if they were never hospitalized for their initial illness. Overall, 85% of participants reported at least four neurological symptoms. The most common symptom was „brain fog“ or trouble thinking, reported by 81% of participants; followed by headaches, reported by 68%; and numbness or tingling, reported by 60% of participants. More than half reported problems with their sense of taste or smell; 47% reported dizziness; 30% reported blurred vision; and 29% reported ringing in the ears. Other common, but not neurological, symptoms included fatigue, depression and anxiety, insomnia and gastrointestinal symptoms. In many patients, their symptoms fluctuated, or came and went, for months. When they were asked how much they felt they had recovered to their pre-COVID-19 level, on average, patients said they felt only 64% recovered after about five months. As COVID-19 causes ME/CFS-relevant symptoms in patients and this increases the need for monitoring of patients for even longer after recovering from COVID-19’s symptoms, in order to prevent complications and the progression of chronic diseases. The similarity and overlap of ME/CFS and long-haul COVID19 symptoms suggest possibility of similar pathological processes.

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S4.L3

THE ROLE OF THE MICROBIOME IN FATIGUE: DOES SEX MAKE A DIFFERENCE?

K. MORTEN[1], I. WILLIAMS[1], J. MACLENNAN[2], J. KENYON[3]

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Microbial imbalance of the intestinal biome is a key associated factor in many chronic conditions including Myalgic Encephalomyelitis (ME/CFS). Our major research goals are too increase our understanding of ME/CFS and open up new treatment options. If a leaky gut is a key component of ME/CFS, restoring a normal gut microbiome balance could be a life changing treatment options. Our collaborator SoftCell Biologicals Research (SBR) have developed approaches examining the host tissue biome. This is an un-tapped area of medicine with the presence of significant levels of wall-less (L-Form) opportunistic pathogens present in many chronic disease states. Using novel L-Form culturing methods SBR have treated L-form cultures from patients with chronic urinary tract infections (CURTIs) using a standard antibiotic panel. Clinicians acting on this information have noticed improvements in a number of patients. Clinical studies, using this approach will allow antibiotics tested in the laboratory to be used to treat patients in a blinded trial setting. In this presentation, I will highlight our research with the Doveclinic exploring levels of gut dysbiosis in a broad range of conditions many of whom suffer with fatigue. The impact of age and sex on the gut microbiome will be explored with a focus on ME/CFS and cancer. Exciting data from a comparison of recent trials of Gut Floral Replacement Therapy (GFTR) to the more conventional Faecal Microbiota transplantation (FMT) will be presented.

S4.L4

CARDIOPULMONARY AND AUTONOMIC CHARACTERISTIC OF FATIGUE

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Fatigue is a physiological phenomenon when it follows prolonged activity, and resolves completely with rest. Overreaching occurs as a result of increase of intensity of physical exercise training program is also considered as its physiological side-effect. However, there are conditions in which fatigue is not resolved with rest easily. Overtraining syndrome (OTS) and chronic fatigue syndrome (CFS) are conditions in which underlying pathophysiology is related to, inter alia, chronic fatigue. In the above study, cardiopulmonary and autonomic profile of subjects with chronic fatigue would be explored. CFS patients were included if they met the diagnostic criteria of, the Fukuda case definition. Initially, 1400 volunteers were assessed for eligibility onto the trial with 1308 being excluded. This left 69 individuals who met the trial inclusion criteria. VO_{2peak}, $VO_{2submax}$ and heart rate (HR) were assessed using cardiopulmonary exercise testing. A Task Force Monitor was used to assess ANS functioning. Results: Two autonomic nervous system function profiles could be distinguished in the above sample (parasympathetic dominant and sympathetic dominant). Moreover, based on indicator of sympathetic nervous system activity, several clusters with distinct clinical profiles could be distinguished. Conclusions: Both cardiopulmonary and autonomic nervous system function could are important features related to chronic fatigue. Future should further explore pathophysiology of OTS. Presumably, knowledge from this field could be applied to development of therapeutic strategies of chronic fatigue treatment in other pathological conditions.

S4.L5

EFFECT OF FATIGUE GENERATED BY EFFORT ON REACTION TIME

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The simple reaction time (SRT), minimal time needed to respond to a stimuli, is a physiological response toward a neutral sense stimulus. The aim of presented study was to estimate the changes of simple reaction time (RT) in fatigue condition induced by two efforts of a different nature. Twenty participants performed incremental test (INC) to volitional exhaust for fitness level and VO_{2max} estimation. The 40-min effort (LE) with intensity of 80% VO_{2max} was performed for fatigue elicitation. Respiratory parameters were measured breath-by-breath (K4b2, Cosmed, Italy). Participants performed a SRT task before (pre-test) and follows the 5 min of recovery (post-test) for incremental and 40-min effort. Visual: red, orange, green light and auditory: one sound, stimuli were given in random order. The mean value of reaction time was calculated excluding the first and last values and separately for each type of stimuli (3 colors and a sound). Blood was collected for estimation of lactate concentration (Dr Lange Kuvettentest, LKM 140, Germany) and venous blood was collected to determine the concentration of selected neurotransmitters (ELISA Test Demeditec Diagnostics GmbH Germany). VO_{2max} in incremental test was 53.79 ± 4.52 ml/kg/min. Lactate concentration in blood reach 9.25 ± 2.77 and 4.25 ± 1.2 (mmol) for INC and LE respectively. Concentration of neurotransmitters: adrenaline, noradrenaline and dopamine in plasma, and serotonin in serum increased significantly as a result of both efforts ($p < 0.05$). Independently on effort performed, the direction of alteration in reaction time was the same and showed decrease. There was no differences in SRT in pre-test measurement while significant effect of conducted efforts on SRT were noted (INC, P=0.04; LE, P=0.003, respectively). Significant decrease in SRT for red and orange light after INC (P=0.05 and P=0.003) and LE (P=0.02, P=0.04), and sound stimuli after LE (P=0.03) effort were noted. We expected the longer reaction time after the efforts made. Five minutes after the tests, RT were still shorter than at rest. Interestingly, the most noticeable reduction in reaction time was noted for red and orange stimuli, but not for green. The increase of neurotransmitters in plasma and serum indicates the development of fatigue, although not translated into a decline of SRT directly after the efforts. It may be that 5 min after the effort the excitation of nervous system enables faster reaction and a biochemical changes resulted by effort occur before fatigue appears in nervous system function.

Acknowledgements: Research granted by MNiSW nr 0022/RS4/2016/54

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S4.L6

PHYSIOLOGICAL ADAPTATIONS TO HEAT STRESS AND EXERCISE IN CELL CULTURE MODELS AND HUMANS

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Cells utilize heat shock proteins to fold de novo synthesized cellular proteins, to refold dysfunctional proteins that were damaged during cellular stress, or to send a protein for degradation if its repair is beyond the capacity of a cell. In eukaryotic cells, there are two main mechanisms responsible for degradation of dysfunctional proteins: proteasomal degradation and autophagy which recycles cellular proteins as well as protein complexes, or cellular organelles. Both protein synthesis and degradation depend on the coordination between autophagy and HSPs. In our studies, we have utilized heat stress or exercise to illustrate the importance of HSPs in the regulation of fever, proinflammatory cytokine expressions, or tight junction barrier in cell culture models, animals, or humans. We have also shown the sequential activation and inhibition of autophagy in the initial phase of exercise (protein degradation) that is followed by a progressive induction of heat shock protein response in the later phase of exercise (protein synthesis). We conclude that HSPs by maintaining internal protein homeostasis are necessary for the physiological adaptations of the cell and the whole organism.

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NEW VIEW ON THE IMPACT OF THE LOW FREQUENCY ELECTROMAGNETIC FIELD (50 HZ) ON STRESS RESPONSES – IS THE ADAPTATION POSSIBLE?

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Problem of the impact of low frequency electromagnetic field (50 Hz) (ELF-EMF) on human health seems to be still far from the definitive explanation. Effects of the ELF-EMF are inconclusive (beneficial or harmful) and there is no clear concept put forward that would give the comprehensive explanation of the observed phenomenon. Whether or not magnetic field exposure is causally related to increased health risks has led many scientists to examine the potential mechanisms by which ELF-EMF might affect human health. Obviously electromagnetic fields accompany the life of the organisms and probably, to certain extent modify some crucial neuronal processes, but we suggested that the impact is not definitely negative, and direction and dynamics of ELF-EMF depend on value of magnetic induction (magnetic flux density). Our research has been directed into 1) determining whether ELF-EMF exhibits hormesis, it means bidirectional action depending on field strength (magnetic induction: 1 or 7 mT) and 2) into verifying the possibility of adaptation to ELF- EMF exposure on animal model. Many studies have suggested an association between chronic ELF-EMF exposure and anxiety and/or depression. Existing data indicate that the exposure to ELF-EMF may count as a mild stress situation and could be a factor in the development of disturbances of brain stress system: hypothalamo-pituitary-adrenal (HPA) axis. Thus, we suggested that effects of low and high intensity ELF-EMF exposure might be related to different activation of HPA axis (changes in the level of HPA axis hormones (corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH) and corticosterone) and their receptors. The exposure to ELF-EMF can establish a new "set-point" for stress systems activity. Corticosterone initiates physiological and behavioural responses through two types of receptors: mineralocorticoid (MR) and glucocorticoid (GR) receptors. Moreover, both MR and GR receptors are abundant in the hippocampus; which regulates the negative feedback of the HPA axis through this MR/GR dual-receptor system of crucial importance for the homeostatic control. The interplay between all components of stress response (hormones and their receptors) seems to determine the final effect of ELF-EMF exposure. We have found the hormetic (bidirectional) effect of ELF-EMF which results in different activation of stress response system hypothalamo-pituitary-adrenal (HPA) axis and as the consequence of that the subsequent changes in stress hormones and their receptors levels also appeared. A single exposure to ELF-EMF with a value of 1 mT resulted in a slight increase in HPA axis activity (CRH in hypothalamus; ACTH in the pituitary gland, CORT in adrenal glands and plasma). However, after each subsequent exposure the level of measured parameters was lower or not different from control level. It may indicate that ELF-EMF of low intensity activates some endogenous adaptive processes. ELF-EMF of 7 mT led to sustained stimulation of stress systems activity which was higher with each next exposure, indicating that the stronger field - 7 mT is a factor, which can be recognised as harmful for organism. We have also found the increase of MR receptors density only in rats exposed to ELF-EMF of 1 mT, however in 7 mT group the level of MRs was not detectable. The level of GR receptors in 1 mT group was similar to control level or slightly decreased, but in 7 mT group the diminished level of GR receptors was clear. MR receptors needs to be present and functional for neuronal survival in the damaged brain regions. The MR expression in 1 mT ELF-EMF exposed group possibly represents an endogenous response that may serve as a compensatory mechanism designed to increase the neuronal plasticity. On the other hand, the strong imbalance between MR/GR receptors expression after exposure to 7 mT ELF-EMF suggests the disturbed control of HPA axis activity, which could result in some harmful processes leading to nervous system disorders. The ELF-EMF-induced dose dependent different activation of HPA axis can in turn can initiate cellular hormesis, it means bidirectional activation of intrinsic signaling pathways: 1) of compensative character promoting the neuroadaptation as the consequence of low intensity ELF-EMF (1 mT), or 2) causing disturbance of intracellular homeostasis leading to increase of the sensitivity to subsequent stress factors in case of high intensity ELF-EMF (7 mT). For the first time we demonstrated the bidirectional (hormetic) mode of action of ELF-EMF in vertebrates. Our research provided the new comprehensive data on the impact of ELF-EMF on mammals' organism with reference to HPA-axis activity with the accent on potential consequences of the ELF-EMF for health. The project can contribute to explaining the fundamental mechanisms of bidirectional responses to ELF-EMF and it can lead to a new view on possible therapeutic properties of magnetic field and provide new data for reliable risk assessment of the exposure to ELF-EMF, what is of crucial importance for the human health.

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S4.L8

FREEZE TO SURVIVE: ROLE OF MICROBIOM

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Animals have evolved special mechanisms to counteract the life-endangering effect of extremely low temperatures and to survive freezing. The mechanism include a large variety of structural and functional adaptations such as changes in the cell membrane fluidity, proteins conformation, reduced metabolic activity, and particular ability to avoid intracellular ice formation resulting from synthesis of cryoprotectants, which overcomes uncontrolled freezing. All above mentioned factors are characteristic of both endotherms and ectotherms that experience seasonal temperature changes and pass long periods of cold-stress in a hypometabolic state called hibernation or overwintering. Recently, the importance of the gut microbiome in freezing tolerance has been highlighted. Environmental temperature is an important factor that affects the composition of gut microbial communities in many animal taxa, including invertebrates and vertebrates, and the microbiome's relationship with the host. Gut bacteria are involved in multiple physiological processes, assisting their hosts with digestion, disease resistance, environmental resistance and cold hardiness during hibernation, and subsequently to maintenance and survival. Gut microbiota upregulate the levels of cryoprotectant transcripts and metabolites, which increases the resistance to long-term low-temperature stress by stimulating the host cryoprotectant pathways. Because microbes are ectotherms, the microbiome of ectothermic animals will be exposed to the same temperature fluctuations as those of their hosts. In mammalian heterotherms, e.g. in hamsters and bats, the thermal conditions experienced by bacteria during winter are likely to change less dramatically in metabolically active animals than they do during hibernation. These fluctuations have a great potential to challenge the host's microbe community, and to modify the community interactions with the host. In ectothermic organisms, both vertebrates and invertebrates, microbes are subjected to the same temperature changes as those of their hosts, therefore, the host overwintering-related changes may be less relevant than those induced by winter itself. It must be stressed that for some ectothermic hosts the only possibility to survive winter is due to certain types of bacteria that control the partial freezing process by acting as ice-nucleating factors. Despite the progress that has been made, understanding of how temperature affects the animals gut microbiota remains still limited. Therefore, we will try to answer the following questions: 1) do microbes influence overwintering entry and exit? and 2) which physiological changes in the host affect the conditions under which different bacterial species compete.

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S4.L9

CAPSAICIN AND THERMOREGULATORY RESPONSES IN THE AMERICAN COCKROACH. THE INVOLVEMENT OF TRANSIENT RECEPTOR POTENTIALS RECEPTORS

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Transient receptor potential (TRP) receptors are cation channels involved in detection of multiple stimuli, with some members acting as temperature sensors (thermo-TRP). In insects thermos-TRP receptors are responsible for sensation of temperatures in normal temperature range (dTRPA1), as well as nociceptive temperatures (painless, pyrexia, TRPL, Brivido or Pkd2). Thermo-TRP are also sensitive to chemicals ligands, which affect channel activity and therefore induce changes in insects' thermal behavior. We demonstrated that capsaicin, an alkaloid that activates mammalian heat receptor (TRPV1), induces thermoregulatory responses in American cockroach. Changes in behavioral thermoregulation (preference for cold), as well as physiological thermoregulation (decrease of head temperature in cockroaches placed at constant ambient temperature) were observed after capsaicin treatment. This alkaloid changed also cockroaches' response to noxious ambient temperature. These results indicate involvement of TRP receptor in cockroaches' thermosensation. We also aimed to determine the role of octopamine (potential neurotransmitter in TRP related processes) in capsaicin-induced thermoregulatory response in the American cockroach.

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S4.L10

SOME FEATURES OF COLD ADAPTATION IN MEN DURING OVERWINTERING IN ANTARCTICA

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Wintering in Antarctica is associated with the impact of extreme environmental factors, including the cold exposure. The adaptation of human to extreme conditions is largely ensured by the vegetative mechanisms of regulation of the organism. We used heart rate variability (HRV) analysis to evaluate the winterer's adaptation to cold. There were 23 winterers of 21 and 23 Ukrainian Antarctic expeditions aged from 22 to 63 years old (all men, average age 39.5 years) took part in the study. Additionally, 17 winterers took part in the study with 3 min cold pressure test (CPT). The CPT was performed by immersing the right hand into a cold water (T water 9.2 ± 1.2°C). The measurements were carried out every month. All participants were informed about the objectives of the study and agreed to participate in it. We found that winterers can be divided into at least 2 groups depending on the type of response to cold. In one group the responses were connected with the sympathetic nervous regulation (an increase in heart rate and blood pressure, a significant predominance of LF components of HRV). But in the other group the heart rate decreased, LF components were only slightly higher than HF ones, and were even less sometimes, indicating about parasympathetic regulation mechanisms activation. Recently it was described the reduction of sympathetic and growth of parasympathetic activity in winterers after overwintering. (Harinath et al, 2005) and we believed that this phenomenon may be related to the one we observed.

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S4.P1

DO ELITE ATHLETES HAVE DIFFERENT LEVELS OF A PHYSIOLOGICAL STRAIN (PSI) IN RESPONSE TO A SIMILAR SUBMAXIMAL EXERCISE PERFORMED UNDER TEMPERATE CONDITIONS AFTER A MEDIUM-TERM ACCLIMATION TO WHOLE BODY HYPERTHERMIA (MWBH) AND WHOLE BODY CRYOSTIMULATION (MWBC)?

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The aim of this study was to indicate the differences in the body physiological strain (PSI) in response to exercise performed under temperate conditions after a medium-term sauna-based heat acclimation (MWBH) and after a series of whole body cryostimulation (MWBC) in elite cross-country skiers. Ten elite cross-country skiers participated in four exercise trials, (2) before and after a series of ten sauna baths (MWBH) or (2) before and after a series of ten MWBC. Thermal and physiological variables were measured before and after the exercise tests. The series of ten sauna baths induced a moderate decrease in the heart rate (HR) at rest, but did not influence the baseline internal (Tac; p=0.31), body ($\overline{T}$b; p=0.53) and skin ($\overline{T}$sk; p=0.38) temperatures. The series of MWBC did not induce an either change in the heart rate (HR) at rest or the baseline internal (Tac; p=0.31) and body ($\overline{T}$b; p=0. 38) temperatures but influenced on the skin temperature ($\overline{T}$sk; p=0.008). In response to exercise, physiological strain (PSI) tended to be lower (p=0.31) after MWBH but not after MWBC (p=0.88). There was a significant difference in *f*HR PSI (p=0.02) and *f*Tac PSI (p=0.02) in response to exercise between MWBH and MWBC groups. The results of this study indicated that level of physiological strain was similar during exercise test performed after MWBH and MWBC acclimations. There were differences in the share of contribution of the cardiovascular fraction and the thermoregulatory fraction to the PSI (circulatory strain, thermoregulatory strain) during exercise trials performed in this study after heat and cold adaptations in athletes.

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S4.P2

THE INFLUENCE OF REGULAR PROFESSIONA TRAINING ON THE RESTING TEMPERATURE DISTRIBUTION OF THE BODY SKIN

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The aim of study was to evaluate the difference in skin temperature in selected muscles zones of limbs at rest in ten male cross-country skiers who train competitively and ten AWF students with normal physical activity. For both groups, measurements were carried out thermal imaging camera FLIR E95. Measurements were made in conditions necessary for proper thermal imaging. Generally, infrared thermography indicated that at rest skin temperature over muscle of non-training people is higher than that of professional cross-country skiers. The analysis of the results showed that the temperature obtained at rest differs statistically significantly in the area of chest and back, while in the lower parts of the body these differences are generally invisible(except for vastus lateralis and knees). The greatest relative differences in skin temperature are for the trapezius and deltoid muscles, and the smallest for the muscles on the back of the calf. Our research shows that professional sports training has an impact on the resting body temperature distribution of an athlete. In our research group (cross-country skiers), it lowered the skin temperature compared to the control group.

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S4.P3

EFFECT OF ANTI-INFLAMMATORY EXTRACTS ON COELOMOCYTES OF THE EARTHWORM LUMBRICUS TERRESTRIS

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Due to the specific habitat conditions in which they live, earthworms are constantly exposed to pathogens. Consequently, they have evolved various immuno-defense mechanisms, including cellular (coelomocytes) and humoral responses, which may help to repair and/or protect host cells and tissues but also can kill ingested pathogens. Earthworm coelomocytes are important for the assimilation and elimination of exogenous compounds and play a key role in the processes of phagocytosis and inflammation. Plants can provide a vast source of active natural products for the discovery of new drugs. Natural products play a significant role in relation to the prevention and treatment of inflammatory conditions. In the present works, we studied the effects of the dermal exposure of *Lumbricus terrestris* (*in vivo*) to different anti-inflammatory extracts: α-bisabolol, licorice, honey and then earthworms coelomocytes (*in vitro*) were exposed to anti-inflammatory extracts. Our results imply that extracts affect the earthworms immune system. We hypothesized that that studying the simpler immune response demonstrated by earthworm is important for understanding the evolution of immune system in higher vertebrates.

This research was supported by the Discipline Research Fund (WPBU/2020/05/00454) Pedagogical University of Krakow.

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S4.P4

GEOGRAPHICAL ORIGIN REFLECTED IN PHYSIOLOGY - DIFFERENCES IN THERMAL BEHAVIOUR OF THREE HONEYBEE *APIS MELLIFERA* SUBSPECIES

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Thermal preferences of three honeybee Apis mellifera subspecies reared in Poland-Caucasian, Carniolan and Central European bee were compared using the thermal gradient. Eighteen virgin honeybee Queens (six repetitions for each subspecies experimental group) with their retinues, counting 5–12 workers (3–14 day-aged), originated from that year's breeding (2019) in breeding apiaries. The 24-hour average ambient temperature selected was slightly lower in the Caucasian bee (*A.m. caucasica* G.), compared with the Carniolan bee (*A.m. carnica* P.) and the Central European bee (*A.m. mellifera* L.). Simultaneously, both in the 16 hours of daily activity and 8-hour of nocturnal rest Caucasian bee (*A.m. caucasica* G.) chose significantly lower ambient temperatures than the Carniolan bee (*A.m. carnica* P.) and the Central European bee (*A.m. mellifera* L.). Caucasian bees during the entire (3-day) registration period showed higher oscillations of the ambient temperature selected than in the other tested subspecies, which most probably results from differences between given subspecies in single individual body size and abundance of families. Our experiments undoubtedly showed the influence of the honeybee subspecies geographical origin on the thermoregulation of those insects.

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S4.P5

BIORITHMOGENIC PROBLEMS OF HUMAN ADAPTATION TO ANTARCTIC CONDITIONS OF ACTIVITY

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A large number of scientific works are devoted to the study of the role of melatonin in the regulation of circadian rhythms of organism systems. With a certain degree of probability, the state of melatonin secretion can be judged by changes in human body temperature, because the correlations between the dynamic changes of these indicators are extremely close. Therefore, in order to establish the characteristic features of regulatory influences on changes in circadian architectonics of indicators of functional systems of the human organism in Antarctica, studies of circadian organization of body temperature were conducted (body temperature was measured at three points oral cavity, under the armpit and on the scalp). The results showed that at the initial stage of winter the body temperature did not have the correct shape of the circadian rhythm, which is known to be characterized by low values at night, a gradual increase in the morning, and peak values in the afternoon. In the Antarctic autumn, night decrease in body temperature did not occur, the acrophase of the minimum shifted to 8 o'clock in the morning with its subsequent increase, but already at 16 o'clock there was a tendency to decrease. In winter, sinusoidal dynamics of periods of decrease and increase in body temperature of winterers (approximately every four hours) during the day was observed, which probably reflected the presence of significant changes in the mechanisms of humoral regulation. In the spring, the circadian architectonics of body temperature leveled off somewhat, but the duration of the low level remained shifted to the morning hours. In summer, the state of circadian rhythms of body temperature deteriorated, which led to the absence of significant changes in body temperature, even at night, when winterers need complete rest. At the same time, the body temperature briefly decreased in the morning, and remained at the same level for most of the day. Thus, the established dynamics of changes in the circadian architectonics of the body temperature of winterers may be indirect evidence of significant changes in the humoral regulatory chain, which occur under the influence of biorhythmogenic factors (season inversion, change of photoperiodicity and time zone, daily alternations and monochromaticity of the environment), which indicates the presence of desynchronous and maladaptive disorders. These changes are confirmed by the parallel results of the study of the dynamics of morpho-functional characteristics of the mitochondrial apparatus, which indicate the rearrangement of subcellular structures that signaling the formation of consequential signs of stress.

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S4.P6

A NEW VIEW ON OVERWINTERING IN SNAILS: THE ROLE OF MICROBIOTA IN FREEZE TOLERANCE

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Snails in the temperate zone are seasonally subjected to extreme climatic conditions with temperatures below freezing point of their body fluids. Because water is necessary for all life processes, animals developed two adaptive mechanisms. The first one is avoidance of freezing (supercooling) and the other one is the ability to endure ice formation. Before winter, land snails empty their gut, reduce body water content, and produce cryoprotectant substances that prevent ice crystals from forming inside their cells. However, the role of cryoprotectants in cold tolerance of *Helix pomatia* snails is still uncertain. We suppose that despite emptying the gut by the snails in the autumn, some bacteria remain in the intestine even during hibernation and are known to have ice-nucleating activity. Gut bacteria are involved in both of those mechanisms related to cold resistance and also in multiple physiological processes, such as digestion, disease and environmental resistance. To test whether freezing tolerance in the wild population of the *H. pomatia* snails is associated with their intestinal microbiota, we conducted a series of experiments on animals collected over the period of their annual activity at two-month intervals, starting from spring, immediately after their arousal from winter torpor. Additional experimental groups were animals acclimated to autumn conditions during summer (8D:16N, low temperature), and to summer conditions during autumn (16D:8N, high temperature). Gut microbiota samples obtained from the intestinal tract were cultivated in 10°C for 14 days on selective media containing colloidal hitine, cellulase and MRS, followed by 16S rRNA gene sequencing as well as the whole genome sequencing. The analysis of 16S rRNA gene sequences allowed us to identify cultivable psychrophilic snail gut bacteria belonging mostly to Alphaproteobacteria and Gammaproteobacteria class in all seasons and to Betaproteobacteria and Mollicutes class in some seasons. The obtained results show that both photoperiod and temperature affecting intestinal microbiota are related to external hibernation signaling in land snails. The conducted experiments have also contributed to expanding the collection of externally cultivable cultures.

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SESSION V

BODY FLUID HOMEOSTASIS
RENAL FUNCTION

Friday (September 17, 2021; 10:00 – 10:45)
Friday (September 17, 2021; 11:45 – 13:35)

Chair:

Prof. Elzbieta Kompanowska-Jezierska
Department of Renal and Body Fluid Physiology, M. Mossakowski Medical Research Institute, Polish Academy of Science, Warsaw, Poland

Prof. Maciej Jankowski
Department of Clinical Chemistry, Medical University of Gdansk, Gdansk, Poland

DETAILED SESSION V SCHEDULE

Opening lecture (September 17, 2021; 11:45 – 12:15; *virtual stream B*)

S5.L1 BLOCKADE OF ENDOTHELIN RECEPTOR AS AN ADJUVANT THERAPY IN THE TREATMENT OF CHRONIC KIDNEY DISEASE – STUDIES IN REN-2 TRANSGENIC RATS. **I. Vaneckova** (Institute of Physiology, Czech Academy of Sciences, Prague, Czech Republic).

Oral presentations (September 17, 2021; 12:15 – 13:35; *virtual stream B*)

S5.L2 RENAL EFFECTS OF β,γ-METHYLENE ATP, P2X RECEPTOR AGONIST, IN NORMO- AND HYPERGLYCEMIC RATS. G. Chyla, E. Kreft, M. Jankowski (Department of Clinical Chemistry, Medical University of Gdansk, Poland).

S5.L3 ANGIOTENSIN II IN THE MEDIAL PREOPTIC AREA MEDIATES CARDIOVASCULAR REGULATION, BUT NOT MICTURITION CONTROL. **S. Daiuto[1], P. Aronsson[2], M. Sato[1]** ([1]Centro Universitario FMABC, Santo Andre, Brazil, [2]Department of Pharmacology, Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden).

S5.L4 HYPOTENSIVE EFFICIENCY OF EPOXYEICOSATRIENOIC ACID ANALOG (EET-A) AND 20-HETE AGONIST (AAA) IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). **I. Baranowska[1], O. Gawrys[1,2], A. Walkowska[1], Z. Huskova[2], Z. Honetschlagerova[2], J.R. Falck[3], J.D. Imig[4], L. Cervenka[2,5], E. Kompanowska-Jezierska[1]** ([1]Department of Renal and Body Fluid Physiology, M. Mossakowski Medical Research Institute, Polish Academy of Science, Warsaw, Poland; [2]Center for Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague, Czech Republic; [3]Department of Biochemistry, University of Texas Southwestern Medical Center, Dallas, TX, U.S.A; [4]Department of Pharmacology and Toxicology, Medical College of Wisconsin, WI, U.S.A; [5]Department of Pathophysiology, 2nd Faculty of Medicine, Charles University, Prague, Czech Republic).

S5.L5 THE ROLE OF ADENOSINE (ADO) IN CONTROL OF RENAL HAEMODYNAMICS AND EXCRETION IN NORMO-(NG) AND HYPERGLYCAEMIC (HG) SPRAGUE DAWLEY RATS. **J.D. Sitek, A. Walkowska, M. Kuczeriszka, L. Dobrowolski** (Department of Renal and Body Fluid Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S5.L6 DIFFERENTIAL EFFECTS OF HIGH-FAT DIETS VARYING IN FATTY ACID COMPOSITION ON THE KIDNEY HISTOLOGY AND EXPRESSION OF GENES RELATED WITH CELLULAR STRESS AND WATER-ELECTROLYTE HOMEOSTASIS. **A. Grzesiak[1], A. Dunislawska[2], M. Grabowska[3], K. Michalek[1], M. Ozgo[1], K. Liput[4], M. Pierzchala[4], A. Herosimczyk[1] A. Lepczynski[1]** ([1]West Pomeranian University of Technology, Szczecin, Poland, [2]University of Science and Technology in Bydgoszcz, Poland, [3]Pomeranian Medical University, Szczecin, Poland, [4]Institute of Genetics and Animal Biotechnology, Jastrzebiec, Poland).

Session summary

Poster session (September 17, 2021; 10:00 – 10:45; *virtual stream C*)

S5.P1 URINARY EXCRETION OF EXTRACELLULAR VESICLES IN PATIENTS IN THE EARLY PERIOD AFTER KIDNEY TRANSPLANTATION. **K. Salaga-Zaleska[1], A. Kuchta[1], B. Bzoma[2], A. Ploska[3], L. Kalinowski[3], A. Debska-Slizien[2], M. Jankowski[1]** ([1]Department of Clinical Chemistry; Medical University of Gdansk, Poland, [2]Department of Nephrology, Transplantology and Internal Diseases, Medical University of Gdansk, Poland, [3]Department of Medical Laboratory Diagnostics - Biobank Fahrenheit BBMRI.pl; Medical University of Gdansk, Poland).

S5.P2 AGING AFFECTS URINARY BLADDER REACTIVITY IN FEMALE WISTAR RATS: AN IN VIVO PREPARATION. **V. Correia[1], C. Magaldi[2], M. Moreno[2], F. Magaldi[2], B. Do Vale[1], L. Maifrino[2], M. Sato[1], E. Cafarchio[1]** ([1]Department of Morphology and Physiology, Centro Universitario FMABC, Santo Andre, SP, Brazil, [2]Universidade Sao Judas Tadeu, Sao Paulo, SP, Brazil).

S5.P3 SODIUM APPETITE IS INDUCED BY SWIMMING EXERCISE IN WISTAR RATS. **D. Vantini[1], G. Petri[2], J. Dos Santos[2], F. Fonseca[3], R. de Almeida[1], M. Sato[1]** ([1]Department of Morphology and Physiology, Centro Universitario FMABC, Santo Andre, SP, Brazil, [2]Department of Animals Care, Technical and Experimental Surgery, Centro Universitario FMABC, Santo Andre, SP, Brazil, [3]Laboratory of Clinical Analysis, Centro Universitario FMABC, Santo Andre, SP, Brazil).

S5.P4 THE ROLE OF PURINE P1 RECEPTORS IN CONTROL OF THE RENAL EXCRETION DEPENDS ON RAT'S AGE AND DURATION OF STREPTOZOTOCIN INDUCED HYPERGLYCAEMIA. **L. Dobrowolski, M. Kuczeriszka, A. Walkowska, J.D. Sitek** ([1]Department of Renal and Body Fluid Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S5.P5 THE ROLE OF ANGIOTENSIN 1-7 IN CONTROL OF BLOOD PRESSURE, RENAL HAEMODYNAMICS, AND EXCRETION IN RATS MODEL OF STREPTOZOCIN-INDUCED DIABETES. **L. Dobrowolski, A. Walkowska, E. Kompanowska-Jezierska, J.D. Sitek, M. Kuczeriszka** ([1]Department of Renal and Body Fluid Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S5.P6 HYPERGLICAEMIA MODULATES P1 RECEPTORS IMPACT ON THE RENAL CIRCULATION AND URINE EXCRETION BUT NOT TISSUE NO. **A. Walkowska, M Kuczeriszka, J.D Sitek, L. Dobrowolski** ([1]Department of Renal and Body Fluid Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S5.L1

BLOCKADE OF ENDOTHELIN RECEPTOR AS AN ADJUVANT THERAPY IN THE TREATMENT OF CHRONIC KIDNEY DISEASE - STUDIES IN REN-2 TRANSGENIC RATS

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Chronic kidney disease (CKD) is a growing problem both in the developed and developing countries. Apart from significant morbidity and mortality and substantial decrease of quality of life, it is a growing financial burden for both the patients and societies. CKD arises as a frequent complication of diabetes, obesity and hypertension. Since it is usually unrecognized for a long time, it often progresses to the end-stage renal disease. Due to the ageing of world population, the prevalence of CKD is sharply increasing in recent decades, affecting more than 10% of the adult population. CKD is characterized by the development of progressive glomerulosclerosis, interstitial fibrosis and tubular atrophy along with a decreased glomerular filtration rate. This is associated with podocyte injury and a progressive rise in proteinuria. Although blockers of renin-angiotensin system (angiotensin converting enzyme inhibitors and angiotensin type 1 receptor blockers) are used as the "gold standard" in the treatment of CKD due to their antihypertensive and renoprotective effects, they only partially slow down the progression of CKD to end stage renal disease. Therefore, new therapeutics are urgently needed. Endothelin receptor blockers belongs to the promising drugs in this field. There are two types of G-protein coupled receptors, ET_A and ET_B – ET_A receptors located on vascular smooth muscle cells mediate vasoconstriction and cell proliferation, while ET_B receptors are located mainly on endothelial cells and mediate vasodilation, ET-1 clearance and inhibition of sodium reabsorption in the renal collecting duct, thus contributing to the regulation of sodium and water homeostasis. As endothelin-1 (ET-1) leads through the activation of ET_A receptors to renal cell injury, inflammation, fibrosis and finally to proteinuria, it is not surprising that ET_A receptor blockers were proven to have beneficial renoprotective effects in both experimental and clinical studies. Hypertensive Ren-2 transgenic rats (TGR) in combination subjected to partial nephrectomy are a good model of chronic kidney disease. Our results in heterozygous TGR rats with ablation nephropathy indicated the positive antiproteinuric effects of ET_A blockade using atrasentan as additional therapy to RAS blockade (especially in combination with diuretics).

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S5.L2

RENAL EFFECTS OF B,Γ-METHYLENE ADENOSINE TRIPHOSPHATE (ATP), P2X RECEPTOR AGONIST, IN NORMO- AND HYPERGLYCEMIC RATS

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Extracellular nucleotides affecting target cells through activation of purinergic receptors P2 (P2X and P2Y) play important role in control of renal hemodynamic and excretion function. This action may be modified in pathophysiological conditions, including hyperglycemia. Thus, we evaluated renal hemodynamic and tubular system sensitivity to action of β,γ-methylene ATP (β,γ-meATP), P2X receptor agonist, in diabetic rats. Clearance studies with β,γ-meATP (intravenous infusion rate 2 μmol/kg + 20 nmol/kg/min) were performed on streptozotocin-induced diabetic Wistar rats. Using laser Doppler flowmetry renal cortical and medullary blood perfusions (CBP, MBP) were measured. Results: β,γ-meATP decreased glomerular filtration rate (GFR) about 14% (1.30±0.05 vs.1.12±0.06 ml/min, $p < 0.01$) and increased CBP about 11% (580 ± 10 vs. 644 ± 16 PU, $p < 0.01$) in normoglycemic rats. However β,γ-meATP did not statistically significant effect affect GFR (0.73 ± 0.07 vs. 0.71 ± 0.08 ml/min) or CBP (570 ± 22 vs. 617 ± 22 PU) in hyperglycemic rats. MBF was not affected by β,γ-meATP in both experimental groups. In normoglycemic rats, β,γ-meATP increased diuresis about 113% (13 ± 2 vs. 29 ± 4 μl/min, $p < 0.01$) and sodium excretion in urine about 66% (1.20 ± 0.11 vs. 1.99 ± 0.21 μmol/min, $p < 0.01$) but in hyperglycemic rats the influence of β,γ-meATP was not observed. Conclusions: P2X receptors are involved in regulation of glomerular filtration, cortical blood flow and natriuresis. The lack of β,γ-meATP effects in diabetic rats suggests that hyperglycemia affecting vascular and tubular responses to agonist of P2X receptors may lead to disturbances in renal function and maintenance of homeostasis.

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S5.L3

ANGIOTENSIN II IN THE MEDIAL PREOPTIC AREA MEDIATES CARDIOVASCULAR REGULATION, BUT NOT MICTURITION CONTROL

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The medial preoptic area (mPOA) is a hypothalamic area known to participate in thermoregulatory control and blood pressure modulation, demonstrated by electrical stimulation or cobalt chloride administration, a non-selective synapse inhibitor. Retrograde labeling of mPOA by pseudorabies virus administrated in the urinary bladder has been previously shown. Immunohistochemical labeling for angiotensin II (Ang II), angiotensinogen mRNA, and AT-1 receptors have also been reported in mPOA neurons. Nevertheless, the role of Ang II in this area is still unknown. This study investigated whether Ang II acts or not in the mPOA to mediate the micturition and/or cardiovascular control. Male Wistar rats (~260 g) were submitted to implantation of a guide cannula in the mPOA 7 days prior to the experiments. On the day of the experiment, animals were anesthetized with 2% isoflurane in 100% O_2, and submitted to catheterization of the femoral artery and vein, and cannulation of the urinary bladder for mean arterial pressure (MAP), heart rate (HR) recordings, infusion of drugs, and intravesical pressure (IP) measurements, respectively. After the baseline MAP, HR and IP recordings for 15 min, Ang II (0.1 nM/µL, 1 µL) or saline (1 µL) was injected into the mPOA, and the variables were measured for additional 30 min. Data was expressed as mean ± SEM and analyzed using the Student's t-test ($P < 0.05$). Results: The injection of Ang II into the mPOA evoked a significant reduction in MAP (-50±11 mmHg, n=6, $P<0.05$) and HR (-42±26 bpm, $P<0.05$) compared to the saline injection (0 ± 0.7 mmHg and 1 ± 2 bpm, n=6). In contrast, no significant changes were observed in IP (9.12±9.68% vs. 5.65±5.65%, saline) after the injection of Ang II into the mPOA. We conclude that The Ang II in the mPOA causes hypotension and bradycardia, but does not seem to be involved in the micturition control.

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S5.L4

HYPOTENSIVE EFFICIENCY OF EPOXYEICOSATRIENOIC ACID ANALOG (EET-A) AND 20-HETE AGONIST (AAA) IN SPONTANEOUSLY HYPERTENSIVE RATS

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The precise pathomechanisms underlying the development of hypertension remain largely unclear and more efficient therapeutic strategies are still in a great demand. Latest studies suggest the important role of cytochrome P-450 dependent metabolites of arachidonic acid (AA) in blood pressure regulation. The epoxyeicosatrienoic acids (EETs) possess vasodilatory activity, they exhibit renoprotective and anti-inflammatory properties. In the present study the efficiency of EET-A (a stable analogue of 14,15-EET), together with AAA, a novel receptor antagonist of 20-HETE was tested. As a model we employed male spontaneously hypertensive rats (SHR) in two stages of disease development (6 and 16 week old rats). Rats were treated daily for 5 weeks with EET-A only, the combination of EET-A and AAA (administered in drinking water in the dose of 10 mg/kg/day each) and compared to age-matched untreated SHR. Systolic blood pressure (SBP) was measured by telemetry. Once a week observations in metabolic cages were performed; urine, blood and tissue samples were collected for further analysis. EET-A given alone had no significant effect on blood pressure of SHR (both young and adult). However the combined treatment with AAA + EET-A was not only effective in young rats, in which we observed significant attenuation of the disease development, but also it was significantly antihypertensive in adult animals (161 ± 5 vs. 180 ± 3 mmHg, $p < 0.05$). Additionally, combined treatment attenuated cardiac hypertrophy, decreased kidney ANG II level and increased the excretion of nitric oxide metabolites in adult rats. Taking into account all the beneficial impact of the combined treatment with EET-A and AAA on cardiovascular and renal function of adult SHR we suggest that it constitute a very promising novel antihypertensive strategy.

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THE ROLE OF ADENOSINE (ADO) IN CONTROL OF RENAL HAEMODYNAMICS AND EXCRETION IN NORMO-(NG) AND HYPERGLYCAEMIC (HG) SPRAGUE DAWLEY RATS

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The aim was to examine if the role of endogenous Ado in the regulation of kidney function in Sprague Dawley (Tac: Cmd: SD) rats depends on the duration of hyperglycemia in a pharmacological model of diabetes induced by streptozotocin (STZ). After administration of STZ (60 mg/kg i.p.) or its solvent to rats aged 6–7 weeks, in NG and HG animals short-term (14 days) or long-term (60 days) observations were conducted including blood glucose levels and body weight (b.w.) monitoring. Then, in anaesthetized (thiopental, 100 mg/kg i.p.), surgically prepared rats the effect of Ado deaminase (ADA, Ado metabolizing enzyme) on total renal blood flow (RBF, renal artery probe) and perfusion of kidney zones (laser-Doppler fluxes): upper cortex (CBF), outer- (OMBF) and inner-medulla (IMBF), along with urine (V) and sodium (UNaV) excretion was recorded. ADA infusion into the renal artery (140 U/kg b.w.) induced significant changes in NG-14 animals only: it increased CBF (5%) and decreased OMBF (9%). However, in NG-60 rats there was an increase in RBF (17%) and CBF (8%), while in HG-60 rats RBF decreased by 23%, CBF by 12%, with a transient decrease in OMBF (–8%) and IMBF (–20%). In NG-14 rats ADA administration did not change UNaV but a slight reduction in V was seen. In contrast, after 60 days' observation, ADA lowered V both in NG and HG rats (–20% and –25%, respectively), but it lowered UNaV in HG only (–34%). Thus, both the age of the animals (younger: 14 days' vs. older: 60 days' observation) and the duration of hyperglycemia influenced the effects of endogenous Ado on the regulation of renal function. In younger rats, irrespective of the glycemia level, the effects of Ado on renal blood perfusion and renal excretory function is slight and transient. On the other hand, in older rats, Ado modifies the perfusion of the kidney cortex; however the direction of changes depends on the level of glycaemia. The effect of Ado on the regulation of medullary circulation and sodium excretion was demonstrated only in the animals with hyperglycemia.

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DIFFERENTIAL EFFECTS OF HIGH-FAT DIETS VARYING IN FATTY ACID COMPOSITION ON THE KIDNEY HISTOLOGY AND EXPRESSION OF GENES RELATED WITH CELLULAR STRESS AND WATER-ELECTROLYTE HOMEOSTASIS

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Development of obesity is closely associated with the consumption of high-calorie diets. One of the diets considered as obesogenic is a western-type diet. It is characterized by a high content of saturated fatty acids (SFA) and a low level of omega-3 PUFA, often accompanied by an imbalance in the n-6/n-3 PUFA ratio. An overconsumption of the n-6 PUFA and SFA is strongly related with pathogenesis of many modern diet-related chronic diseases including chronic kidney disease (CKD). The high-fat diet consumption may lead to renal metabolic disorders and concomitantly may enhance both oxidative stress and inflammation. The above is a hallmark of apoptosis and a leading cause of the structural changes in the kidney microarchitecture. On the other hand n-3 PUFA consumption reduces the prevalence of CKD. Considering the above, we hypothesized that feeding mice with three different high-fat diets with a saturated fatty acids and a significant proportion of different ratios of unsaturated n-6 and n-3 FA would differentially impact the kidney histological structure and expression pattern of the selected genes. The analysis were performed on 24, two-month-old, Swiss-Webster mice. Animals were divided into 4 dietary groups (n=6) and for 12 weeks were fed the following diets: the standard diet (STD group), the high-fat diet (HFD) rich in SFAs (SFA group), and HFDs dominated by PUFAs with linoleic acid to α-linolenic acid ratios 14:1 (14:1 group) and 5:1 (5:1 group). After the experimental period animals were euthanized using CO_2, than kidney were collected for further analysis. Histological analysis included (H&E, PAS, trichrome and TUNEL staining and IHC labeling of aquaporins – AQPs 2, 3).RT qPCR was used to assess the expression pattern of genes related with inflammation (*Kim-1, Ccl2, Il-6*), oxidative stress (*Sod1, Cat*), PUFA metabolism (*Cox2, Lox5, Cyp2c29, Lepr*) and water-electrolyte homeostasis (Ang, Ren, Aqp3). Morphological analysis of the kidney revealed the lipid vacuoles in the proximal tubules in the kidney of mice from SFA and 14:1 groups. These morphological changes were accompanied by an enhanced expression of *Kim-1* gene which is known as a marker of the proximal tubule epithelial cells injury. The same tendency was observed for apoptotic cell count measured by TUNEL assay which was significantly higher in the kidney of animals from SFA and 14:1 groups. The oxidative stress-related genes such as Sod1 and Cat were significantly up-regulated in the 14:1 group. However, in the light of the fact that lipotoxicity may decrease the activity of an antioxidative enzymes we were suspecting significant ROS generation in the group of mice fed the SFA diet. Expression of *Cyp2c29* gene that encodes the protein involved in the synthesis of active renoprotective metabolites of both n-6 and n-3 PUFA, respectively epoxyeicosatrienoic acids and epoxydocosapentaenoic acids was significantly upregulated in the kidney of animals fed all HFDs. Conversion of aforementioned eicosanoids to their less active forms is catalyzed by a soluble epoxide hydrolase expression. The *Ephx2* gene encoding this protein was significantly up-regulated in the kidney of animals fed both PUFA rich HFDs. Cox2 gene was significantly down-regulated in the kidney of 4:1 group in comparison to the STD group. Both PUFA rich HFDs influenced local renin angiotensin system-related genes. The animals of 4:1 group showed significantly decreased renin gene expression. The angiotensinogen gene was significantly down-regulated in the kidney of animals of both 14:1 and 5:1 groups. Expression of *Aqp3* gene was significantly increased in the both SFA and 14:1 group, however the ICH analysis showed decrease of both AQP2 and AQP3 protein expression in the respectively apical and basolateral membrane of collecting duct epithelial cells in animals fed the SFA rich HFD. The high fat diets varying in fatty acids composition differentially influenced kidney morphology. The severity of observed pathophysiological lesions seems to show trend to decrease with increased content of alpha linoleic acid in the HFD. Observed morphological changes are probably related with the generation of the oxidative stress. It seems that the SFA-based HFD may affect the facultative water reabsorption in the collecting duct as an effect of AQP2 and 3 down-regulation. On the other hand n-3 PUFA may be involved in the regulation of local renal RAA system. Above may suggest that the westernized diet with a high SFA and/or n-6 PUFA content may exert a negative impact on renal morphology and function.

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S5.P1

URINARY EXCRETION OF EXTRACELLULAR VESICLES IN PATIENTS IN THE EARLY PERIOD AFTER KIDNEY TRANSPLANTATION

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Extracellular vesicles have a size about 30–300 nm and can be found in various body fluids, including urine. Increased excretion of extracellular vesicles may have a diagnostic value in the initial early stages of renal dysfunction. The aim of the study was to investigate the urinary excretion of extracellular vesicles in patients in the early period after kidney transplantation. The study was approved by the Medical Ethics Committee of Medical University of Gdansk and the director of University Clinical Center in Gdansk. The preliminary study involved adult Patients from the Department of Nephrology, Transplantology and Internal Diseases at the University Clinical Centre in Gdansk, Poland, in the early period after kidney transplantation (1–4 weeks, n=3) and healthy volunteers (n=3). Urinary extracellular vesicles were isolated by ultracentrifugation-based method from the same volume of each first morning urine sample. The expressions of the specific marker CD63, nephrin and podocin were verificated by Western blot. The total number of extracellular vesicles per milligram of creatinine was determined by nanoparticle tracking analysis (NTA). All values are expressed as mean ± SEM. Statistical significance between the two group was determined by unpaired t test. Human urinary extracellular vesicles were identified by showing the expression of the exosomal marker CD63 in all samples. In early period after kidney transplantation the urinary excretion of extracellular vesicles was 1.5-fold higher compared to healthy volunteers ($2.6*10^{10} \pm 4.4*10^{9}$ vs. $3.9*10^{10} \pm 5.0*10^{9}$ particles/mg creatinine, p=0.1218), however, this difference was not statistically significant. The presence of nephrin and podocin were confirmed on isolated extracellular vesicles. The research is preliminary and prompted us to further analyze of urinary excretion of extracellular vesicles proteins in a larger group of patients, looking for early markers of renal graft function.

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S5.P2

AGING AFFECTS URINARY BLADDER REACTIVITY IN FEMALE WISTAR RATS: AN IN VITRO PREPARATION

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Urinary bladder diseases affect mostly women worldwide and the number of patients with bladder disorders increases with aging. This study investigated the urinary bladder reactivity to the neurotransmitters of the autonomic nervous system in elderly female rats. Female nulliparous Wistar rats with 8, 15 and 18 months-old were anesthetized with 2% isoflurane in 100% O_2 and submitted to the catheterization of the femoral artery and vein and cannulation of the urinary bladder for mean arterial pressure (MAP), heart rate (HR), and intravesical pressure (IP) recordings, respectively, in a data acquisition system (PowerLab 16 SP, ADInstruments). After a baseline recording of MAP, HR and IP, acetylcholine (Ach, 2.0 µg/mL, 0.1 mL), or noradrenaline (Nor, 2.0 µg/mL, 0.1 mL), or saline (vehicle, 0.1 mL) were topically(*in situ*) administrated onto the urinary bladder, and all the parameters were recorded for additional 15 min. Data are expressed as mean ± SEM and were submitted to paired Student's t-test or One-way ANOVA ($P < 0.05$). The rats with 8, 15 and 18 months-old (n=6/group) showed significant increases in IP after Ach (500.00 ± 22.81%, 174.55 ± 20.88%, and 83.01 ± 0.80%, respectively) and significant decreases in IP (–67 ± 12%, –27.83 ± 12.69%, and –31.41 ± 0.28%, respectively) compared to saline (–0.97 ± 2.54%, 3.71 ± 0.68%, and –1.69 ± 1.97%, respectively). The IP responses to Ach were significantly attenuated in 15 and 18 months-old compared to 8 months-old female rats. No changes were observed in MAP and HR after Ach or Nor or saline *in situ* onto the urinary bladder in all groups. The findings suggest that aging reduces the urinary bladder reactivity to Ach and Nor, the neurotransmitters of the autonomic nervous system, and the reactivity to Ach was the most affected by elderly.

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S5.P3

SODIUM APPETITE IS INDUCED BY SWIMMING EXERCISE IN WISTAR RATS

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The loss of water and sodium evoked by physical exercise has been described in several studies. This study investigated if chronic swimming exercise induces sodium appetite in rats. Adult male Wistar rats were submitted to swimming exercise (SE) or maintained sedentary (SED) after a gradual adaptation period to the individual tanks with warmed water. Afterwards, the animals underwent daily bouts of exercise, with 1 h of duration, 5 consecutive days/week, for 6 weeks with 5% of body weight (b.w.) load. At the end of the 6 weeks of swimming, the animals were left in a recovery period for 3 weeks. Daily water and 0.3 M NaCl intakes were measured using drinking bottles, in SE and SED rats (n=6/group). Another group of animals underwent the same SE and SED (n=6/group) procedures, but they only had access to water in the drinking bottle. Urine sodium and potassium were analyzed at the adaptation period, after 3 and 6 weeks of exercise, and after 3 weeks of recovery from the exercise bouts in all groups. Plasma sodium and potassium were evaluated in blood samples of all animals at the end of the experiment protocol. Data area as mean ± SEM and submitted to two-way ANOVA followed by Tukey post-test ($P < 0.05$). We observed a significant higher sodium intake in SE rats compared to SED rats was observed after 2 weeks (4.6 ± 0.7 vs. 1.1 ± 0.4 mL/100 g of b.w.), 4 weeks (5.7 ± 0.7 vs. 1.8 ± 0.3 mL/100 g of b.w.), 5 weeks (6.3 ± 1.0 vs. 2.0 ± 0.3 mL/100 g of b.w.) and during the 2 weeks of recovery from SE bouts, without corresponding increase in water intake. No difference was observed in water intake in rats without 0.3 M NaCl comparing SE and SED groups. Urine and plasma sodium showed no difference in all groups. Urine potassium only reduced after 6 weeks of SE in rats with access to 0.3 NaCl (189.4 ± 22.9 mEq/L) compared to SED animals (260.5 ± 9.6 mEq/L). Our data demonstrated that SE with 5% b.w. load for 6 wks increases sodium appetite in rats, which remained higher even after the cessation of the exercise bouts, suggesting that long-term mechanisms activated by this approach of exercise can mediate the change in this ingestive behavior.

Acknowledgments: FAPESP and NEPAS.

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S5.P4

THE ROLE OF PURINE P1 RECEPTORS IN CONTROL OF THE RENAL EXCRETION DEPENDS ON RAT'S AGE AND DURATION OF STREPTOZOTOCIN-INDUCED HYPERGLYCAEMIA

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The impact of purine P1 receptors (P1R) on renal function is altered under pathological conditions, e.g. in diabetes mellitus (DM). Recently, we found that the P1R role depends on the animals' age, however, this was studied only in normoglycaemic (NG) animals subjected to the treatment with theophylline (Theo), a nonselective P1R antagonist. Here, we examined the effects of Theo and CSC (8-(3-chlorostyryl)caffeine, a selective antagonist of A2a type of P1R) on renal excretion during short- (2-wks, DM-2) or long-term (8-wks, DM-8) streptozotocin (STZ, 60 mg/kg i.p.) induced hyperglycaemia and compared the effects with those in NG age-matched male Sprague Dawley rats. In NG and DM anaesthetized rats (thiopental, 100 mg/kg i.p.), we measured urine flow (V), urine osmolality (Uosm), total solute (UosmV), sodium (UNaV) and potassium excretion (UKV). Theo infusion (14 mg/kg/h i.v.) induced a transient elevation of V, UosmV, UNaV; the slight decrease of Uosm did not differ between the NG two age groups and DM-14 or DM-60 rats. Remarkably, a long-lasting increase of Uosm after cessation of Theo infusion was shown in the NG older rats only. CSC given into the renal artery (1.7 µmol/kg/h) did not affect renal excretion in either NG age group. The exception was a twofold UNaV increase noted after cessation of CSC infusion in older rats. However, in diabetic rats, a distinct decrease of V, UosmV, UNaV, UKV was shown in DM-14 group only; in DM-60 rats an increase in UKV was seen. Neither antagonist affected the arterial blood pressure, which suggests that the effects on RE depended mainly on the drug's direct action on the tubular transport. Our data show that short-term hyperglycaemia does not modify the joint effect of all P1R on renal excretion but can alter the contribution of individual subtypes, such as P1A2aR. On the other hand, long-term diabetes blunts the P1R impact on sodium excretion and urine concentration and abolishes P1RA2a contribution to the control of renal excretory function.

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S5.P5

THE ROLE OF ANGIOTENSIN 1-7 IN CONTROL OF BLOOD PRESSURE, RENAL HAEMODYNAMICS, AND EXCRETION IN RATS MODEL OF STREPTOZOTOCIN-INDUCED DIABETES

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We examined if angiotensin 1-7 (Ang1-7) could modulate blood pressure and renal function in animal model of diabetes (DM). In Sprague Dawley rats 3wks after STZ (60 mg/kg i.p.) or solvent injections (normoglycaemic control, NG), osmotic minipumps with Ang1-7 (400 ng/kg/min, s.c.) or 0.9% NaCl were implanted for 3 weeks. Along with the 5 wks water intake, diuresis and systolic blood pressure (SBP, tail-cuff method) were observed; thereafter in thiopental anaesthetized rats we recorded: mean arterial blood pressure (MABP), whole kidney blood flow (RBF) and perfusion of renal zones (laser-Doppler fluxes): cortex (CBF), outer - (OMBF) and inner- (IMBF) medulla also with urine flow (V), total solutes (UosmV) and sodium (UNaV) excretion. Regardless of the Ang1-7 treatment, a significant increase in water intake was shown in DM rats. However, this was associated with elevation of diuresis only in DM+Ang1-7 rats which was more pronounced than in NG+Ang1-7 rats. There was a significantly higher SBP in NG+Ang1-7 than in NG rats, while no difference in SBP was observed in DM rats after the addition of Ang1-7. MABP, RBF, CBF and OMBF did not differ among groups. Regardless of Ang1-7 treatment, IMBF was significantly higher in NG than in DM rats. V was significantly decreased by Ang1-7 in NG but increased in DM rats. Also, UNaV was lowered by Ang1-7 in NG rats. Only UosmV differs between NG and DM rats, it was higher in the latter and in addition increased in Ang1-7. In summary, data from chronic studies indicate that Ang1-7 contributes to blood pressure control in NG rats only while in DM rats could modulate water intake and urine excretion. Data from acute studies suggest that angiotensin 1-7 rather not contribute to systemic (no MABP changes) and renal haemodynamics both in NG and DM. However, independent of/from glycaemia Ang1-7 can modify tubular water and solutes reabsorption but in the opposite way, to improve in normo- and to impair in hyperglycaemia. This could depend on the selective affinity of Ang1-7 to the AT-1 receptors, which density is simultaneously increased in diabetes.

Acknowledgements: Supported by 217/01/X/NZ4/02053 Miniatura.

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S5.P6

HYPERGLICAEMIA MODULATES P1 RECEPTORS IMPACT ON THE RENAL CIRCULATION AND URINE EXCRETION BUT NOT TISSUE NITRIC OXIDE

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Chronic hyperglycaemia could affect in the kidney paracrine factors like adenosine (Ado), their P1 receptor (P1R) density and nitric oxide (NO) bioavailability. The impact of these modifications on renal function is unclear. Ado can induce either vasoconstriction or vasodilatation, depending on the prevailing stimulation of A1 or A2 receptors (A1R, A2R). Ado-induced renal excretion alterations may be secondary to haemodynamic changes, or reflect a direct influence on tubular transport by P1R located along the nephron; both could be mediated by fluctuated intrarenal NO activity. We compared the effects of an antagonist of A1R and A2R (theophylline, Theo) in anaesthetized normoglycaemic rats (NG) or after two weeks hyperglycaemia induced by streptozotocin, (DM). Whole kidney blood flow (RBF) and perfusion of the outer and inner medulla (OMBF, IMBF, respectively) were measured, together with renal excretion of water (V), total solute ($U_{osm}V$), and sodium ($U_{Na}V$), and measurement of cortical and medullary tissue NO changes using selective microprobes. *I.V*. Theo did not affect systemic blood pressure. However, renal haemodynamics and excretion were modified differently in NG and DM rats. RBF transiently increased in NG (10%), significantly in contrast to a gradual decrease in DM rats (18%). Simultaneously, a slight OMBF decrease without IMBF alteration were shown in both groups. Interestingly, the renal tissue NO signal increased similarly (13–15%) in the cortex and medulla, independent of glycaemia. Theo-induced renal excretion changes were uniform, which indicates they were independent of haemodynamics alterations. Notably, increases of V, $U_{osm}V$ were greater in NG than DM rats (236% and 178% vs. 76% and 51%, respectively), while $U_{Na}V$ increase did not differ between both groups (223 vs.193%, respectively). Thus, in DM, in opposite to NG, within the cortex A2R prevails over A1R effects, reflected by RP1 antagonist vasoconstriction, whereas within medulla a balance between receptors persisted. A1R/A2R impact on tubular transport of water and solutes (but not sodium) were also modified by hyperglycaemia. However, these alterations of P1R action on renal haemodynamics and excretion seem to not be dependent on *NO* bioavailability.

Supported by National Science Centre, Poland: grant # 2017/25/B/NZ5/01292, Joanna D. Sitek – ”POWEROch!DOK” project participant.

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SESSION VI

HEART
CARDIOVASCULAR AND RESPIRATORY REGULATION

Thursday (September 16, 2021; 9:45 – 17:30)

Chair:

Prof. Barbara Malinowska
Department of Physiology and Experimental Pathophysiology,
Medical University of Bialystok, Bialystok, Poland

Prof. Agnieszka Cudnoch-Jedrzejewska
Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Sciences, Medical University of Warsaw, Warsaw, Poland

Prof. Katarzyna Kaczynska
Department of Respiration Physiology, Mossakowski Medical Research Centre,
Polish Academy of Sciences, Warsaw, Poland

DETAILED SESSION VI SCHEDULE

Part I – **HEART. CARDIOVASCULAR REGULATION.**

Opening lectures (Thursday, September 16, 2021; 11:30 – 13:00; *virtual stream A*)

S6.L1 IS OXYGEN STARVATION RESPONSIBLE FOR PROGRESSION TO RIGHT VENTRICULAR FAILURE IN PULMONARY ARTERIAL HYPERTENSION? **M. Okninska, Z. Zambrowska, A. Paterek, U. Mackiewicz, M. Maczewski** (Department of Clinical Physiology, Centre of Postgraduate Medical Education, Warsaw, Poland).

S6.L2 PURINERGIC SIGNALING AND ITS DISTURBANCES IN THE PATHOLOGY OF VESSELS AND HEART VALVES. **R.T. Smolenski** (Department of Biochemistry, Medical University of Gdansk, Gdansk, Poland)

S6.L3 HIGH SALT INTAKE PROMOTES ENDOTHELIAL DYSFUNCTION AND IMPAIRS BRAIN FUNCTION. ROLE OF THE IMMUNE SYSTEM. **A. Sawicka, M. Aleksandrowicz, E. Kozniewska** (Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland)

S6.L4 RECIPROCAL RELATIONSHIP BETWEEN ARTERIAL BLOOD PRESSURE AND GUT MICROBIOTA. **M. Ufnal, K. Jaworska, D. Chabowski** (Department of Experimental Physiology and Pathophysiology, Medical University of Warsaw, Warsaw, Poland)

Oral presentations (Thursday, September 16, 2021; 13:00 – 14:50; *virtual stream A*)

S6.L5 ROLE OF STEAROYL-COA DESATURASE 1 IN CONTROL OF THE HEART FUNCTION THROUGH LIPID METABOLISM CHANGES IN HYPERTHYROIDISM. **A. Olichwier[1], A. Binczak[2], M. Duda[2], P. Dobrzyn[1]** ([1]Nencki Institute of Experimental Biology, Warsaw, Poland, [2]Medical Center of Postgraduate Education, Warsaw, Poland).

S6.L6 STEAROYL-COA-DESATURASE 1 AFFECTS DAMAGED MITOCHONDRIAL DYNAMICS AFTER DOXORUBICIN TREATMENT. **O. Blesznowska, V. Baltskyi, A. Olichwier, P. Dobrzyn** (Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland).

S6.L7 THE EFFECT OF ISOPROTERENOL ON THE DEVELOPMENT OF HEART FAILURE IN C57BI/6J MICE. **A. Jedrzejewska, M. Zabielska-Kaczorowska, P. Mierzejewska, B. Kutryb-Zajac, O. Krol, E. M. Slominska, R.T. Smolenski** ([1]Department of Biochemistry, Medical University of Gdansk, Poland, [2]Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S6.L8 THE EFFECT OF KISSPEPTIN-10 ON THE REGULATION OF COLLAGEN METABOLISM IN THE HEART. **P. Radwanska, M. Galdyszynska, L. Piera, J. Drobnik** (Department of Pathophysiology, Chair of General and Experimental Pathology, Medical University of Lodz, Lodz, Poland).

S6.L9 THE INFLUENCE OF GUT DYSBIOSIS CAUSED BY HIGH FAT DIET ON THE MYOCARDIAL FUNCTION. **P. Dubinski[1], K. Czarzasta[1], D. Sztechman[1], L. Puhalska[1], D. Mirowska-Guzel[2], A. Cudnoch-Jedrzejewska[1]** ([1]Chair and Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland, [2]Department of Experimental and Clinical Pharmacology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland).

S6.L10 EFFECTS OF PERIPHERAL CB_1 RECEPTOR INVERSE AGONIST JD5037 IN MONO- AND POLYTHERAPY WITH METFORMIN IN A MONOCROTALINE-INDUCED RAT MODEL OF PULMONARY ARTERIAL HYPERTENSION. **P. Remiszewski, A. Pedzinska-Betiuk, K. Minczuk, J. Weresa, A. Krzyzewska, B. Malinowska** (Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.L11 HOW BEETROOT JUICE NITRATES CAN MODULATE THE FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM? A THEORETICAL FRAMEWORK. **M. Wyciszkiewicz, R. Seredynski, B. Paleczny, B. Ponikowska** (Wroclaw Medical University, Wroclaw, Poland).

Questions and answers. Session summary.

Part II – **CARDIO-RESPIRATORY REGULATION**

Opening lecture (Thursday, September 16, 2021; 14:55 – 15:25; *virtual stream A*):

S6.L12 BREATHING DISORDERS IN ALZHEIMER'S DISEASE. **K. Kaczynska, K. Andrzejewski** (Mossakowski Medical Research Institute Polish Academy of Sciences, Warsaw, Poland).

Oral presentations (Thursday, September 16, 2021; 15:25 – 16:15; *virtual stream A*):

S6.L13 DEFICIT OF MONOAMINES IN RESERPINE PARKINSON'S DISEASE MODEL ALTERS THE HYPOGLOSSAL NERVE ACTIVITY. **K. Andrzejewski[1], M. Jampolska[1], M. Zaremba[2,3], I. Joniec-Maciejak[2], M. Orlowska[1], K. Kaczynska[1]** ([1]Department of Respiration Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [2]Department of Experimental and Clinical Pharmacology, Centre for Preclinical Research (CePT), Medical University of Warsaw, Warsaw, Poland, [3]Laboratory of Experimental Therapies, Military Institute of Hygiene and Epidemiology, Warsaw, Poland).

S6.L14 DAILY SITTING TIME AFFECTS LACTULOSE-INDUCED CHANGES IN HYPOXIC RESPONSIVENESS IN HUMANS. **K. Pawlowska-Seredynska[1], R. Seredynski[2], B. Ponikowska[2], W. Umlawska[1], B. Paleczny[2]** ([1]Department of Human Biology, University of Wroclaw, Wroclaw, Poland; [2]Department of Physiology, Wroclaw Medical University, Wroclaw, Poland).

S6.L15 VASOPRESSIN AND V1a RECEPTORS IN HEMODYNAMIC AND RESPIRATORY REGULATION IN NORMOTENSIVE AND HYPERTENSIVE RATS. **M. Proczka[1], A. Trzcinski[2], T. Zera[2]** ([1]Department of Experimental and Clinical Physiology, Doctoral School, Medical University of Warsaw, Poland, [2]Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Poland).

Session summary

Poster session – Part I (Thursday, September 16, 2021; 9:45 – 11:20; *virtual stream C*)

S6.P1 CHEMOSENSITIVITY DURING MECHANO AND METABOREFLEX ACTIVATION IN HEALTHY SUBJECTS CHARACTERIZED BY LOW AND HIGH EXERCISE CAPACITY. **W. Lopusiewicz, A. Lis, T. Okupnik, B. Paleczny, B. Ponikowska** (Wroclaw Medical University, Poland)

S6.P2 CARDIAC PHYSIOLOGY AFTER OSTARINE TREATMENT – *IN VITRO* STUDY ON H9C2 CARDIOMYOCYTES AND FIBROBLASTS. **N. Leciejewska[1], P. A. Kolodziejski[1], E. Malek[2], K. Mielnik[1], E. Pruszynska-Oszmalek[1]** ([1]Department of Animal Physiology, Biochemistry and Biostructure, Poznan University of Life Sciences, Poznan, Poland, [2]Department of Preclinical Sciences and Infectious Diseases, Faculty of Veterinary Medicine and Animal Science, Poznan University of Life Sciences, Poznan, Poland).

S6.P3 EVALUATION OF THE ANTI-INFLAMMATORY AND ANTI-PROLIFERATIVE PROPERTIES OF CANNABIDIOL IN AN EXPERIMENTAL MODEL OF MONOCROTALIN-INDUCED PULMONARY HYPERTENSION. **A. Krzyzewska[1], M. Baranowska-Kuczko[1,2], I. Kasacka[3], H. Kozlowska[1]** ([1]Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland, [2]Department of Clinical Pharmacy, Medical University of Bialystok, Bialystok, Poland, [3]Department of Histology and Cytophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.P4 THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS ANACETRAPIB AND TORCETRAPIB ON LIVER DDAH1 ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA. **E. Krzewicka-Romaniuk, D. Siedlecka, A. Pradiuch, G. Wojcicka** (Department of Pathophysiology, Medical University of Lublin, Lublin, Poland).

S6.P5 THE CHARACTERISTICS OF A SUB-CHRONIC MODEL OF NON-ATOPIC ASTHMA. **D. Zajac, E. Russjan, K. Kaczynska** (Department of Respiration Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland).

S6.P6 THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS, ANACETRAPIB AND TORCETRAPIB, ON PLASMA AND LIVER PARAOXONASE 1 (PON 1) ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA. **D. Siedlecka, E. Krzewicka-Romaniuk, A. Pradiuch, G. Wojcicka** (Department of Pathophysiology, Medical University of Lublin, Lublin, Poland).

S6.P7 LONG-TERM EFFECT OF PERIPARTUM DEPRESSION ON THE CARDIOVASCULAR SYSTEM OBSERVED IN THE ADULT RAT FEMALE OFFSPRING. **J. Kruszewska[1], D. Sztechman[1], V. Skital[1], J. Malik[1], A. Segiet-Swiecicka[1], K. Czarzasta[1], E. Sajdel-Sulkowska[2]** ([1]Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland; [2]Department of Psychiatry, Harvard Medical School, Boston, MA, USA).

S6.P8 ELECTROPHYSIOLOGICAL, HEART RATE VARIABILITY, AND BIOCHEMICAL DISTURBANCES IN A RAT MODEL OF 5-FLUOROURACIL INDUCED CARDIOTOXICITY ARE PARTIALLY REVERSED BY CHRONIC VITAMIN D SUPPLEMENTATION. **M. Jurczyk[1], P. Stach[1], V. Aleksandrovych[1], A. Midro[1], M. Krol[1], B. Kusnierz-Cabala[2], P. Mazur[3], K. Jasinski[4], A. Poniatowski[1], K. Gil[1]** ([1]Department of Pathophysiology, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Diagnostics, Chair of Clinical Biochemistry, Jagiellonian University Medical College, Krakow, Poland, [3]Department of Medical Diagnostics, Faculty of Pharmacy, Jagiellonian University Medical College, Krakow, Poland, [4]Institute of Nuclear Physics of the Polish Academy of Sciences, Department of Magnetic Resonance Imaging, Krakow, Poland).

S6.P9 TUMOUR NECROSIS FACTOR RECEPTORS TYPE 1 AND TYPE 2 ARE EXPRESSED IN THE BRAINSTEMS OF NORMOTENSIVE AND HYPERTENSIVE RATS. **A. Segiet-Swiecicka[1], K. Czarzasta[1], T. Zera[1]** ([1]Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland).

S6.P10 DEVELOPMENT OF HEART FAILURE IN SPONTANEOUSLY HYPERTENSIVE RATS (SHR). **O. Krol[1], P. Mierzejewska[1], M. Zabielska-Kaczorowska[1,2], T. Borkowski[3], A. Jedrzejewska[1], E. M. Slominska[1], R.T. Smolenski[1]** ([1]Department of Biochemistry, Medical University of Gdansk, Gdansk, Poland, [2] Department of Physiology, Medical University of Gdansk, Gdansk, Poland, [3]Department of Medical Laboratory Diagnostics, Medical University of Gdansk, Gdansk, Poland).

S6.P11 STEAROYL-COA DESATURASE 4 DEFICIENCY PROTECTS AGAINST HIGH FAT DIET-INDUCED HEART DYSFUNCTION IN MOUSE. **M. Wolosiewicz[1], A. Filip[1], M. Duda[2], A. Olichwier[1], V. Navrulin[1], P. Dobrzyn[1]** ([1]Laboratory of Molecular Medical Biochemistry, Nencki Institute of Experimental Biology, Polish Academy of Sciences, Warsaw, Poland, [2]Department of Clinical Physiology, Postgraduate Medical School, Warsaw, Poland).

S6.P12 ASSOCIATION BETWEEN DEPRESSION AND UNFAVORABLE NUTRITIONAL, CARDIAC AND LABORATORY OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE. **G. Opielak[1], T. Powrozek[1], A. Skwarek-Dziekanowska[2], G. Sobieszek[2], T. Malecka-Massalska[2]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Department of Cardiology, 1st Military Clinical Hospital with the Outpatient Clinic, Lublin, Poland).

S6.P13 RELATION BETWEEN THE HEART RHYTHM ASYMMETRY AND THE RESPIRATORY PHASE IN HEALTHY PEOPLE AND PATIENTS WITH ARTERIAL HYPERTENSION. **D. Wejer[1], B. Graff[2], G. Graff[3], K. Narkiewicz[2], D. Makowiec[4]** ([1]University of Gdansk, Faculty of Mathematics, Physics and Informatics, Institute of Experimental Physics, Gdansk, Poland, [2]Medical University of Gdansk, Department of Hypertension and Diabetology, Gdansk, Poland, [3]Gdansk University of Technology, Faculty of Applied Physics and Mathematics, Gdansk, Poland, [4]University of Gdansk, Faculty of Mathematics, Physics and Informatics, Institute of Theoretical Physics and Astrophysics, Gdansk, Poland).

Poster session – Part II (Thursday, September 16, 2021; 16:30 – 17:30; *virtual stream C*)

S6.P14 POST-EXERCISE HYPOTENSION IN ELDERLY: THE EFFECT OF SINGLE SESSION OF WATER BASED EXERCISE. **C. Reis[1], W. Barbosa[1], L. Barcellos[1], P. Zovico[1], C. Leite[1], R. Rica[2], D. Bocalini[1]** ([1]Federal University of Espirito Santo, Vitoria, Brazil, [2]Estacio de Sa University, Vitoria, Brazil).

S6.P15 THE EFFECTS OF ENHANCED ENDOCANNABINOID TONE INDUCED BY CHRONIC ADMINISTRATION OF DUAL FAAH/MAGL INHIBITOR JZL195 IN SPONTANOUSLY HYPERTENSIVE RATS. **M. Toczek, A. Kicman, B. Malinowska** (Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.P16 EFFECT OF MUSIC ON TRAINING PARAMETERS AND MOOD STATE IN HIIT BODY WORK SESSIONS. **P.V.C. Zovico[1], R.A.A. Filho[1], J.J.G. Oliveira[1], W.A Barbosa[1], R.L. Rica[2], D.S. Bocalini[1]** ([1]Federal University of Espirito Santo, Vitoria, Brazil, [2]Estacio de Sa University, Vitoria, Brazil).

S6.P17 THE EFFECT OF GENETICALLY ALTERED AMP DEAMINASE ACTIVITY IN EXPERIMENTAL ISOPROTERENOL-INDUCED HEART FAILURE. **M. Zabielska-Kaczorowska[1,2], P. Mierzejewska[1], E.M. Slominska[1], R.T. Smolenski[1]** ([1]Department of Biochemistry, Medical University of Gdansk, Gdansk, Poland, [2]Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S6.P18 THE INFLUENCE OF CANNABIDIOL ON ISOLATED RAT ATRIA UNDER NORMOXIC, HYPOXIC AND REOXYGENATION CONDITIONS. **A. Pedzinska-Betiuk, J. Weresa, B. Malinowska** (Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.P19 NEUROPEPTIDE FF COUNTERACTS OPIOID INDUCED RESPIRATORY DEPRESSION. **P. Wojciechowski, K. Andrzejewski, K. Kaczynska** (Department of Respiration Physiology, Mossakowski Medical Research, Institute Polish Academy of Sciences, Warsaw, Poland).

S6.P20 INFLUENCE OF CANNABINOID CB1 AND CB2 RECEPTOR ANTAGONISTS ON CARDIOSTIMULATORY EFFECTS OF ISOPRENALINE IN HUMAN ATRIAL TRABECULAE. **J. Weresa, A. Pedzinska-Betiuk, B. Malinowska** Department of Experimental Physiology and Pathophysiology, Medical University of Bialystok, Bialystok, Poland).

S6.L1

IS OXYGEN STARVATION RESPONSIBLE FOR PROGRESSION TO RIGHT VENTRICULAR FAILURE IN PULMONARY ARTERIAL HYPERTENSION?

M. OKNINSKA, Z. ZAMBROWSKA, A. PATEREK, U. MACKIEWICZ, M MACZEWSKI

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Pulmonary arterial hypertension (PAH) initially results in compensatory right ventricular (RV) hypertrophy, but eventually in RV failure. This transition is poorly understood, but may be triggered by hypoxia. Indeed in PAH oxygen delivery is impaired due to increased extravascular compression of RV coronary vessels (due to both RV hypertrophy and increased RV pressures) and reduced coronary perfusion pressure (due to reduced aortic pressure as a consequence of reduced LV cardiac output), while increased RV afterload results in proportionally increased energy demand. Last but not least, capillary rarefaction was found in various animal PAH models as well as in humans. We have recently demonstrated that in PAH RV pO_2 is reduced by almost half, while that in LV is maintained. Acute administration of new agent that facilitates oxygen dissociation from hemoglobin, myo-inositol trispyrophosphate (ITPP), partially restored RV pO_2, providing beneficial effects on RV contractility. This indicates that oxygen balance is impaired in PAH and as such can be an important target for PAH therapy. ITPP may be one of such potential therapies.

S6.L2

PURINERGIC SIGNALLING AND ITS DISTURBANCES IN THE PATHOLOGY OF VESSELS AND HEART VALVES

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Purinergic signaling is primarily attributed to function of purinergic receptors that respond to nucleotide ligands such as adenosine triphosphate (ATP) P2 receptors or nucleosides such as adenosine P1 receptors. However, purinergic signaling is far more complex. First, many other compounds are involved as signaling molecules that include pyrimidine nucleotides such as UTP or nicotinamide derivatives. Then, origin of purinergic mediators could involve intracellular pathways with its release into extracellular space or formation of purinergic mediators in the extracellular space. This underlies the importance of membrane transport systems such as nucleoside transporters for adenosine or pannexin channels for ATP. Purinergic signaling is tightly controlled by ectoenzymes such as ecto-nucleoside triphosphate diphosphohydrolases (eNTPD) and ecto-5'-nucleotidase (e5'NT). Our group identified also another element of the ectoenzyme cascade that is involved in modulation of purinergic system which is ecto-adenosine deaminase (eADA). Purinergic signaling controls broadest range of physiological functions of the organisms and different elements often induce opposite effects. For instance activation of P2 receptors stimulates platelet aggregation while activation of P1 receptors has anti-platelet effect. This provides broad range of therapeutic opportunities, but this is also important disadvantage as it is difficult to achieve specificity and avoid unwanted effects. Despite that, there are several success stories of clinical applications with anti-platelet drug clopidogrel (P2Y12 receptor antagonist) as an as an example. Purinergic signaling is especially important in vascular pathologies. Our group identified purinergic receptors and ectoenzymes on the surface of cellular elements of the aortic valves. Activity of e5'NT responsible for adenosine production on the surface of the aortic leaflets was found to be the highest in the human body. We found profound alterations of the ectoenzymes activities on the surface of the aortic valves in calcific aortic valve disease in humans which include reduction of e5'NT activity and elevation of eADA activity. Mice genetically altered to delete e5'NT activity was found to develop alterations of aortic valve leaflets. This has several practical implications: genetic variations of purinergic receptors or enzymes could relate to valve disease. Purinergic drugs (clopidogrel, ticagrelor, ticlopidine, dipyridamole, deoxycoformycin or newer A1 or A2b activators) could be effective in prevention of aortic valve disease. Finally, prevention of degeneration of implanted biological valves could be achieved by its engineering to enhance adenosine production and to block ATP/ADP signaling.

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S6.L3

HIGH SALT INTAKE PROMOTES ENDOTHELIAL DYSFUNCTION AND IMPAIRS BRAIN FUNCTION. ROLE OF THE IMMUNE SYSTEM

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consumption of sodium chloride (HSD) is well known risk factor for cardiovascular diseases including hypertension and ischemic stroke. We, and others have documented that long lasting HSD leads to dysfunction of the endothelium manifested by a decreased shear stress-dependent production of a potent vasodilator nitric oxide (NO) and decreased response of brain blood vessels to endothelium-dependent vasodilators in rodents, in the absence of increased blood pressure. One of the reasons why HSD leads to endothelial dysfunction may be damage of the endothelial glycocalyx which plays essential role in shear stress activation of endothelial NO synthase. Dysfunction of the endothelium may lead to the impairment of functional hyperemia and produce symptomatic neuronal dysfunction. Recently, neuronal dysfunction and cognitive impairment was reported in rats fed HSD for several weeks. It is not known, however, how excess dietary salt leads to NO deficit and vascular morphological changes as there is no increase in plasma concentration of sodium ions during consumption of HSD. This challenges the direct effect of sodium ions on blood vessels. Considering that gastrointestinal tract is in direct contact with ingested sodium, the participation of the gut microbiota cannot be excluded. Particularly, in view of the results reported in the literature demonstrating that HSD may lead to the increase of plasma trimethylamine N-oxide (TMAO) concentration and gut dysbiosis. We were, however, unable to demonstrate an increase in TMAO plasma concentration in the rats fed HSD for 4 weeks. Recently published results convincingly demonstrate that dietary salt promotes neurovascular and cognitive impairment through a gut initiated TH17 response.

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S6.L4

RECIPROCAL RELATIONSHIP BETWEEN ARTERIAL BLOOD PRESSURE AND GUT MICROBIOTA

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Trillions of microbes inhabit the human gut. Recent scientific advances demonstrate that their role goes beyond assisting in food breakdown and nutrient extraction. Metabolites produced by commensal microbiota are beginning to be recognized as biologically active compounds. Given the striking similarity of the gut microbiota-derived metabolites to the signaling molecules generated natively by the host, the microbiota can orchestrate a plethora of responses from the host and recognize and respond to endogenous signals. For instance, short-chain fatty acids, which are the products of dietary fiber bacterial fermentation, have been found to dilate blood vessels and lower blood pressure, whereas trimethylamine, a gut bacteria metabolite of carnitine and choline, has recently emerged as a potentially toxic molecule. The interaction between the host and gut bacteria is bidirectional. On the one hand, gut bacteria may affect the host's homeostasis *via* blood-borne bacterial products. On the other, the host can affect the gut bacteria by dietary habits and ingestion of antibacterial food preservatives, medicinal products, or other substances that may alter the gut environment. To enter the bloodstream, microbiota products cross the gut-blood barrier, a multilayer system of the intestinal wall. Experimental and clinical studies show that cardiovascular diseases may compromise the gut-blood barrier function and increase gut-to-blood penetration of microbiota-derived molecules. This paper explores how gut microbiota-derived metabolites impact the regulation of arterial blood pressure. It also discusses recent findings demonstrating how hypertension-induced changes in intestines may affect gut microbiota composition.

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S6.L5

ROLE OF STEAROYL-COA DESATURASE 1 IN CONTROL OF THE HEART FUNCTION THROUGH LIPID METABOLISM CHANGES IN HYPERTHYROIDISM

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Thyroid hormones (TH) and stearoyl-CoA desaturase 1 (SCD1), an enzyme responsible for monounsaturated fatty acids (FAs) synthesis, are both involved in reprograming of cardiac metabolism, what affects heart function and structure. TH *via* thyroid hormone receptors (TR) can modulate expression of the genes involved in heart function, e.g. myosin heavy chain α and β (*Myh6* and *Myh7*) and lipid metabolism, e.g. fatty acid synthase (*Fas*) and sterol regulatory element-binding protein 1 (*Srebf*). The mechanism identifying the role of TH-SCD1 cross-talk in the control of heart work is still unknown. Therefore, the aim of the presented study was to determine the interrelation between SCD1 and TH in the regulation of the lipid metabolism and heart function in hyperthyroidism. To induce hyperthyroidism wild type (WT) and SCD1$^{-/-}$ mice were injected with triiodothyronine (T3). Performed analyses show increase of T3 and free T3 plasma level both in WT and SCD1$^{-/-}$ hyperthyroid mice and additional elevation of thyroid stimulating hormone (TSH) in SCD1$^{-/-}$ mice. Ablation of SCD1 in hyperthyroidism led to decrease in the left ventricle (LV) end-diastolic dimension with a simultaneous increase in LV wall thickness and an improvement in systolic and diastolic functions, when compared to WT littermates. Moreover, decreased triglyceride content was observed in hyperthyroid SCD1$^{-/-}$ mice, unlike to increase of FAs and diacylglycerol in hyperthyroid WT. Those changes were caused by simultaneous activation of lipolysis (increase of adipose tissue specific triglyceride lipase (ATGL) and elevated phosphorylation of hormone-sensitive lipase (HSL)) and lipogenesis (elevated SREBP-1 and FAS protein levels) in WT hyperthyroid mice, in contrast to activated only lipolysis in SCD1$^{-/-}$ hyperthyroid mice. Furthermore, changes in lipid metabolism were associated with increase in TRα and TRβ protein levels in WT hearts after TH administration, what was not observed in SCD1$^{-/-}$ mice. Additionally, in hyperthyroid SCD1$^{-/-}$ hearts, *Myh6* expression was not changed, what is consistent with unchanged TR levels. Collectively, these results indicate that SCD1 is a key factor in the regulation of TH-dependent changes in lipid metabolism in cardiomyocytes, what can affect heart function, structure and contractility.

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S6.L6

STEAROYL-COA-DESATURASE 1 AFFECTS DAMAGED MITOCHONDRIAL DYNAMICS AFTER DOX TREATMENT

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Doxorubicin (DOX) is a widely used drug in cancer therapy which also exerts cardiotoxic effects. DOX affects function and structure of mitochondria in cardiomyocytes and thus causes changes in mitochondrial dynamics, ATP production and oxidative phosphorylation chain (OXPHOS). One of the main lipogenic enzyme, stearoyl-CoA-desaturase 1 (SCD1) is an important point in regulation of heart function and structure, however its role in DOX induced cardiotoxicity is unknown. Therefore, the aim of the present study was to determine if SCD1 is involved in regulation of mitochondrial structure, dynamics and activity, and development of cardiomyocytes dysfunction caused by DOX. Murine HL-1 cardiomyocytes were treated with DOX and SCD1 inhibitor A939572. Performed analyses show that SCD1 inhibition in cardiomyocytes increases number of mitochondria, modulates their shape and does not affect mitochondrial membrane potential. Interestingly, SCD1 inhibition in DOX treated cardiomyocytes increases number of mitochondria when compared to DOX condition. Additionally SCD1 inhibition decreases expression of mitochondrial fission genes Mfn1 and Mfn2 reversing upregulation caused by DOX. Mitochondrial homeostasis disruption is associated with changes in mitochondrial structure and activity, ATP production and anion transporting protein levels (e.g. uncoupling protein 3 (UCP3)). Blocked SCD1 activity in DOX condition elevates UCP3 protein level and reduces ATP production. Moreover DOX treatment decreases protein level of complex 1 (OXPHOS chain) and SCD1 inhibition reverses this effect. ATP production is related to peroxisome proliferator-activated receptor alpha (PPARα), transcription factor that is involved in control of β-oxidation of fatty acids (FAs) in mitochondria. Elevated PPARα protein level and decreased free FAs level was observed in cardiomyocytes treated with both DOX and SCD1 inhibitor when compared to cardiomyocytes treated only with DOX. Obtained results suggest that SCD1 inhibition can improve and stabilize mitochondrial functionality after DOX treatment.

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S6.L7

THE EFFECT OF ISOPROTERENOL ON THE DEVELOPMENT OF HEART FAILURE IN C57BI/6J MICE

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Isoproterenol is a nonselective beta-adrenergic agonist used widely for inducing heart failure in mice. The main purpose of this study was to confirm the cardiotoxicity of isoproterenol based on in vitro and in vivo models. *In-vitro* model: to analyze the mitochondrial function rat cardiomyocytes (H9c2 cells) were cultured in a DMEM medium. The mitochondrial function was assessed using the Agilent Seahorse XF Cell Mito Stress equipment after 48 h treatment with 10, 20, 50 and 100 μM isoproterenol. Respiration was quantified by sequential addition of 1.5 μM oligomycin, 1.0 μM FCCP, and 0.5 μM rotenone with antimycin B. *In-vivo* model: male mice (n=4–6) were treated with isoproterenol (100 mg/kg) administered subcutaneously for 4 or 8 days. For the transthoracic echocardiography, mice were anesthetized with ketamine (100 mg/kg) and xylazine (10 mg/kg) intraperitoneally. After chest hair removal, animals were placed on a heated platform to maintain the body temperature at 37°C. The transducer was placed above the anterior chest wall and hemodynamic parameters, including stroke volume (SV), left ventricular ejection fraction (EF) and fractional shortening (FS) as well as cardiac output (CO) and left ventricular (LV) Mass were collected. The statistical analysis was performed using Graph Pad Prism 7 (Graph Pad Software). Paired Student t-test was used for comparisons between two groups. A p-value <0.05 was considered a significant difference. The analysis of the mitochondrial function of the H9c2 cells showed a significant reduction in the oxygen consumption rate (OCR) at 50 μM isoproterenol treatment. This dose caused a significant reduction in basal respiration ($p<0.01$), as well as ATP-linked respiration ($p < 0.001$). Interestingly, the 100 μM dose turned out to be toxic to the H9c2 cells. After 4 days of treatment, no deterioration in cardiac function was observed. Furthermore, a significant decrease in EF ($p<0.001$) and FS ($p<0.05$), and an increase of LV Mass ($p<0.05$) was observed after 8 days compared to the control group. These results indicate the deterioration of left ventricular function induced by the 8-day administration of isoproterenol. Based on *in vitro* and *in vivo* studies, we have shown that isoproterenol reduces heart function and develops heart dysfunction both at the structural and cellular levels.

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S6.L8

EFFECT OF KISSPEPTIN-10 ON THE REGULATION OF COLLAGEN METABOLISM IN THE HEART

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Myocardial fibrosis is connected with remodeling of the connective tissue of the heart. It is mainly caused by overproduction of collagen by fibroblasts. The main factors that regulate collagen metabolism in the heart include cytokines, endopeptidases, reactive oxygen species and hormones. Kisspeptin-10 (KiSS-10) is the product of the *kiss-1* gene and belongs to the RF-amide peptide family. The aim of the present study was determination of the collagen metabolism in cardiac fibroblasts under the influence of KiSS-10. The effect of KiSS-10 on collagen metabolism within the heart of mice was also examined. The experiments were performed on human cardiac fibroblast cell line and male BALB/c mice. This *in vitro* model was used to assess intracellular collagen content, expression of α1 chains of procollagen type I and III, C-terminal propeptides of procollagen type I and III (PICP and PIIICP), metalloproteinases (MMP-1, -2, -9), tissue inhibitors of metalloproteinases (TIMPs 1-4), transforming growth factor β1 (TGF-β1). The *in vivo* studies were carried out to determine the serum level of PICP and PIIICP. The collagen content and expression of α1 chains of procollagen type I and III within the hearts of mice were also measured. KiSS-10 significantly elevates the content of collagen in the heart and cardiac fibroblasts cultures. These changes correlate with an increase in the level of the PICP and PIIICP in human cardiac fibroblast culture medium as well as mouse PIIICP in serum. *In vitro*, this hormone inhibits the release of matrix metalloproteinases (MMP-1, -2, -9) and stimulates the secretion of their tissue inhibitors (TIMP-1, -2, -4). KiSS-10 also increases the expression of α1 chains of procollagen type I and III *in vitro*. However, the introduction of KiSS-10 to the cardiac fibroblasts cultures does not affect release of TGF-β1. The results indicate that KiSS-10 is involved in the regulation of heart fibrosis. Augmentation, by KiSS-10, of the collagen deposition is dependent on the protein synthesis elevation, inhibition of matrix metalloproteinases (increase of TIMPs release) or decrease of matrix metalloproteinases (MMP-1, 2, 9) concentration. The effect of KiSS-10 is related to direct action of this compound on cardiac fibroblasts. However, the profibrotic activity of KiSS-10 is not dependent on release of TGF-β1. The present study points at KiSS-10 as the novel target for antifibrotic therapy.

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S6.L9

INFLUENCE OF GUT DYSBIOSIS CAUSED BY HIGH FAT DIET ON THE MYOCARDIAL FUNCTION

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High fat diet can induce intestinal dysbiosis and lead to chronic, systemic inflammation that affects myocardial function. The aim of the project was to investigate whether the pro-inflammatory effects of intestinal dysbiosis and a high fat diet are related to dysfunction of the rat heart muscle. The studies were conducted on 15 male Sprague Dawley rats, divided into the two groups: rats on normal fat diet (NFD), n=7, contained: 3.6% fat, 17.4% protein, 60% carbohydrates, 0.2% sodium, 2864 kcal/kg (Labofeed B, Kcynia, Poland), and rats on high fat diet (HFD), n=7, contained: 31% fat, 17.1% protein, 35.5% carbohydrates, 0.18% sodium, 3842kcal/kg (Laboffed B, Kcynia, Poland). Faeces for microbiota analysis were collected from randomly selected 12-week old rats on NFD (n=3) and on HFD (n=3). The same rats on NFD (n=3) and HFD (n=3) from which feces were collected for microbiological analysis were subjected to the ECHO study. Immediately after ECHO test all rats on NFD (n=7) and on HFD (n=7) were euthanized in order to plasma and left ventricular (LV) tissue collection for biochemical analysis. The multiplex real time PCR analysis was conducted for determining the rat TLR4 and TLR6 receptor. Plasma LPS concentrations were also determined using ELISA. In the fecal cultures of NFD rats, there were obtained a higher number of bacteria in the phylum *Proteobacteria*: *Escherichia coli* and phylum *Firmicutes*: *Enterococcus spp*. Whereas in the fecal cultures of HFD rats were received a higher number of bacteria in the phylum *Bacteroidetes*: *Bacteroides spp*. In the ECHO analysis in the HFD rats were noted mild generalized LV hypertrophy accompanied by a larger left atrium. Additionally, left ventricular diastolic dysfunction was also indicated in the HFD rats in comparison with the NFD rats. RT-PCR analysis showed significantly higher expressions of TLR4 mRNA and TLR6 mRNA in the LV in the HFD rats compared to the NFD rats. The plasma concentration of LPS in HFD rats was slightly elevated compared to NFD rats. In conclusion, presented study indicates that gut dysbiosis in rats on a HFD may have a pro-inflammatory effect related to myocardial dysfunction.

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S6.L10

EFFECTS OF PERIPHERAL CANNABINOID CB_1 RECEPTOR INVERSE AGONIST JD5037 IN MONO- AND POLYTHERAPY WITH METFORMIN IN A MONOCROTALINE-INDUCED RAT MODEL OF PULMONARY ARTERIAL HYPERTENSION

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Pulmonary arterial hypertension (PAH) is an incurable disease leading to an increased pressure in the pulmonary artery and right heart failure. It has been proved that the adenosine monophosphate-activated protein kinase (AMPK) activator, metformin (MET), plays a protective role in chronic PAH. Peripheral CB_1 receptor antagonists reduce the number of pathological changes in experimental lung fibrosis. The aim of this study was to evaluate the effect of the peripheral cannabinoid CB_1 inverse agonist JD5037 given in mono- or polytherapy with MET in an experimental PAH model and in PAH-free control animals. Experiments were performed on Wistar rats, in which PAH was induced by a single injection of monocrotaline (MCT) (60 mg/kg, s.c.) at day 0. The control group was injected with saline. During the experiment, which was conducted for 21 days, animals were given JD5037 (3 mg/kg), MET (100 mg/kg), combination of these compounds or its vehicles (DMSO, Tween, 0.9% NaCl or 0.9% NaCl, respectively) by oral gavage once a day. The MCT-induced PAH caused an increase in the right ventricular systolic pressure (RVSP), Fulton index (the right ventricle weight to left ventricle plus septum weight), lung hypertrophy and decrease of oxygen saturation. MET preventive treatment has shown a tendency to reverse these changes. JD5037 did not modify positively any of the parameters except for the tendency to increase the oxygen saturation. Polytherapy with JD5037 and MET has shown various changes. Not only did it tend to decrease right ventricle hypertrophy, but also caused a significant increase of the oxygen saturation and reduction of RVSP. In conclusion, the monotherapy with JD5037 does not influence PAH-related changes in physiological parameters significantly. However, the polypharmacological treatment with MET possesses better potency than any of these compounds alone.

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S6.L11

HOW BEETROOT JUICE NITRATES CAN MODULATE THE FUNCTION OF THE AUTONOMIC NERVOUS SYSTEM? A THEORETICAL FRAMEWORK

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According to the literature, beetroot juice contains a number of compounds that can have a significant impact on health, e.g. nitrates. Nitrates in the body are finally reduced to nitric oxide (NO), which has a positive effect on the cardiovascular system, inter alia, by regulating blood pressure. There are two ways of NO formation in the human body - the endogenous one using L-arginine and NO synthase (NOS) and the exogenous one using dietary nitrates, which are processed in the nitrate-nitrite-NO pathway. A frequently proposed mechanism of NO action in the circulatory system is a local effect leading to an improvement in blood flow by relaxing the blood vessels or by improving the function of the peripheral vascular endothelium. We have suggested that nitrogen oxide from beetroot juice may also improve cardiovascular parameters by modulating the autonomic nervous system (AUN), possibly influencing the reflex pathway, including the baroreceptor and peripheral chemoreceptor reflexes. In this presentation, we proposed a possible model for the effects of beetroot juice nitrates on AUN, pre-identifying possible challenges for scientists in this field.

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S6.L12

BREATHING DISORDERS IN ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a neurodegenerative, age-related disorder and most common reason for dementia, with over 45 million people worldwide affected. Its main features are cognitive and neuropsychiatric symptoms leading to progressive impairment and disability. The characteristic neuropathological abnormalities such as progressive accumulation of amyloid-β plaques (Aβ), intracellular neurofibrillary tangles of hyperphosphorylated tau protein, and decreased synaptic density are believed to result in neurodegeneration and depletion of brain neurotransmitters. Apart from impaired cognitive function, disturbances in respiration are a frequent occurrence in AD patients. Among them the leader is sleep apnea, but respiratory dysrhythmias, shortness of breath, bronchitis, and pneumonia are also observed. Despite serious respiratory problems that reduce quality of life, they are often undiagnosed and untreated and their causes are not well understood. There have been recent attempts to study respiratory changes in an animal model of disease induced by streptozotocin (STZ) injection into the lateral brain ventricles. Studies, imitating sporadic AD, showed significant astrogliosis in the commissural part of the nucleus tractus solitarii and blunted ventilatory response to hypoxia exposure (Ebel 2017, Brown 2019). Another study displayed only increased sensitivity to CO_2, attributed to augmented Aβ expression in the locus coeruleus (LC), an important chemosensitive area in the brainstem (Vincente, 2018). Unfortunately, the results differ despite fairly similar experimental conditions. In our study we investigated hypoxic and hypercapnic ventilatory responses in transgenic mice model of AD (AβPP V717I-'London mutation'). Transgenic mice with APP gene mutation and extensive AβPP overexpression recapitulate a number of features of familial early-onset AD cases. Our research displayed unchanged hypoxic ventilatory response and increased ventilatory response to hypercapnic stimulus. In further steps we examined whether treatments used in AD therapy have any impact on breathing. APP^+ mice were treated intraperitoneally with cholinesterase inhibitor-rivastigmine or NMDA receptor antagonist-memantine, in attempt to turn over augmented hypercapnic ventilatory response. Although memantine had no impact on respiration of APP^+ mice, rivastigmine was effective in reducing chemoreflex respiratory response due to decrease of tidal volume and frequency of breathing. Nevertheless, hypercapnic response did not return to the level present in control APP^- mice suggesting that dysfunction of another neurotransmitter system may be involved in an altered response to hypercapnia, and this leaves room for further research.

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S6.L13

DEFICIT OF MONOAMINES IN RESERPINE PARKINSON'S DISEASE MODEL ALTERS THE HYPOGLOSSAL NERVE ACTIVITY

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Hypoglossal (HG) and phrenic (PHR) nerves are the main nerves involved in respiratory muscle control. The respiratory deficits observed in Parkinson's disease (PD) may manifest as HG and PHR nerve dysfunction and may result not only from dopamine, but also serotonin and noradrenaline deficiencies. Therefore aim of this study was to analyze the activity of HG and PHR nerves in reserpine rat model imitating deficit of biogenic monoamines. Experiments were performed on anesthetized, paralyzed and vagotomized adult male Wistar rats divided into two groups; with reserpine 5 mg/kg and alpha-methyl-p-tyrosine 250 mg/kg pretreatment (n=7) and with vehicle injections (n=9). By the use bipolar electrodes the amplitude and frequency of discharges of both nerves in normoxia, acute hypoxia (8% O_2 in N_2) and during recovery after apnea were recorded. Following electrophysiological experiments brains were collected and striatum and brainstem were dissected to monoamine level detection by the HPLC analysis. Reserpine treated rats, in contrast to sham, showed decreased baseline amplitude and minute HG activity, and also blunted depressive phase after hypoxic exposition. The pre-inspiratory activity of HG nerve in reserpine treated rats was reduced by shortening the pre-inspiratory time of HG activity and the ratio of pre-inspiratory time to total respiratory cycle length and by decreasing the ratio of pre-inspiratory to inspiratory amplitude during normoxia, hypoxia and recovery. We suggest that the massive depletion in the brainstem of not only dopamine (75%), but also noradrenaline (92%) and serotonin (72%), has an impact on the pre-inspiratory activity of the HG. The pre-inspiratory HG activity is responsible for maintaining the appropriate diameter of the upper airway in the pre-inspiratory phase, preparing for inspiration. Altered pre-inspiratory activity in the reserpine rats may shed some light on the cause of obstructive sleep apnea development in some PD patients. New therapeutic strategy involving the supplementation of amine depletion other than dopamine is suggested.

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S6.L14

DAILY SITTING TIME AFFECTS LACTULOSE-INDUCED CHANGES IN HYPOXIC RESPONSIVENESS IN HUMANS

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Despite growing interest in the role of gut microbial signaling in the regulation of multiple physiological systems, our understanding of the contribution of gut microbiota to respiratory control in humans remains very limited. We have recently demonstrated in a group of healthy subjects that the increased gut microbial fermentation is associated with augmented ventilatory responses to transient hypoxia, which implied the altered function of peripheral chemoreceptors. In this report, we have evaluated whether such changes in hypoxic responsiveness might be related to the subjects' body composition and declared physical activity. Sixteen healthy volunteers (8 men; mean ± SD age 25.9 ± 5.2 years) underwent two separate trials, receiving lactulose (stimulating gut microbial fermentation) or placebo. Ventilatory and haemodynamic responses to the acute hypoxia were evaluated before and two hours after the test meal. Hydrogen breath tests were applied to evaluate gut fermentation intensity. All participants underwent anthropometric measurements and body composition analysis, and filled IPAQ-SF questionnaire. Declared sitting time (ST; hours per day) negatively correlated with the magnitude of the lactulose-induced changes in the following hypoxic responses: minute ventilation response ($r= –0.57$, $p=0.022$); heart rate response ($r= –0.64$, $p=0.007$); systemic vascular resistance response ($r= –0.69$, $p=0.005$). No such correlations were obtained in placebo test. Neither ST, nor aforementioned changes in hypoxic responses were found related to the body composition parameters (BMI, body fat content, skinfold thicknesses; $p >0.05$). Daily sitting time modulates the effect of increased gut microbial fermentation on the hypoxic responsiveness in humans. These results emphasize the need of further research linking gut microbiome, physical activity and respiratory control mechanisms.

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S6.L15

VASOPRESSIN AND V1A RECEPTORS IN HEMODYNAMIC AND RESPIRATORY REGULATION IN NORMOTENSIVE AND HYPERTENSIVE RATS

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Vasopressin (AVP) and its V1a receptor (V1aR) have been implicated in pathophysiology of essential hypertension. V1aRs have been found in the cardiovascular and respiratory neurons of the brainstem and in the carotid bodies. AVP has been shown to affect both circulatory and respiratory function in normotensive animals. In our study we investigated the role of AVP and V1aRs in the regulation of cardiorespiratory parameters under normo- and hypertensive conditions. Male normotensive Wistar-Kyoto (WKY) (n=7) and spontaneously hypertensive (SHR) (n=7) rats were instrumented with: vascular catheters implanted into the femoral vein (intravenous (i.v.) infusions) and the femoral artery (hemodynamic parameters); the tracheal tube (respiratory parameters); and subcutaneous ECG electrodes (heart rate; HR). The responses to AVP (10 ng/100 µL i.v.) and pharmacologically evoked arterial chemoreflex (KCN; 30 microg/100 microL i.v.) were tested before and after administration of V1aR antagonist ((d(CH2)51,Tyr(Me)2,Arg8)-vasopressin; 5 µg/100 µL i.v.). Resting mean arterial blood pressure (MABP) and minute ventilation (MV) were significantly higher and the chemoreflex-evoked changes of MABP and MV were significantly greater in SHR than in WKY rats. In SHR rats administration of AVP resulted in a significantly greater increase in MABP than in WKY controls, but only in SHR it was accompanied by reduction in MV and respiratory rate (RR). Blockade of V1aRs caused a decrease of MABP in both groups and increase in MV and RR only in SHR rats. V1aR antagonist decreased the pressor response of the chemoreflex and abolished all responses to AVP in both groups. Our findings confirm increased sensitivity of the arterial chemoreflex and enhanced pressor and respiratory responses to AVP in SHR rats that are dependent on V1aRs.

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S6.P1

CHEMOSENSITIVITY DURING MECHANO AND METABOREFLEX ACTIVATION IN HEALTHY SUBJECTS CHARACTERIZED BY LOW AND HIGH EXERCISE CAPACITY

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The behavior of the peripheral chemoreceptor reflex during: (i) concomitant stimulation of the muscle mechanoreceptors alone, or (ii) combined stimulation of mechano- and metaboreceptors remains poorly known and the nature of the interaction between these reflexive mechanisms is likely to be influenced by the level of aerobic and/or anaerobic capacity. This study aimed to explore this issue in a group of 19 healthy, young volunteers: 9 men; age: 28.5 ± 3.8 years, body mass index: 24.0 ± 3.7 kg/m2 (mean ± SD). Anaerobic fitness was tested by the Wingate test, while aerobic fitness was tested with the progressive RAMP test. A bicycle ergometer was used for both tests. Peripheral chemoreflex sensitivity (PChS) was assessed by the transient hypoxia method at rest, during passive pedaling (activation of muscle mechanoreflex), and passive pedaling with circulatory occlusion of the lower limbs (simultaneous activation of muscle mechano- and metaboreflex). The subjects were divided into the low- and high-anaerobic fitness groups and the low- and high-aerobic fitness groups according to medians of the Wingate test and the RAMP test, respectively, and the PChS at rest, during passive pedaling and passive pedaling with circulatory occlusion of the lower limbs were compared between low- vs. high-fitness groups. We found no difference in the PChS at rest, during passive pedaling and passive pedaling with circulatory occlusion of the lower limbs between the high- and low-fitness groups. It can be concluded that the level of the aerobic and anaerobic capacity does not affect the nature of the interaction between the peripheral chemoreflex and the mechano- and metaboreflexes in humans.

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S6.P2

CARDIAC PHYSIOLOGY AFTER OSTARINE TREATMENT – *IN VITRO* STUDY ON H9C2 CARDIOMYOCYTES AND FIBROBLASTS

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Selective androgen receptor modulators (SARMs) are a dynamically developing group of anabolic substances. While many SARMs have been tested in clinical trials, none have been yet approved by the drug committee (FDA). The most popular of them is ostarine (enobosarm, GTx-024), a compound that is becoming more and more popular as a doping agent, using often in high doses. Easy access and interest in these compounds means that the actual number of SARMs users is large and steadily growing. The dangerous effects of anabolic androgenic steroids (AAS) on the heart are being investigated - i.e. myocyte hypertrophy, disturbation in the lipid profile or promote fibrotic changes have been described. However, ostarine has not been studied for its effects on the heart. We decided to investigate the effect of ostarine on the metabolism and functioning of the heart using *in vitro* techniques. H9C2 myoblast lines and isolated fibroblasts from the hearts (CF) of young rats were used. Cells were treated with ostarine at selected doses for 24 and 48 hours, then we determined protein content, survival and proliferation using MTT and BrdU. Additionally, CF were treated for 24, 48 and 72 h to assess the expression of the fibrosis genes. We have shown that ostarine affects cell proliferation, survival, and protein content in tested cells. We also showed an increase of gene expression - fibronectin and αSMA involved in the processes of fibrosis. According to our results, ostarine may have a negative impact on the functioning of the heart. The use of ostarine may be a potential risk factor in the development of cardiovascular disease, but more research is needed.

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S6.P3

EVALUATION OF THE ANTI-INFLAMMATORY AND ANTI-PROLIFERATIVE PROPERTIES OF CANNABIDIOL IN AN EXPERIMENTAL MODEL OF MONOCROTALIN-INDUCED PULMONARY HYPERTENSION.

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Pulmonary hypertension (PH) is a rare disease of multifactorial etiology leading to right ventricular failure and remodeling of pulmonary arteries of small diameter (40–100 μm). Additionally, in development of PH inflammatory process is involved and level of inflammatory mediators positively correlates with the advancement of the disease. Cannabidiol (CBD), isolated from *Cannabis sativa* L. var. *indica*, is characterized by a lacks of psychoactive properties and its potential therapeutic use in diseases related to inflammation and proliferation has been suggested. The aim of the study was to evaluate the effect of CBD on the selected parameters of inflammation and remodeling in the lungs of rats with PH induced with the plant alkaloid - monocrotaline (MCT) - MCT-PH rats. The studies were carried out on rats with and without PH (control group). CBD (10 mg/kg) or its solvent was administered in a preventive model, once daily intraperitoneally for 3 weeks (from day 1 to 21) after administration of MCT at a dose of 60 mg/kg (in groups with MCT-PH) or solvent for MCT (in groups without PH). ELISA, western blot and immunohistochemistry methods were used. A very strong expression of galectin-3, a marker of inappropriate pulmonary remodeling and inflammation, was found in the lungs of rats with MCT-PH and the alveolar macrophages of these rats showed morphological signs of activation. MCT-PH group showed increased concentration of inflammatory parameters in lung tissue (tumor necrosis factor-α and nuclear factor-κB) and serum (M-CSF). Administration of CBD to MCT-PH rats resulted in a marked reduction of galectin-3 and interleukin-1 immunoreactivity, and inflammatory mediators. In conclusion, CBD could be used as an adjunct therapy in the treatment of PH because of its potential property of stopping or slowing down the remodeling process caused e.g. by inflammation, and thus limiting the adverse effects of the development of PH.

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S6.P4

THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS ANACETRAPIB AND TORCETRAPIB ON LIVER DIMETHYLARGININE DIMETHYLAMINOHYDROLASE-1 ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA

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Dimethylarginine dimethylaminohydrolase (DDAH) is an enzyme found in all mammalian cells. There are two isoforms of DDAH - DDAH1 and DDAH2, with some differences in tissue distribution of the two isoforms. DDAH1 predominates in tissues that express neuronal NOS (nitric oxide synthases), while DDAH II predominates in tissues expressing endothelial NOS. DDAH degrades methylarginines, specifically asymmetric dimethylarginine (ADMA) and NG-monomethyl-L-arginine (MMA). Inhibition of DDAH activity causes methylarginines to accumulate, blocking nitric oxide(NO) synthesis and causing vasoconstriction. An impairment of DDAH activity appears to be involved in the elevation of plasma ADMA, and impairment of vascular relaxation observed in humans with cardiovascular disease or risk factors. The activity of DDAH is impaired by oxidative stress. The cholesteryl ester transfer protein (CETP) inhibitors have ability to elevate high density lipoprotein (HDL) level. It is supposed that protective effect of CETP inhibitors on endothelial function may be HDL-independent and related to its effect on DDAH/ADMA/NO pathway. The present study was undertaken in order to answer the question whether the treatment of anacetrapib or torcetrapib affect liver DDAH1 activity/expression and therefore modulate endothelial function. Fructose-induced (FRU) dyslipidemic rats were treated for 1 week with anacetrapib (ANA) (3.0 mg/kg p.o) or with torcetrapib (TOR) (10 mg/kg, p.o). Liver activity of DDAH1 and plasma NO concentration were measured spectrophotometrically. The expression of DDAH1 protein was determined by ELISA method. The administration of both drugs increased plasma NO level in fructose-fed rats. Both ANA and TOR had no effect on liver DDAH1 activity. The significant increase of DDAH1 expression was found in liver of fructose-fed rats treated with torcetrapib (FRU+TOR) vs. fructose-fed rats (FRU) and fructose-fed rats treated with anacetrapib (FRU+ANA). We concluded that treatment with CETP inhibitors increased plasma NO level and affected DDAH1 expression in rats' liver. Therefore, treatment with CETPi most probably modulate endothelial function in dyslipidemia.

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S6.P5

THE CHARACTERISTICS OF A SUB-CHRONIC MODEL OF NON-ATOPIC ASTHMA

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Non-atopic asthma is, contrary to the allergy-related form of the disease, more severe and more difficult in treatment, less responsive to corticosteroids, and involves neutrophils instead of eosinophils in its progression. There are only a few animal models of the disease, none of them being proven to be chronic. Therefore, there is a high need for stable models of non-atopic asthma enabling a chronic or sub-chronic administration of potential drugs. The aim of the study was a verification if the hapten-induced murine model of asthma remains stable for at least two weeks after final induction. For this purpose, adult Balb/c mice were twice skin-sensitized with DNFB, and 4 days later were challenged intratracheally with DNS. A methacholine test was performed to access the airway hyperreactivity. Later, the animals were kept for two weeks in the local animal facility under standard conditions. Then, the mice were once again challenged with DNS and the methacholine test was repeated. At the end, the number of inflammatory cells in BALF was determined. Control recordings showed a typical pattern of airway hyperreactivity (AHR) in non-atopic asthma with growing PenH values in response to increasing methacholine concentrations. After two weeks, the pattern of AHR changed and the reaction to methacholine was weaker at its higher concentrations. Parallelly, basic ventilatory parameters including ventilation, breathing frequency, and inspiratory/expiratory times did not change. The total number of inflammatory cells increased while the percentage of neutrophils declined compared to single DNS challenge mice. The results suggest a decrease of airway hyperreactivity, a stabilization of the airway inflammation at the level of cellular influx and a probable shift towards other forms of asthma, the non-neutrophilic ones. This leads to the conclusion that the DNFB/DNS-induced model of non-atopic asthma is not stable during two weeks after induction. To maintain the proper level of features of non-atopic asthma, a re-sensitization repeated each week should be considered.

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S6.P6

THE EFFECT OF CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) INHIBITORS, ANACETRAPIB AND TORCETRAPIB, ON PLASMA AND LIVER PARAOXONASE 1 (PON 1) ACTIVITY AND EXPRESSION IN RATS WITH FRUCTOSE INDUCED DYSLIPIDEMIA

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The paraoxonase family consists of three proteins: PON1, PON2 and PON3. They are differentially expressed and have different functions. PON1 is an antioxidant glycoprotein synthesized in the liver and secreted to the bloodstream. It binds high-density lipoproteins (HDL) and therefore potentiates their antioxidant and antiatherogenic properties. The cholesteryl ester transfer protein (CETP) inhibitors are a new class of lipid-lowering drugs that can elevate HDL level. However, the development of various cardiovascular diseases is related to HDL function, rather than HDL level. The present study was undertaken in order to answer the question whether the treatment of anacetrapib or torcetrapib can modulate PON1 activity and expression, the HDL-associated antioxidant enzyme. Fructose-induced (FRU) dyslipidemic rats were treated for 1 week with anacetrapib (ANA) (3.0 mg/kg p.o) or with torcetrapib (TOR) (10 mg/kg, p.o). Plasma and liver activity of PON1 was measured spectrophotometrically. PON1 protein expression was assessed by enzyme immunoassay technique. Eight 8 weeks of fructose administration resulted in decrease of plasma PON1 activity. By contrast, the significant increase of PON1 activity was found in the liver of fructose-fed rats (FRU). The treatment with anacetrapib and torcetrapib resulted in the significant reduction in PON1 activity in the liver. Moreover, TOR increased the PON1 expression in the liver. Both drugs did not affect PON1 plasma PON1 activity and concentration. We conclude CETP inhibitors can impact PON1 activity and expression in the liver but they had no effect on and HDL antioxidant function.

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S6.P7

LONG-TERM EFFECT OF PERIPARTUM DEPRESSION ON THE CARDIOVASCULAR SYSTEM OBSERVED IN THE ADULT RAT FEMALE OFFSPRING

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Peripartum depression is a significant clinical problem affecting both the mother and her offspring. We have previously reported that maternal depression results in altered neurodevelopment and cardio development when examined in adolescent (35-day-old) rat offspring evidenced by significantly increased heart rate and left ventricular (LV) diastolic dysfunction. The present study examined the possibility that the effect of peripartum depression on the cardiovascular system may persist until adulthood. The study was carried out on 14 Sprague Dawley rat dams and their offspring. Half of the dams underwent chronic immobilization stress to induce depression. A urinary corticosterone concentration confirmed immobilization-induced development of the depressive state in dams. The effect of peripartum depression was measured in depressed female offspring (DO) and control females offspring (CO) at six months of age in terms of blood pressure and heart functions (ECHO). Maternal peripartum depression did not significantly affect body weight and LV weight of the offspring. The DO offspring had significantly higher values of both systolic and diastolic blood pressure compared to the CO offspring. ECHO analysis revealed mild LV hypertrophy in the DO offspring. The interventricular septum thickness at end-diastole (IVSd) and LV posterior wall thickness at end-diastole (LVPWd) were both increased in the DO offspring compared to CO offspring. Additionally, LV diastolic dysfunction suggested by the decrease in the speed of the wave e' and the increased ratio of E/e' was observed in the DO offspring. These results suggest that peripartum depression can have a long-term effect on the cardiovascular system persisting until adulthood.

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S6.P8

ELECTROPHYSIOLOGICAL, HEART RATE VARIABILITY, AND BIOCHEMICAL DISTURBANCES IN A RAT MODEL OF 5-FLUOROURACIL INDUCED CARDIOTOXICITY ARE PARTIALLY REVERSED BY CHRONIC VITAMIN D SUPPLEMENTATION

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5-fluorouracil (5-FU) is the most commonly used drug belonging to the fluoropyrimidines. Disturbances of cardiac muscle are one of the most common and dangerous side effects of fluoropyrimidines, including: chest pain, arrhythmias, heart failure, and myocardial infarction. Cardiovascular complications most commonly occur during the first dose. The aim of the study was to evaluate electrophysiological, heart rate variability (HRV), and biochemical changes observed after subsequent doses of 5-fluorouracil and after attempting to reduce cardiotoxicity using vitamin D supplementation. 60 adult male Wistar rats were included in the study. The rats were randomized into 4 groups: in group 1, the rats received 0.9% saline p.o. daily; in group 2, the rats received vitamin D (500 IU/kg) p.o. daily; in group 3, the rats received up to 4 doses of a 0.9% saline i.p. injection every two weeks with 0.9% saline p.o. daily; in group 4, the rats received up to 4 doses of 5-FU (150 mg/kg) i.p. every two weeks with vitamin D (500 IU/kg) p.o. daily. The first injection of 5-FU decreased mean heart rate (289 vs. 275 (beats/min)), sBP (119 vs. 103 (mmHg)), and increased both SDNN (3.22 vs. 4.08 (ms)) and the HRV triangular index (1.51 vs. 1.72). Vitamin D supplementation partially reverse these changes. ECG parameters were affected, including QRSt (34.4 vs. 40.1 (ms)) and QTt (55.8 vs. 62.1 (ms)). Biochemical parameters and ELISA revealed increases in troponin levels after the first and fourth dose (6.65 and 11.92 (ng/ml), respectively). Conclusions: Both electrophysiological and heart rate variability disturbances were observed after subsequent 5-FU administrations, predominantly after the first dose of 5-FU. Chronic vitamin D supplementation reduced partially these cardiotoxic effects of 5-FU in rat model.

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S6.P9

TUMOUR NECROSIS FACTOR RECEPTORS TYPE 1 AND TYPE 2 ARE EXPRESSED IN THE BRAINSTEMS OF NORMOTENSIVE AND HYPERTENSIVE RATS

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Tumor necrosis factor (TNF) is a pleiotropic cytokine involved in the regulation of the cardiovascular system. Accumulating evidence indicates that increased levels of TNF in the brain are associated with arterial hypertension. Proinflammatory effects of the cytokine are mediated by TNF type 1 receptors (TNFR1), whereas activation of TNF type 2 receptor (TNFR2) exerts anti-inflammatory actions. The evidence of expression of both receptors in the cardiovascular centres of the brainstem is limited. We seeked to determine the expression of TNF receptors in the brain regions encompassing cardiovascular centres in normo- and hypertensive rats. In normotensive Wistar-Kyoto (WKY) (n=6) and in spontaneously hypertensive (SHR) (n=6) rats systolic blood pressure (SBP) was measured with tail-cuff method and brains were harvested. Expression of TNFR1 and TNFR2 mRNA was evaluated with RT-PCR in the dorsal and ventral aspects of the medulla containing respectively NTS and RVLM and in the hypothalamus. Immunostaining of TNFR1 and TNFR2 in the brainstem and in the hypothalamus was carried out in WKY and SHR rats (n=2). SHR rats had significantly higher SBP than WKY controls. There were no significant differences in the mRNA expression of TNFR1 and of TNFR2 in the investigated regions between SHR and WKY rats. Immunostaining revealed presence of both subtypes of TNF receptors in the brainstem and in the hypothalamus in both groups. TNF type 1 and type 2 receptors are expressed in the central nervous system, however, surprisingly mRNA levels of the receptors are similar between normotensive WKY and hypertensive SHR rats.

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S6.P10

DEVELOPMENT OF HEART FAILURE IN SPONTANEOUSLY HYPERTENSIVE RATS

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Spontaneously hypertensive rats (SHR) rats are an animal model that strictly reflects to the one of the most common cardiovascular diseases in humans- hypertension. SHR rats are characterized by the development of spontaneous arterial hypertension from 5-6 weeks of age. This study aimed to test whether SHR rats will develop heart failure based on long-term hypertension. Rats were housed in a conventional animal facility with a 12/12 h day/night cycle, in a room with stabilized temperature and humidity (22 ± 2°C, 55 ± 10% humidity). Wistar Kyoto (WKY) rats were the control group, the test group was SHR rats. The studies were conducted after the rats were 6-, 12- and 18-month-old (n=5 in each group). Rats were anesthetized with ketamine (20 mg/kg) and xylazine (10 mg/kg) intraperitoneally. After chest hair removal, animals were placed on a heated platform to maintain the body temperature at 37°C. Transthoracic echocardiography was performed on each animal using a Vevo 1100 (VisualSonics Inc, Canada) equipped with a 40 MHz linear transducer. Images were obtained at a frame rate consistently above 200 frames/s. The transducer was placed above the anterior chest wall. The obtained acquired images were used to calculate hemodynamic parameters such as systolic volume (V systol), diastolic volume (V diastol), stroke volume (SV), LV ejection fraction (EF), and fractional shortening (FS) as well as cardiac output (CO). To measure blood pressure parameters, such as systolic, diastolic, and mean blood pressure, likewise heart rate the CODA tail-cuff system was used. The statistical analysis was performed using Graph Pad Prism 8 (Graph Pad Software). Paired Student t-test was used for comparisons between two groups. Results are presented as mean ± SEM. Based on a statistical analysis of hemodynamic parameters, changes in heart function in SHR rats over time were observed. Left ventricular systolic dysfunction was not observed based on the ejection fraction (EF) in 6-month-old SHR rats (74.26 ± 4.34 vs. 70.32 ± 2.88 (%])). However, in the group of 12-month-old SHR rats, a statistical decrease of this parameter was observed compared to the WKY group (68.86 ± 3.17 vs. 78.73 ± 1.97 (%)). Moreover, in a group of 18-month-old rats, this occurrence was even more pronounced (61.83 ± 1.3 vs. 75.29 ± 2.24 (%)). Another important parameter describing the systolic function of the left ventricle is fractional shortening (FS). The deterioration trend of left ventricular function based on FS was the same as in the of EF (WKY vs. SHR: 6-month: 45.02 ± 3.02 vs. 39.73 ± 2.17; 12-month: 47.36 ± 1.81 vs. 39.06 ± 2.48; 18-month: 44.21 ± 2.16 vs. 32.99 ± 0.85 (%)). All examined SHR rats developed advanced arterial hypertension (systolic/diastolic BP: 198 ± 5.83/145 ± 7.8 (mm Hg); heart rate: 354 ± 11.37 (bpm)). The presented results indicate the development of left ventricular heart failure based on long-term hypertension in SHR rats. This allows the SHR model to be used in experimental *in-vivo* studies in the field of heart failure.

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S6.P11

STEAROYL-COA DESATURASE 4 DEFICIENCY PROTECTS AGAINST HIGH FAT DIET-INDUCED HEART DYSFUNCTION IN MOUSE

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Stearoyl-CoA desaturase (SCD) is an enzyme involved in biosynthesis of monounsaturated fatty acids, what was shown as a crucial point in the regulation of cardiac metabolism. SCD4 is expressed exclusively in the heart and its expression is significantly increased after a high-fat diet (HFD). Therefore, the aim of the present study was to determine the impact of SCD4 deletion on heart function in HFD induced steatosis. Our study showed that HFD in wild type (WT) mice led to remodeling of left ventricle by increased relative wall thickness, decreased end-diastole diameter and stroke volume, but also reduced cardiac output. Simultaneously, no changes in cardiac structure and function were observed in $SCD4^{-/-}$ mice after HFD. Additionally, no changes in expression of hypertrophy markers i.e. α- and β-myosin heavy chain, was observed after HFD in both genotypes. Interestingly, brain natriuretic peptide expression (peptide hormone involved in inhibition of fibrosis, hypertrophy and cardiac steatosis) was decreased in WT hearts after HFD. In $SCD4^{-/-}$ mice this effect was not observed, suggesting beneficial effect of SCD4 deficiency on heart function after HFD. Furthermore, in WT mice in contrast to $SCD4^{-/-}$ proteins involved in Ca2+ dependent cardiac contractility control like Ca^{2+}/calmodulin-dependent protein kinase II and sarcoplasmic reticulum Ca^{2+}-ATPase 2 were decreased and phospholamban was increased after HFD. These changes are consistent with decreased stroke volume noticed only in WT HFD mice. Summarizing, obtained results show that SCD4 is an important point in regulation of heart function and SCD4 is involved in control of induced by HFD changes at morphological and molecular levels in the heart.

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S6.P12

ASSOCIATION BETWEEN DEPRESSION AND UNFAVORABLE NUTRITIONAL, CARDIAC AND LABORATORY OUTCOMES IN PATIENTS WITH CHRONIC HEART FAILURE

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To date, there are no literature reports combining the relationship between depression and chronic heart failure (CHF) in relations to selective nutritional, cardiac and laboratory parameters. The aim of this study was to assess how depression condition in CHF parameters reflects nutritional and laboratory parameters in comparison with non-depressive patients. We enrolled 94 CHF individuals to assess depression prevalence and to compare values of cardiac, laboratory and nutritional parameters between depressed and non-depressed patients. Depression was diagnosed in 66 individuals (70.2%). We noted significant reduction of EF% in group of depressive patients compared to disease-free individuals (mean EF%: 42 ± 12 and 49 ± 9; p=0.030) and worse outcomes in NYHA examination (p <0.001). Depressed patients demonstrated lower body weight (p=0.023), BMI (p=0.044), serum albumin concentration (p=0.015), hemoglobin concentration (p=0.042) and elevated level of CRP (p=0.025) in contrast to non-depressed group. Moderate or severely depressed group demonstrated decreased level of EF% (p=0.019) and increased LAD (p=0.040) comparing with group suffering from mild depression. We observed greater susceptibility to develop cachexia in patients diagnosed as moderately or severely depressed (p=0.030). Moreover, in the mentioned group of patients, the lower values of body weight (p=0.037), FFM (p=0.022) and hemoglobin concentration (p=0.007) was found. Depression in CHF patients is associated with worse cardiac, laboratory and nutritional outcomes. Unfavorable clinical characteristics of CHF patients is related to depression severity.

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S6.P13

RELATION BETWEEN THE HEART RHYTHM ASYMMETRY AND THE RESPIRATORY PHASE IN HEALTHY PEOPLE AND PATIENTS WITH ARTERIAL HYPERTENSION

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Heart rate asymmetry (HRA) is a physiological phenomenon in a healthy subject. We used Guzik's Index (GI) and Porta's Index (PI) to assess HRA in healthy subjects and patients with hypertension. All subjects were examined in a supine position, and 20-minute recordings of ECG and respiration were obtained. In the following, we analyse data from 18 healthy adults (CG: age: 45 ± 14) and 19 patients with hypertension (HG; age: 53 ± 13) who had regular breathing pattern. For each patient, we assign RR-intervals to one of four states corresponding to the phase of breathing: inspiration (IN) or expiration (EX), and two possible breathing phase transitions: from inspiration to expiration (IN›EX) or from expiration to inspiration (EX›IN). Poincare plots for pairs of RR-intervals from subsequent respiratory phases for both groups were obtained. Then the HRA was estimated by the two indices (GI and PI). Both indices estimate the distribution of the points concerning the line of identity. In standard assessment (without considering respiratory phase), GI tended to be different in healthy subjects and hypertensive patients (p <0.07), and the value of GI for healthy subjects was significantly different from 50% (p <0.005), which means that asymmetry has been found in the CG. Nonetheless, the asymmetry of RR-intervals was not detected by PI. At the same time, values of asymmetry indices (GI and PI) obtained from RR-intervals in various respiratory phases were statistically different. Although, in this kind of analysis CG and HG groups presented similar characteristics.

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S6.14

POST-EXERCISE HYPOTENSION IN ELDERLY: THE EFFECT OF SINGLE SESSION OF WATER BASED EXERCISE

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Among cardiovascular diseases, hypertension has been considered with high prevalence. In this way, countless treatments are often attributed as disease management strategies, in this way, the physical activity is highlighted above all for being able to reduce blood pressure. However, the hypotensive effect in acute sessions performed in an aquatic environment still remains inconclusive. Thus, the objective of the study was to verify the hypotensive effect of a water based exercise in normotensive and hypertensive elderly people. Twenty eight physically independent elderly women were distributed in two groups being normotensive (N, n: 10) and hypertensive of stage 1 (H, n: 18). All subjects were submitted to single session of 45-minute of water based exercise session, consisting of 5 minutes of warm-up, 35 minutes of the main part and 5 minutes of calm down. The intensity was monitored by the subjective perception of effort, indicating that throughout the main part the exercises were performed between 6 and 7 on the 0-10 scale. The following parameters were analyzed before and after 60 minutes of the exercise session: systolic (SBP), diastolic (DBP) and mean (MBP) blood pressure, heart rate (HR) and rate pressure product (RPP). Differences were analyzed by t test or ANOVA repeated measures as appropriate and significance level of $p < 0.05$. No significant differences ($p > 0.05$) were found between age and anthropometric parameters between groups N and H. No differences were found in both groups in HR ($F=0.194$, $p=0.66$), SBP ($F=1.685$, $p=0.20$), DBP ($F=2.52$, $p=0.125$), MAP ($F=1.54$, $p=0.22$) and SD ($F=2.02$, $p=0.16$) after immersion. Analyzing the hypotensive response induced by the exercise session, a significant effect was found in SBP (time: $F=12.74$, $p=0.001$; group: $F=77.96$, $p<0.001$; interaction: $F=7.25$, $p=0.012$), MBP (time: $F=11.09$, $p=0.002$; group: $F=118.7$, $p<0.001$) and RPP (time: $F=9.65$, $p=0.004$; group: $F=22$, 05, $p<0.001$; interaction: $F=4.52$, $p=0.043$). Thus, 60 minutes after the exercise session, significant reductions ($p<0.05$) were found in the SBP (N: –1.6 ± 3.48, H: –9.57 ± 8.96;%), DBP (N: 0.98 ± 3.09, H: –3.10 ± 5.59;%), MBP (N: –1.26 ± 2.10, H: –4.37 ± 5.00; %) and RPP (N: –2.28 ± 3.71, H: –11.27 ± 12.29;%). Conclusion: an acute session of water based exercise was able to promote a reduction in systolic, diastolic and mean and rate pressure product in hypertensive elderly women.

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S6.P15

THE EFFECTS OF ENHANCED ENDOCANNABINOID TONE INDUCED BY CHRONIC ADMINISTRATION OF DUAL FAAH/MAGL INHIBITOR JZL195 IN SPONTANOUSLY HYPERTENSIVE RATS

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Two major endocannabinoid degrading enzymes are fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL). We have previously demonstrated that chronic administration of FAAH inhibitor induced different (also positive) age- and model-dependent effects on various cardiovascular system in normotensive and hypertensive rats. The therapeutic potential of stronger enhancement of endocannabinoid tone by dual FAAH/MAGL blockade in hypertension is unknown. Thus, the aim of our study was to examine the influence of dual FAAH/MAGL inhibitor JZL195 on the cardiovascular system in spontaneously hypertensive rats (SHR). Experiments were performed on 8–11 weeks old SHR and their appropriate normotensive control Wistar Kyoto rats (WKY). JZL195 10 mg/kg or its vehicle were injected intraperitoneally once daily for two weeks. Blood pressure (BP) and heart rate (HR) were measured in conscious animals using the tail-cuff method. Blood glucose in tail capillary blood, rectal temperature and organ weight (expressed as organ weight to body mass or tibia length ratio) were measured at the end of experiments. Systolic, mean and diastolic BP and HR measured before the first injection of JZL195 was higher in SHR than in WKY. JZL195 tended to decrease BP slightly (in SHR but not in WKY) and did not affect HR. Hypertensive rats had cardiac hypertrophy, lower body mass and kidney weight (but only expressed as tibia length ratio), comparable rectal temperature and lung and liver weight in comparison to normotensive animals. JZL195 did not affect any of these parameter. In conclusion, chronic administration of JZL195 did not exhibit significant benefit influences (but also did not evoke adverse effects) in hypertension, so further investigations are necessary to determine its real antihypertensive potential.

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S6.P16

EFFECT OF MUSIC ON TRAINING PARAMETERS AND MOOD STATE IN HIIT BODY WORK SESSIONS

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Use of music in exercise sessions has been considered an interesting strategy for both psychophysical and psychophysiological effects. However, considering the high intensity interval training (HIIT), the effects of music remain inconclusive. In this way, the objective of the study was to evaluate the influence of music in HIIT sessions using body weight (HIIT-C) in internal training load parameters and in the mood of university students. Eight physically healthy and independent men were randomly submitted to three sessions of HIIT-C with the influence of song they like (SL), dislikes (DL) and without music (WM). The HIIT body weight session consisted of 20 sets of 30 s stimulus with all-out intensity and 30 s of passive recovery using the following exercises: jumping jack, burpee, mountain climber and squat jump. The following parameters were analyzed: heart rate (HR), lactate (La), number of movements (NM), perceived exertion (PE), perception of pleasure (PP) and the state of humor (BRUMS). Differences were analyzed by ANOVA-two-way with a significance level of $p<0.05$. Results: Although an increase ($p<0.05$) in HR, La and PE was found after the HIIT-C session, no difference was found in HR (WM: 167.83 ± 6.96; DL: 168.66 ± 11.67; SL: 163.33 ± 15.59 bpm; F=0.33; p=0.724), La (WM: 14.38 ± 3.11; DL: 16.01 ± 3.77; SL: 15.70 ± 3.20 $mMol.L^{-1}$; F=0.32; p=0.730) and PE between exercise sessions. Condition SL promoted greater (F=18.83; p=0.001) NM compared to DL and WM which also differed from each other. Considering the PP, the effect of music was found between the protocols (F=26.07; p=0.0001) indicating that the SL session promoted an increase in pleasure, different from the DL session that caused displeasure and the WM that did not promote modification. According to the Brunel mood scale, the feeling of fatigue was increased after HIIT-C (F=15.79; p=0.0054) with no difference between sessions, the WM condition and SL were able to decrease the sensation of tension after exercise. Increases in the parameter of mood disorder were observed both for the condition WM and DL, while the SL did not have a significant effect Conclusion: HIIT-C sessions using SL presented a higher NM and positive PP when compared to sessions with DL and WM without promoting changes in internal training load parameters. Although all sessions of HIIT-C increased the feeling of fatigue, the sessions of HIIT-C that use SL and WM showed less tension when compared to the session with DL. In addition, the WM and DL sessions were able to increase the mood disorder, with no effect for the SL session.

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S6.P17

THE EFFECT OF GENETICALLY ALTERED AMP DEAMINASE ACTIVITY IN EXPERIMENTAL ISOPROTERENOL-INDUCED HEART FAILURE

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Studies on the influence of AMP deaminase (AMPD) activity on the progression of heart disease are conflicting, possibly due to the diverse effect in different clinical conditions. Isoproterenol is a non-selective β-adrenergic agonist that has been used widely to mimic the heart failure state. Our study aims to investigate the effect of isoproterenol (ISO)- induced heart failure on cardiac function in murine hearts lacking AMPD3. In this study we used male wild type and AMPD3 knockout mice (n=6–8). We injected intra-peritoneally ISO in the experimental animals at a dose of 100 mg/kg body weight/day for 12 days. ISO-treated and control mice (saline) from each group were examined with echocardiography. At the age of 12 months old, mice were anesthetized intraperitoneally with ketamine (100 mg/kg) and xylazine (10 mg/kg). After chest hair removal, animals were placed on a heated platform to maintain the body temperature at 37°C. The transthoracic echocardiography was performed using the Vevo 1100 (VisualSonics Inc, Canada) equipped with a 40-MHz linear array transducer. Images were acquired at a frame rate consistently above 200 frames/s. The transducer was placed above the anterior chest wall and hemodynamic parameters, including stroke volume (SV), left ventricular (LV) ejection fraction (EF) and fractional shortening (FS) as well as cardiac output (CO) and LV mass were collected. The statistical analysis was performed using Graph Pad Prism 7 (Graph Pad Software). Paired Student t-test was used for comparisons between two groups. A p-value <0.05 was considered as a significant difference. To characterize the implications of the AMPD KO for the ISO-induced development of cardiac dysfunction, we conducted two-dimensional echocardiographic measurements. The measurement of SV and CO did not differ in the studied groups, both WT and AMPD KO and after the treatment with ISO. A significant decrease in EF was observed in WT mice treated with isoproterenol compared to WT. Interestingly, the effect of ISO on EF was abolished in AMPD KO mice. EF was not different between WT and AMPD KO mice not treated with ISO. Moreover, a similar effect was observed with the FS measurement. There was a considerable reduction in FS in the WT group treated with ISO compared to the WT group and a suppression of the ISO impact on FS in the AMPD KO group. FS measurement did not differ between the non-treated WT and AMPD KO groups. Furthermore, a significant increase in left ventricular mass was observed in ISO-treated WT mice compared to WT. In turn, ISO did not affect left ventricular mass in AMPD KO mice. LV Mass did not differ between the untreated animals, WT and AMPD KO. This study shows that reduced AMPD activity has a beneficial effect on cardiac function in isoproterenol-induced heart failure. Possibly the enhanced activation of protective AMPK cascade is likely to be the mechanism. The use of specific AMPD inhibitors may offer significant therapeutic potential.

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S6.P18

THE INFLUENCE OF CANNABIDIOL ON ISOLATED RAT ATRIA UNDER NORMOXIC, HYPOXIC AND REOXYGENATION CONDITIONS

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The antioxidant, anti-inflammatory and antiapoptotic properties as well as the comprehensive mechanism of action of cannabidiol (CBD) may play potential cardioprotective role in myocardial injury. The aim of this study was to examine the effect of CBD on the rate and force of contractions of isolated rat atria under control (normoxia) and hypoxic/reoxygenation (H/R) conditions. The experiments were conducted with atria under basal conditions and in the presence of β-adrenoceptors stimulation with a non-selective agonist isoprenaline (ISO). Both, positive chronotropic (spontaneously beating right atria) and inotropic (electrically stimulated left atria) effects were evaluated. Hypoxia was achieved by replacement of carbogen gas by 95% N_2 and 5% CO_2 in the organ baths. After 30-min incubation with 1 μM CBD (or its vehicle) atria were exposed to 30 min hypoxia followed by 30 min reoxygenation. The increasing concentrations of ISO (0.01 nM–10 μM) were administered before or after H/R. Atrial rate and force of contractions decreased during hypoxia. Rate of contractions of right atria returned after reoxygenation to values comparable to the basal while the force of contractions of left atria reached approximately 50% of the basal. CBD prevented the decrease in rate of contractions of right atria during the hypoxia (about 50%). However, this protective effect of CBD was abolished by previous adrenergic stimulation with ISO. On the contrary, in left atria stimulated with ISO, CBD accelerated the recovery of left atrial contractile force during reoxygenation in comparison to the tissue not treated with CBD. Additionally, incubation with CBD potentiated the inotropic effect of ISO in left atria given after H/R. In summary, CBD exerts cardioprotective effect and can affect the ability to endure cardiac hypoxia and reoxygenation but in different manner in right and left rat atria.

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S6.P19

NEUROPEPTIDE FF COUNTERACTS OPIOID INDUCED RESPIRATORY DEPRESSION

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The activity of opioids undergoes the regulation by a homeostatic anti-opioid system involving i.a. neuropeptide FF (NPFF) - a member of RF-amidated neuropeptides. The contribution of this peptide to the modulation of pain perception, opioid-induced tolerance, and dependence seems to be well documented while there is scarce information about its effect on respiratory pattern and opioid-induced respiratory depression. The aim of the present study was to examine the influence of intracerebroventricular (icv) administration of NPFF on respiration and its effect on post-opioid cessation of breathing (apnea). Urethane-chloralose anaesthetized male Wistar rats spontaneously breathing room air were injected icv with various doses of NPFF 5 min prior to intravenous (iv) endomorfin-1 (EM-1) administration. Respiratory parameters, arterial blood pressure and heart rate were measured. Neither vehicle (saline) nor doses of NPFF (1, 10 and 20 μg) injected into the right cerebral ventricle affected all measured variables. However, icv pre-treatment with NPFF at a dose of 20 μg abolished the presence of post-EM-1 apnea of median duration of 7 s and diminished the maximal drop in the median arterial blood pressure from 30 mmHg to 10 mmHg. These effects were completely blocked by NPFF receptor antagonist - RF9 (20 μg) - given icv in a mixture with NPFF (20 μg) before systemic challenge with EM-1. Our experiments showed that centrally administered neuropeptide FF weakens the respiratory depression induced by icv EM-1 injection. This suggests the important role of NPFF and its receptors localized centrally in the manifestation of vagally mediated opioid-induced apnea.

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S6.P20

INFLUENCE OF CANNABINOID CB_1 AND CB_2 RECEPTOR ANTAGONISTS ON CARDIOSTIMULATORY EFFECTS OF ISOPRENALINE IN HUMAN ATRIAL TRABECULAE

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We have demonstrated that cannabinoid CB_1 and CB_2 receptor antagonists AM251 and AM630 differentially modulate positive chronotropic and inotropic effect of the non-selective β-adrenoceptor agonist isoprenaline in right and left atria isolated from Wistar rats (Weresa *Pharmacol Rep* 2019, 71, 82-89). The aim of the current study was to examine whether the modulatory effects of CB_1 and CB_2 cannabinoid receptor antagonists on cardiostimulatory effects of isoprenaline will also occur in human atrium. Experiments were carried out in paced human atrial trabeculae (1 Hz) obtained from patients who underwent cardiosurgery. The trabeculae were incubated for 30 min with AM251 or AM630 (0.1, 1 or 3 μM). Then concentration response curves for isoprenaline (0.1 nM–30 μM) were constructed. Isoprenaline exerted the concentration-dependent increase in cardiac tissue force (positive inotropic effect). AM251 (0.1 and 3 μM) and AM630 (0.1 μM) decreased the inotropic effects of isoprenaline by about 70%. In contrast, the blockade of CB_1 or CB_2 receptor with both CB-R antagonists in the intermediate concentration (1 μM) led to increase in force of contraction (by about of 20% for AM251 and 45% for AM630). In conclusion, in human atrial trabeculae, cannabinoid CB_1 and CB_2 receptor antagonists modulate cardiostimulatory effects of isoprenaline in a different manner, dependent on antagonist concentration. Therefore, due to increasing interests of cannabinoid antagonists as a therapeutic agents we underline that caution should be taken by their application, especially under conditions associated with enhanced sympathetic tone.

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SESSION VII

FUNCTIONS OF BLOOD
HEMOSTASIS

Thursday (September 16, 2021; 15:30 – 18.00)

Chair:

Prof. Ewa Chabielska
Department of Biopharmacy, Medical University of Bialystok, Poland

Assoc. Prof. Andrzej Mogielnicki
Department of Pharmacodynamics, Medical University of Bialystok, Poland

DETAILED SESSION VII SCHEDULE

Opening lectures (Thursday, September 16, 2021; 16:30 – 17:30; *virtual stream A*)

S7.L1 THE ROLE OF PLATELET JUNCTION ADHESION MOLECULE-A IN HAEMOSTASIS AND ATHEROSCLEROSIS. **T. Przygodzki** (Department of Blood Clotting Disorders, Department of Biomedical Sciences, Medical University of Lodz, Lodz, Poland).

S7.L2 STRIATIN - A NOVEL MEDIATOR OF STEROID HORMONES EFFECTS IN HEMOSTASIS. **A. Gromotowicz-Poplawska[1], N. Marcinczyk[1], R. Flaumenhaft[2,3], J.R. Romero[3,4], G.H. Williams[3,4], E. Chabielska[1]** ([1]Department of Biopharmacy, Medical University of Bialystok, Bialystok, Poland, [2]Division of Hemostasis and Thrombosis, Beth Israel Deaconess Medical Center, Boston, USA, [3]Harvard Medical School, Boston, USA, [4]Division of Endocrinology, Diabetes, and Hypertension, Brigham and Women's Hospital, Boston, USA).

Oral presentations (Thursday, September 16, 2021; 17:30 – 18:00; *virtual stream A*)

S7.L3 THE EFFECTS OF PROTAMINE SULFATE ON THE HEMOSTASIS, CARDIOVASCULAR AND RESPIRATORY FUNCTIONS IN DIFFERENT ANIMAL MODELS. **J. Miklosz[1],B. Kalaska[1], P. Podlasz[2], M. Chmielewska-Krzesinska[2], M. Zajaczkowski[3], M. Rusak[4], A. Kosinski[3], D. Pawlak[1], A. Mogielnicki[1]** ([1]Department of Pharmacodynamics, Medical University of Bialystok, Bialystok, Poland, [2]Department of Pathophysiology, Forensic Veterinary Medicine and Administration, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland, [3]Department of Clinical Anatomy, Medical University of Gdansk, Gdansk, Poland, [4]Department of Haematological Diagnostics, Medical University of Bialystok, Bialystok, Poland).

Session summary

Poster presentations (Thursday, September 16, 2021; 15:30 – 16:25; *virtual stream C*)

S7.P1 CONTRIBUTION OF GASEOUS TRANSMITTERS TO THE OZONE EFFECT ON BLOOD OXYGEN TRANSPORT FUNCTION UNDER HYPOCAMPIC CONDITIONS. **V. Zinchuk[1], E. Biletskaya[1], A. Muravyov[2]** ([1]Grodno State Medical University, Grodno, Belarus, [2]Yaroslavl State Pedagogical University named after K.D. Ushinsky, Yaroslavl, Russia).

S7.P2 THE INFLUENCE OF ANTIMICROBIAL NEUTROPHIL EXTRACT AND PENTOXIFYLLINE ON OVINE NEUTROPHILS ISOLATED DURING THE INSERTION TITANIUM IMPLANT IN A SHEEP MODEL. **J. Zdziennicka[1], J. Wessely-Szponer[1], T. Szponder[2], M. Latalski[3]** ([1]Sub-Department of Pathophysiology, Department of Preclinical Veterinary Sciences, Faculty of Veterinary Medicine, University of Life Sciences, Lublin, Poland, [2]Department and Clinic of Animal Surgery, Faculty of Veterinary Medicine, University of Life Sciences, Lublin, Poland, [3]Department of Pediatric Orthopedics, Medical University, Lublin, Poland).

S7.P3 IMPACT OF FUNCTIONALIZED SILVER NANOPARTICLES ON AGGREGATION OF HUMAN BLOOD PLATELETS. **J. Hajtuch[1], E. Tomczyk[2], M. Wojcik[2], M.J. Santos-Martinez[3], I. Inkielewicz-Stepniak[1]** ([1]Department of Pharmaceutical Pathophysiology, Medical University of Gdansk, Gdansk, Poland, [2]Faculty of Chemistry, University of Warsaw, Warsaw, Poland, [3]School of Pharmacy and Pharmaceutical Sciences, Trinity College Dublin, Dublin 2, Ireland).

S7.P4 NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A FACTOR PREDICTING RADIOTHERAPY INDUCED ORAL MUCOSITIS AND OVERALL SURVIVAL IN HEAD NECK CANCER PATIENTS TREATED WITH RADIOTHERAPY. **I. Homa-Mlak[1], A. Brzozowska[2], R. Mlak[1], A. Szudy-Szczyrek[3], T. Malecka-Massalska[1]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland; [2]Department of Oncology, Medical University of Lublin, Lublin, Poland, [3]Department of Hematooncology and Bone Marrow Transplantation, Medical University of Lublin, Lublin, Poland).

S7.P5 UTILITY OF THE PLATELET-ENDOTHELIAL CELL ADHESION MOLECULE 1 (PECAM-1) AS A MARKER OF PLATELET ACTIVITY IN THE FLOW CHAMBER MODEL OF THROMBOSIS IN ANIMAL AND HUMAN STUDY. **N. Marcinczyk[1], T. Misztal[2], A. Gromotowicz-Poplawska[1], T. Rusak[2], E. Chabielska[1]** ([1]Department of Biopharmacy, Medical University of Bialystok, Bialystok, Poland, [2]Department of Physical Chemistry, Medical University of Bialystok, Bialystok, Poland).

S7.P6 THE ROLE OF LDG CELLS AS A POTENTIAL FACTOR IN THE DEVELOPMENT AND INTENSITY OF INFLAMMATION IN PSORIASIS. **W. Domerecka[1], I. Homa-Mlak[1], R. Mlak[1], A. Wilinska[2], T. Malecka-Massalska[1]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Department of Clinical Genetics, Medical University of Lublin, Lublin, Poland).

S7.P7 CHANGES IN ARTERIAL OXYGEN SATURATION IN HEALTHY PERSONS DURING BACK MASSAGE PROCEDURE. **P. Radziejowski[1], M. Radziejowska[1], V. Dychko[2], O. Romaniv[1]** ([1]Department of Innovations and Safety Management Systems, Faculty of Management, Czestochowa University of Technology, Czestochowa, Poland, [2]Department of Physical Therapy, Physical Education and Biology, Donbass State Pedagogical University, Slavyansk, Ukraine).

S7.L1

THE ROLE OF PLATELET JUNCTIONAL ADHESION MOLECULE-A IN HAEMOSTASIS AND ATHEROSCLEROSIS

T. PRZYGODZKI

Department of Haemostasis and Haemostatic Disorders, Chair of Biomedical Sciences, Medical University of Lodz, Lodz, Poland

Junctional adhesion molecule-A (JAM-A) is a transmembrane protein which belongs to the immunoglobulin superfamily of cell adhesion molecules. JAM-A is present in epithelial cells, endothelial cells, leukocytes and blood platelets. In epithelial and endothelial cells it takes part in formation of tight junctions. In these structures, molecules of JAM-A located on adjacent cells form homodimers and thus take part in stabilization of cellular layer integrity. In leukocytes, JAM-A was shown to play role in their transmigration through the vascular wall. Paradoxically, the function of JAM-A in blood platelets, where it was primarily discovered, is much less understood. Blood platelets are most often considered in terms of two biological processes: haemostasis and development of atherosclerosis. Existing evidence allow to assume that platelet pool of JAM-A takes part in both of them. The studies of platelet JAM-A involvement in haemostasis provide ambiguous results. Functional blockade of homophilic interactions of JAM-A inhibited platelet aggregation induced by selected agonists. Preliminary studies suggest that such functional blockade decreased thrombus formation at high shear rates. On the contrary, genetic deletion of JAM-A in mouse platelets resulted in their hyper-reactivity. This was explained by the finding that JAM-A allowed to maintain the αIIbβ3 integrin in a quiescent state. Therefore, the protein seems to play a complex, plausibly regulatory role in platelet aggregation. The potential role of platelet JAM-A in the process of development of atherosclerosis is substantiated by several observations. Upon endothelium activation, JAM-A translocates from tight junctions to the luminal surface of the vascular wall. There, it can facilitate recruitment of flowing cells to the vascular wall. Such a phenomenon has been shown for monocytes and for platelets. The functional blockade of homophilic interactions of JAM-A diminished platelet adhesion to inflamed endothelium in static *in vitro* conditions as well as *in vivo*. What is more, JAM-A has been shown to take part in deposition of pro-atherogenic platelet-derived microparticles on inflamed endothelium. Finally, the functional blockade of JAM-A decreased growth of atherosclerotic plaques and prolonged survival in mouse model of atherosclerosis. Therefore JAM-A, similarly to other molecules such as P- selectin, seems to be a factor connecting platelets and inflamed vascular wall in the context of atherogenesis. Understanding of the role of platelet JAM-A in haemostasis and atherosclerosis may lead to development of novel antithrombotic anti-atherosclerotic strategies.

S7.L2

STRIATIN - A NOVEL MEDIATOR OF STEROID HORMONES EFFECTS IN HEMOSTASIS

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Recent data suggest that striatin, a caveolin-1-binding protein, is a mediator of steroid hormones effects in cardiovascular system (CVS) and serves as a novel link between the actions of the mineralocorticoid (MR) and estrogen (ER) receptors. It was shown that striatin colocalizes with the MR and that MR activation increases striatin levels in endothelial cells. On the other hand, lowering striatin levels in endothelial cells reduces aldosterone, MR-dependent nongenomic signalling. A similar role in nongenomic steroid receptor signaling has been described for striatin ER-dependent nongenomic effects, suggesting that striatin is involved in the estrogen-mediated protection of arteries after injury. The contribution of striatin to the nongenomic steroid receptor signalling in CVS is well documented, however the role of striatin in hemostasis is still unknown. Although, there are some data suggesting a potential role of striatin in aldosterone-mediated thrombotic response. It was demonstrated that individuals who carry rs2540923, a single nucleotide polymorphic gene variant of striatin, exhibit salt sensitivity of blood pressure (BP). A mouse model of striatin deficiency showed that the mechanisms for salt sensitivity of BP is related to reduced striatin levels, increased aldosterone levels, enhanced vasoconstriction, decreased vascular relaxation and reduced eNOS expression. We showed previously in animal models of thrombosis, that increased aldosterone levels enhances thrombotic response in the mechanism related to platelet and coagulation activation, fibrinolysis inhibition, reduced eNOS expression and vascular relaxation as well. These results suggest that in humans and rodent models, striatin deficiency plays a role in vascular thrombotic response mediated by excess aldosterone. Recently, we showed that striatin deficiency in mice was associated with increased aldosterone level and significant increases in laser-induced thrombotic process, in a mechanism that was likewise associated with increased platelet accumulation and fibrin deposition. These results demonstrate a novel protective role of striatin in aldosterone-mediated hemostatic effects and suggest that subjects who carry the polymorphic striatin gene variant may have a procoagulant phenotype and as such are at increased risk of thrombotic events.

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S7.L3

THE EFFECTS OF PROTAMINE SULFATE ON THE HEMOSTASIS, CARDIOVASCULAR AND RESPIRATORY FUNCTIONS IN DIFFERENT ANIMAL MODELS

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Protamine-induced thrombocytopenia is an immuno-hematological disorder described in patients treated with heparin and protamine during cardiopulmonary bypass. It was proposed that protamine and heparin form multimolecular complexes which may induce production of platelet-activating antibodies, and thus severe thrombocytopenia and thromboembolic complications. However, the link between protamine, heparin, platelets and thrombosis is not clear. The aim of the study was to elucidate the effect of protamine and its heparin complexes on platelets and to investigate its possible early and late thromboembolic complications. All procedures involving animals were approved by the Local Ethical Committee. We explored the toxicity of protamine and its complexes with heparin in zebrafish and rodents. Male Wistar rats and BALB/c mice were divided into 4 groups treated with vehicle, heparin, protamine alone and together with heparin once a week for 5 weeks. The bone marrow and the heart histology, platelet count and aggregation in blood, activated partial thromboplastin time (aPTT) in plasma, cardiac troponin T type 2, P-selectin, thrombopoetin, platelet factor 4 and β-thromboglobulin concentrations in serum were assessed in mice. Thrombus weight, platelet count and aggregation in blood, aPTT, prothrombin time, fibrinolysis indicators, D-dimers, fibrinogen, prostacyclin metabolite and anti-Xa activity in plasma were assessed in rats with electrically induced arterial thrombosis. In the acute experiment, platelet aggregation, their number and cardiovascular and respiratory functions were evaluated during one hour from single administration of tested agents. The involvement of nitric oxide, cationicity of protamine and hERG channels in the above effects was investigated. We found a short-term antiplatelet activity and long-term platelet-independent antithrombotic activity of protamine. Protamine and heparin complexes do not cause cardio-respiratory failure, but an overdose of protamine may affect blood pressure and respiratory parameters. Above effects seems to be charge-dependent and involve enhanced release of nitric oxide.

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S7.P1

CONTRIBUTION OF GASEOUS TRANSMITTERS TO THE OZONE EFFECT ON BLOOD OXYGEN TRANSPORT FUNCTION UNDER HYPOCAPNIC CONDITIONS

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Ozone (O_3) improves tissue oxygenation that enable to use it in hypoxic conditions, which are often accompanied by hypocapnia. The contribution of gaseous transmitters to the effect of ozone (6 mg/L) on blood oxygen transport function under hypocapnic conditions (4.2% CO_2; 5.3% O_2, 90.5% N_2) *in vitro* experiments at exposure of 30 min was studied. The following parameters of blood oxygen transport function were determined: oxygen partial pressure (SO_2), blood oxygen saturation (SO_2), hemoglobin affinity for oxygen according p50 value (with pO_2 equal 50%). Ozonised isotonic sodium chloride solution in a volume of 1 ml and donors of nitrogen monoxide and hydrogen sulfide gaseous transmitters were added to blood samples (nitroglycerin at a final concentration of 0.05 mmol/L and sodium hydrosulfide at a final concentration of 0.38 mmol/L). Introducing O_3 into the blood samples led to an increase in the main parameters of the blood oxygen transport function, such as SO_2, pO_2, $p50_{real}$, $p50_{stand}$ and the shift of the oxyhemoglobin dissociation curve to the right compared to control group. When treated with hypocapnic gas mixture, these parameters decreased compared to the control. Incubation of the blood samples in hypocapnic conditions enhanced the effect of O_3 on blood oxygen transport function parameters. Nitroglycerin caused a significant increase in this effect under given conditions of pO_2 and SO_2 that is parameters increased compared to the group of preliminary hypocapnia with the ozone addition. The $p50_{real}$ parameter increased and the shift of the oxyhemoglobin dissociation curve to the right became more pronounced. Sodium hydrosulfide did not have this effect. Concentration of NO_3^-/NO_2^- and H_2S in blood plasma at action of O_3 under conditions of hypocapnia did not change compared to the group in which only ozone was administered. The addition of nitroglycerin and sodium hydrosulfide under these conditions led to a significant increase of NO_3^-/NO_2^- and H_2S compared with group ozonised under hypocapnic conditions. Thus, the experimental data prove the contribution of these gaseos transmitters to the modification of the blood oxygen transport function.

Acknowledgements: This work was supported by international projects No. M20P-428 – BRFFR and No. 20-515-00019-RFBR.

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S7.P2

THE INFLUENCE OF ANTIMICROBIAL NEUTROPHIL EXTRACT AND PENTOXIFYLLINE ON OVINE NEUTROPHILS ISOLATED DURING THE INSERTION TITANUM IMPLANT IN A SHEEP MODEL

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Titanium (Ti) is the metal commonly used in orthopedic field. Titanium is highly resistant to corrosion. However, Ti ions might slowly diffuse into surrounding tissue where they would be transported into circulation and may interact with blood cells, causing their excessive activation. Autologous neutrophil extract (AMP) was previously considered as factor to decrease of excessive response of leukocytes. Pentoxifylline (PTX) is a competitive non-selective phosphodiesterase inhibitor, which acts anti-inflammatory, enhances microcirculation, blood flow and tissue oxygenation. It also stimulate bone formation and could be considered in management of osseointegration. The aim of this study was to assess of neutrophil *in vitro* response to implantation of biomaterial into the tibia with or without treatment with AMP or PTX. The study was conducted on 8 sheep, females, BCP local breed, 4 months old, from the Bezek Experimental Farm. The procedure consisted of inserting a Ti implant into the proximal tibial physis. Blood sampling necessary to obtain AMP was done 7 days before implantation. For the determination of neutrophil activity, blood was collected at three time points: 7 days before implantation, 1 h and 24 h after implantation. The secretory activity of neutrophils was estimated on the basis of the degranulation and free radicals generation at above time-points, after *in vitro* stimulation with 20 µg/mL AMP or PTX added to final concentrations of 0, 1, and 100 µg/ml of culture of ovine neutrophils. The obtained results show that the addition of AMP and PTX in concentration of 1 µg/ml to the neutrophil suspension decrease of activity of neutrophils. Our study showed that AMP and PTX added at the stated concentrations to the neutrophil suspension isolated during implantation of a Ti implant into the proximal tibial physis reduces the pro-inflammatory response of neutrophils.

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S7.P3

IMPACT OF FUNCTIONALIZED SILVER NANOPARTICLES ON AGGREAGTION OF HUMAN BLOOD PLATELETS

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Nanomedicine is a relatively new field of science and technology. Specifically designed functionalized nanoparticles can impart enhanced cellular internalization ability, non-cytotoxicity, and improved payload binding capacity necessary for effective intracellular delivery. Among metal nanoparticles, silver nanoparticles (AgNPs) are emerging as an attractive tool for many nanomedical applications. They are endowed with anticancer, antibacterial, antifungal and antiviral properties. The field of the nanopharmaceutical development of antithrombotic drugs, has not been explored yet. Based on our previous research, we decided to evaluate the effect of functionalized AgNPs on platelet aggregation and cytotoxicity on human cells. We hypothesized that AgNPs, a known antimicrobial agent, can be used as blood-compatible, ideal material in medical devices or as a drug delivery system. The aim of the research was the synthesis of functionalized AgNPs (glutathione (GSH), polyethylene glycol (PEG), lipoic acid (LA)), evaluation of cytotoxicity and determination of interactions between AgNPs and platelets. A quartz crystal microbalance was used to measure the effect of AgNPs on platelet aggregation. Flow cytometry was used to determine surface platelet receptors. The lactate dehydrogenase assay was used to evaluate the potential cytotoxicity of AgNPs against human platelets, endothelial cells. ELISA tests were used to measure the levels of thromboxane B_2 (TXB_2) and the metalloproteinases released by platelets. All tested functionalized AgNPs inhibited platelet aggregation, increased in total P-selectin and GPIIb/IIIa, TXB_2 formation, release of metalloproteinases at non-toxic concentrations. The results of our research indicate that functionalized AgNPs can potentially be used as an antiplatelet agent in the design of medical materials and equipment.

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S7.P4

NEUTROPHIL-TO-LYMPHOCYTE RATIO AS A FACTOR PREDICTING RADIOTHERAPY INDUCED ORAL MUCOSITIS AND OVERALL SURVIVAL IN HEAD NECK CANCER PATIENTS TREATED WITH RADIOTHERAPY

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Epithelial tumors in the head and neck area (head and neck cancer-HNC) are ones of the most frequently tumors with as many as 650,000 new cases every year. The treatment of HNC patients include surgery, radiotherapy (RT), chemotherapy (CTH) or the combination of these methods. Radical RT, often combined with chemotherapy (C-RT), leads to complications including severe acute radiation reaction in the area of mucosa (oral mucositis - OM). OM occurs in the majority of irradiated patients (80%), which constitutes a serious problem in everyday clinical practice. The objective of this research conducted in HNC patients was the assessment of the relationship between neutrophil-to-lymphocyte ratio (NLR) the incidence of severe RT induced OM as well as overall survival (OS). The study involved 207 patients in advanced stages (III–IV) of HNC. RTOG/EORTC scale was used to assess OM. The pre-treatment NLR was specified as the absolute neutrophil count divided by the absolute lymphocyte count. Starting from 2nd to 7th week of RT we observed significant, positive correlation between NLR values and OM grade. From 2nd to 7th week of RT higher NLR values were related with significant increases (from 2 to over 24-fold) in the risk of occurrence of more severe OM (multivariate analysis confirmed its independent influence). Moreover, multivariate analysis for survival revealed that both higher TNM stage (HR=1.84; p=0.0043) and higher NLR values (HR=1.48; p=0.0395) were independent prognostic factors. We conclude that NLR is a simple and accurate parameter useful in the evaluation of the risk of more severe OM as well as independent prognostic factor of OS in patients subjected to RT due to HNC.

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S7.P5

UTILITY OF THE PLATELET-ENDOTHELIAL CELL ADHESION MOLECULE 1 (PECAM-1) AS A MARKER OF PLATELET ACTIVITY IN THE FLOW CHAMBER MODEL OF THROMBOSIS IN ANIMAL AND HUMAN STUDY

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Platelet endothelial cell adhesion molecule 1 (PECAM-1) is considered as an antithrombotic molecule. In our previous study we introduced the parameter PECAM-1/thrombus ratio which indicates the proportion of PECAM-1 in a laser-induced thrombus in a mouse mesenteric vein. The higher the PECAM-1/thrombus ratio is, the less activated platelets in thrombus are. The present study aimed to assess the utility of PECAM-1/thrombus ratio in a model of thrombus formation on collagen fibers under controlled flow (flow chamber model) which can reflect arterial or venous conditions. This approach extends the possibility of determining the PECAM-1/thrombus ratio to human blood. Flow chamber model enables the observation of thrombotic process *ex vivo* and *in vitro* as well as simultaneous assessment of platelet activity (expressed as the PECAM-1/thrombus ratio) and platelet aggregation (expressed as the thrombus area). In our preliminary study with mice we have shown that the antiplatelet drug acetylsalicylic acid (ASA, 30 mg/kg, i.v.) increased PECAM-1/thrombus ratio by 32.7% (n=7, p <0,001 vs. VEH) and decreased thrombus area by 76.8% (n=7, p <0.001 vs. VEH). We showed for the first time that PECAM-1/thrombus ratio is suitable parameter in the platelet activation assessment in flow chamber model. Experiments with human blood are performed.

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S7.P6

THE ROLE OF LOW-DENSITY GRANULOCYTES CELLS AS A POTENTIAL FACTOR IN THE DEVELOPMENT AND INTENSITY OF INFLAMMATION IN PSORIASIS

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Two populations of cells are observed in human peripheral blood, i.e. polymorphonuclear leukocytes (PMN), with their characteristic granular structure, and peripheral blood mononuclear cells (PBMC). Low-density granulocytes (LDG) are neutrophils which, after separation by a density gradient, remain in the peripheral blood mononuclear fraction of PBMCs. Post-inflammatory LDGs can damage endothelial cells and release a large amount of tumor necrosis factor (TNF) as well as type I and II interferons. They are characteristic of autoimmune diseases, including psoriasis, which occurs in about 2% of the population. The inflammatory process in the course of psoriasis is systemic and manifests itself mainly on the skin, but also affecting internal organs. The diagnosis and monitoring of the disease is based on the clinical picture. The assessment of disorders of other organs requires additional tests. In the study, it was observed that in the PBMC fraction of patients with psoriasis, LDG cells appear in a much greater number, on average about 6 times higher than in healthy people from the control group. In patients suffering from psoriasis, it was on average about 2.77% of the PBMC population, while healthy donors had on average 0.46% of LDG. It is worth noting that in patients suffering from psoriasis, this population was up to approx. 32% of PBMCs, compared to healthy donors, whose maximum was approx. 3.5%. It was also shown that this population is characterized by an increased ability to release the MPO enzyme in psoriasis patients compared to healthy people (28% vs. 0.73%). In sick patients, an increased activity of MPO is observed, on average about 39 times higher than in healthy donors. Presumably, LDGs are an epiphenomenon of ongoing inflammation, and not the primary cause of psoriasis pathogenesis. It is possible that LDG cells present in abundance at inflammatory sites play an active role in the development and maintenance of autoimmune responses. To establish the potential of LDG as a biomarker in inflammatory autoimmune diseases, larger groups should be analyzed to discover potential correlations with disease severity or prognosis.

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S7.P7

CHANGES IN ARTERIAL OXYGEN SATURATION IN HEALTHY PERSONS DURING BACK MASSAGE PROCEDURE

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The aim of this study was to assess changes in arterial oxygen saturation (S_aO_2) in healthy persons during a procedure of back massage. Relevance of this studies is justified by the fact that it is crucial to control the level of S_aO_2 when massaging persons who recovered from COVID-19 in order to assess efficiency of any therapeutic measures, including physiotherapy, for instance massage therapy. The studies included 3 women and 3 men aged 43.5 ± 1.5 years, BMI=24.84 ± 2.03 kg/m^2. All subjects signed a written consent to take part in the study (permission of the Kazimiera Milanowska College of Education and Therapy Bioethical Commission, Resolution No. 006/2018/2019 of 10.05.2019). The intensity of the classical back massage was controlled with thermovision pictures (thermovision camera Flir E6, Estonia) taken before and after the procedure what enabled, through the assessment of temperature distribution in the massaged area, to even out the level of stimulation caused by the mechanical influence of manual massage (the increase in the massaged area temperature was 3.02 ± 0.38°C). The procedure lasted for 20 minutes. The massage was conducted according to the rules of the safe classical massage methodology. Oxygen saturation and heart rate were measured with pulse oximeter (OxyShuttle, USA) before the procedure, with a patient lying down, during the procedure, and within 5 minutes after the procedure was completed. The baseline S_aO_2 was 96.83 ± 0.75%. The highest deviation from the baseline was observed during the massage of left and right side intercostal muscles (7th and 14th minute of the procedure, respectively); S_aO_2 decreased to 94.0 ± 0.63% (7th minute, left side) and 94.16 ± 0.75% (14th minute, right side). Decrease in S_aO_2 to 94.5 ± 0.55% was also noted at the completion of the procedure, after employing the tapotement techniques (hacking and cupping). Five minutes after the massage, the level of S_aO_2 increased to 97.0 ± 0.63%. Changes in S_aO_2 observed during the massage procedure can indicate that during the massage the vesicular ventilation to blood flow velocity ratio changes similarly to low intensity physical activity due to increased temperature of the massaged area.

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SESSION VIII

ENDOCRINE REGULATIONS
CONTROL OF BODY WEIGHT

Thursday (September 16, 2021; 9:00 – 10:10)
Thursday (September 16, 2021; 11:30 – 12:15)

Chair:

Prof. Magdalena Olszanecka-Glinianowicz
Health Promotion and Obesity Management Unit, Department of Pathophysiology Medical Faculty in Katowice, Medical University of Silesia, Katowice, Poland

Assoc. Prof. Marek Skrzypski
Department of Animal Physiology and Biochemistry, Poznan University of Life Sciences, Poznan, Poland

DETAILED SESSION VIII SCHEDULE

Oral presentations (Thursday; September 16, 2021; 9:00 – 10:10; *virtual stream A*)

S8.L1 THE POSITIVE IMPACT OF VITAMIN D SUPPLEMENTATION ON GLUCOCORTICOSTEROID-DEPENDENT NEUROIMMUNOLOGICAL CHANGES. **D. Korewo [1], M.J. Karnia[1], D. Myslinska [2], P. Berezka, Z.M. Ciepielewski[2], J.J. Kaczor[1]** ([1]Gdansk University of Physical Education and Sport, Gdansk, Poland, [2]Faculty of Biology, University of Gdansk, Gdansk, Poland).

S8.L2 MOTS-C A NEW QUAINT ENDOCRINE PLAYER. **J. Bien, P. Kolodziejski, E. Pruszynska-Oszmalek, N. Leciejewska, D. Szczepankiewicz, K.W. Nowak, L. Nogowski, M. Sassek** ([1]Poznan University of Life Sciences, Department of Animal Physiology, Biochemistry and Biostructure, Poznan, Poland).

S8.L3 METABOLIC PARAMETERS IN OVARIECTOMIZED, ESTRADIOL-IMPLANTED SHEEP RESULTING FROM A LONG-TERM CHANGES IN BODY WEIGHT AND RESISTIN. **W. Biernat, M. Szczesna, K. Kirsz, D.A. Zieba** (Department of Animal Nutrition and Biotechnology, and Fisheries, Faculty of Animal Sciences, University of Agriculture in Krakow, Krakow, Poland).

S8.L4 EFFECT OF WHOLE BODY VIBRATION ON BONE NANOCOMPOSITES ORGANISATION AND PREVENTION OF BONE MINERAL DENSITY LOSS IN RATS WITH OBESITY AND LIMITED MOBILITY **N. Kostyshyn, M. Gzhegotskyi M.** (Danylo Halytsky Lviv National Medical University, Lviv, Ukraine).

Session summary

Poster session (Thursday, September 16, 2021; 11:30 – 12:15; *virtual stream C*)

S8.P1 LEPTIN, OMENTIN-1, MELATONIN AND VITAMIN D IN PATIENTS WITH CANCER OF LIP, ORAL CAVITY AND PHARYNX. **J. Nuszkiewicz, M. Budek, K. Szewczyk-Golec** (Department of Medical Biology and Biochemistry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz Nicolaus Copernicus University in Torun, Bydgoszcz, Poland).

S8.P2 CROSS-TALK BETWEEN THYROID HORMONES AND VITAMIN D. **E. Smolinska-Fijolek[1], J. Wierzbicka[2], M. Zmijewski[2]** ([1]Department of Physiology, Medical University of Gdansk, Gdansk, Poland; [2]Department of Histology, Medical University of Gdansk, Gdansk, Poland).

S8.P3 THE IMPORTANCE OF LEPTIN AND LIPIDS IN SHEEP'S MILK FOR HUMAN HEALTH. **E. Molik[1], Z. Flis[1], E. Marciniak[3], H. Pustkowiak[2]** ([1]Department of Animal Nutrition and Biotechnology, and Fisheries, University of Agriculture in Krakow, Poland, [2]Department of Genetics and Animal Breeding, and Ethology, University of Agriculture in Krakow, Krakow, Poland, [3]The Kielanowski Institute of Animal Physiology and Nutrition, Polish Academy of Sciences, Jablonna, Poland).

S8.P4 SINGLE NUCLEOTIDE POLYMORPHISM OF THE PROMOTER OF TNFRSF1A GENE (-610T>G, RS4149570) AS A USEFUL PREDICTOR OF MALNUTRITION IN PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY DUE TO HEAD AND NECK CANCER. **I. Homa-Mlak[1], R. Mlak[1], M. Mazurek[1], A. Brzozowska[2], T. Powrozek[1], T. Malecka-Massalska[1]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Department of Oncology, Medical University of Lublin, Lublin, Poland).

S8.P5 REGULATORY EFFECT OF IRISIN ON CARDIAC FIBROBLASTS PROLIFERATION IS DEPENDENT ON GLUCOSE CONCENTRATION. **M. Drobnik[1], M. Galdyszynska[1], J. Szymanski[2], P. Radwanska[1]** ([1]Laboratory of Connective Tissue Metabolism, Department of Pathophysiology, Medical University of Lodz, Lodz, Poland, [2]Central Scientific Laboratory, Medical University of Lodz, Lodz, Poland).

S8.P6 EFFECT OF N-ACETYLCYSTEINE SUPPLEMENTATION ON FATTY ACID TRANSPORTERS IN ADIPOSE TISSUE. **M. Wolosowicz[1], M. Maciejczyk[2], E. Zebrowska[1], B. Lukaszuk[1], A. Chabowski[1]** ([1]Department of Physiology, Medical University of Bialystok, Bialystok, Poland, [2]Department of Hygiene, Epidemiology and Ergonomics, Medical University of Bialystok, Bialystok, Poland).

S8.L1

THE POSITIVE IMPACT OF VITAMIN D SUPPLEMENTATION ON GLUCOCORTICOSTEROID-DEPENDENT NEUROIMMUNOLOGICAL CHANGES

D. KOREWO[1], M.J. KARNIA[1], D. MYSLINSKA[2], P. Berezka, Z.M. CIEPIELEWSKI[2], J.J. KACZOR[1]

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Dexamethasone (DEX) is used in treating a wide range of conditions. However, long-term exposure to its action affects immune system homeostasis disorders, memory, anxiety, and stress impairment response to the activation of inflammatory mediators in the brain. The study aimed to investigate whether vitamin D_3 supplementation would positively affect DEX-induced neuroimmunological changes measured by hippocampus and thymus total mass in long-term DEX administration. The research lasted 28 days and was carried out on 21 male Wistar rats randomly divided into three groups. These included two groups treated by abdominal injection of DEX at a dose of 2 mg/kg/day supplemented with vegetable oil (DEX PL; *n*=7) or with vitamin D_3 600 IU/kg/day (DEX SUP; *n*=8), respectively, and a control group treated with an abdominal injection of saline (CON; *n*=6). Blood, hippocampus, and thymus were collected and weighed immediately after sacrifice. The vitamin D metabolites concentration were measured. We found decreased serum $25(OH)D_3$ level and a lower hippocampus and thymus mass in both DEX-treated groups; however, vitamin D_3 attenuates this adverse effect in a statistically significant manner.

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S8.L2

MOTS-C - A NEW QUAINT ENDOCRINE PLAYER

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D. SZCZEPANKIEWICZ, K.W. NOWAK, L. NOGOWSKI, M. SASSEK

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MOTS-c is a recently discovered mitochondrial-derived peptide. Its coding sequence was found *in silico* in mitochondrial genome, exactly in 12S rRNA part of it. It has very conservative amino acid sequence in different animal species such as mouse, rat, bonobo and human. Moreover this newly discovered peptide proved to be biologically active. There are studies that show its attenuating effect in insulin resistance and diet induced obesity in mice. It this study we examined the influence of MOTS-c peptide on secretion of two main pancreatic hormones: glucagon and insulin. We used two types of models to test this: laboratory cell lines INS-1E and αTC-1 and isolated rat pancreatic islets. Insulin secretion increases significantly from both pancreatic islets and INS-1E cells, when the glucagon secretion lowers significantly from αTC-1 cells and isolated rat pancreatic islets. These results are promising since MOTS-c is still not well examined and someday it may play a significant role in curing type 2 diabetes and obesity.

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S8.L3

METABOLIC PARAMETERS IN OVARIECTOMIZED, ESTRADIOL-IMPLANTED SHEEP RESULTING FROM A LONG-TERM CHANGES IN BODY WEIGHT AND RESISTIN

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Both long-term undernutrition and overnutrition disturb metabolic balance, which is mediated partially by the action of two adipokines, leptin and resistin (RSTN). In this study, we manipulated the diet of ewes to produce either a thin (lean) or fat (fat) body condition and investigated how RSTN affects endocrine and metabolic status under different leptin concentrations. In the current study, we manipulated the diet of ewes over 4 months to produce either a thin (Lean) or fat (Fat) body condition and investigated how resistin affects metabolic status under low (thin sheep) or high (fat sheep) circulating levels of leptin (fat sheep). Twenty ovariectomized ewes with estrogen replacement were assigned to one of four groups. Plasma was assayed for RSTN, leptin, GH, glucose, insulin, total cholesterol, nonesterified fatty acid (NEFA), high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol and triglycerides. The results indicate that long-term alterations in body weight affect RSTN-mediated effects on metabolic parameters. Body weights of Lean and Fat groups were 41.2 ± 0.92, and 78.1 ± 1.78 kg, respectively ($P < 0.01$). Abdominal fat weight was 0.2 ± 0.02 kg in Lean and 5.3 ± 0.4 kg in Fat animals ($P < 0.01$) postmortem. Jugular blood samples (5 ml) were collected at 10-min intervals over 4 h *via* indwelling catheters to establish metabolic hormone status before and after resistin challenge. Within nutrition groups, mean (± SEM) pretreatment plasma concentrations of leptin were over 5-fold lower ($P < 0.01$) in Lean compared to Fat group, plasma NEFA was greater ($P < 0.05$) in Lean compared to Fat sheep. Resistin treatment increased ($P < 0.01$) plasma concentrations of leptin in both Lean and Fat groups. RSNT enhanced ($P < 0.05$) plasma total cholesterol in Fat group compared to Lean one, and decreased ($P < 0.05$) HDL fractions in Lean relative to Fat group. Mean GH concentrations were increased ($P < 0.05$) by resistin in Lean ewes, whereas insulin concentrations were increased ($P < 0.001$) by resistin treatment in Fat ewes. In conclusion, we have shown that alterations in BW influence the effects of RSTN on metabolic parameters in sheep. RSTN appears to be another adipokine, in addition to leptin, that is strongly involved in the regulation of body conditions in female sheep.

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S8.L4

EFFECT OF WHOLE BODY VIBRATION ON BONE NANOCOMPOSITES ORGANISATION AND PREVENTION OF BONE MINERAL DENSITY LOSS IN RATS WITH OBESITY AND LIMITED MOBILITY

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Several studies indicate that obesity is associated with increased bone mass due to excessive mechanical stress. However, these data are controversial, and the risk of fractures in this group is high. This study aimed to investigate the influence of high-frequency whole body vibration on metabolic and structural responses of rats' bone tissue with limited mobility and obesity. Obesity combined with a sedentary lifestyle can present the potential for negative health effects. However, whole body vibration can be used as a means of non-pharmacological correction of bone mineral density. For characterization of bone nanocomposites organisation and prevention of mineral density loss X-ray diffraction method was used. Markers of bone remodeling in the rats' blood: leptin, osteocalcin, tartrate resistant acid phosphatase 5b, alkaline phosphatase. Using a high-calorie diet and low-mobility model, we proved that bone mineral mass had been decreasing since 8th week. It should be noted that the decrease in the relative amount of crystalline phase - hydroxyapatite, continued throughout the experiment, up to 24 weeks ($p < 0.05$). These structural changes were accompanied by changes in quantitative indicators of the bone remodeling markers. Rats had lower bone mineral density compared to the animals that were on the normal diet and were further affected by whole body vibration. We observed the increase of the crystalline phase volume fraction from 84% to 93% ($p < 0.05$) in group with additional whole body vibration and the decrease of the mineral component in rats with limited mobility condition and high-calorie diet. Therefore, vibration could improve structural conditions of bone and prevent fat accumulation and obesity-associated biochemical markers in obese rats. This can be an effective method to improve the structural and functional state of the bones while preventing the loss of bone mineral density.

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S8.P1

LEPTIN, OMENTIN-1, MELATONIN AND VITAMIN D IN PATIENTS WITH CANCER OF LIP, ORAL CAVITY AND PHARYNX

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Tumors of the lip, oral cavity and pharynx (LOCP) are classified as cancers of the head and neck. LOCP neoplasms have been determined to account for approximately 6% of all tumors. In the course of LOCP neoplasms, the organism homeostasis is disturbed, leading to endocrine and metabolic changes. Adipose tissue hormones, known as adipokines, regulate metabolism, food intake and modulate inflammation. Melatonin and calcitriol, an active form of vitamin D, are hormones found to influence the synthesis and secretion of adipokines. They are also compounds with antioxidant activity. Clinicians point to the deficiency of both melatonin and vitamin D worldwide. The aim of the study is to determine the concentration of melatonin, vitamin D and two adipokines, namely leptin and omentin-1, in patients diagnosed with LOCP cancer. The study group consisted of 25 patients with LOCP neoplasm (10 female and 15 male, mean age 58.24) and the control group consisted of 25 healthy subjects (14 female and 11 male, mean age 55.36). Blood serum samples were obtained after collecting venous blood. $P < 0.05$ was considered as statistically significant. A significantly lower concentration of vitamin D was observed in the LOCP cancer patients. Similar results were observed for leptin level. There were no statistically significant differences in the level of omentin-1 and melatonin. The obtained results indicate the occurrence of vitamin D deficiency in patients with LOCP cancer. Lower levels of leptin in cancer patients may indicate the body depletion accompanying the disease.

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S8.P2

CROSS-TALK BETWEEN THYROID HORMONES AND VITAMIN D

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Vitamin D is actively produced in the skin subjected to UV radiation. Its biological faction is complex and multidimensional, resulting from its pleiotropic properties. In addition to its well established impact on calcium-phosphate homeostasis vitamin D is known modulator of cell proliferation and differentiation, including keratinocytes. The long-recognized “thyroid-skin conection” encompasses many layers of complexity and it has become a hot frontier in dermatoendocrinology. Thyroid disorders are known to involve all organ systems of the body and the skin is no exception. Cutaneous manifestations generally appear subsequent to the development of thyroid disease, but may be the first presenting sign or even precede the diagnosis by many years. However, the relationship between vitamin D and “thyroid-skin connection” has not been well elucidated. The aim of the research was to analyze the *in vivo* effect of vitamin D on the keratinocytes and thyrocytes cells lines. Cytotoxic and anti-proliferative activities of $1,25(OH)_2D_3$ against thyrocyte were tested. Gene expression profiling was performed by real-time qPCR on keratinocytes or thyrocytes treated with vitamin D. No remarkable cytotoxicity activity of vitamin D was observed in the range of tested conditions in HaCaT keratinocytes, while inhibition of proliferation of thyrocytes in a dose-dependent manner was shown. Testing the effects of vitamin D on human keratinocyte and thyrocyte transcriptional pattern, we found that this compound modulated of expression of receptors and enzymes responsible for thyroid hormone synthesis and activity. Our results suggest that expression of genes involving in metabolism and intracellular activities of the thyroid hormones in skin and in thyroid follicular cell can be modulate by the vitamin D. Our results suggest that expression of genes involving in metabolism and intracellular activities of the thyroid hormones in skin and in thyroid follicular cell can be modulate by the vitamin D.

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S8.P3

THE IMPORTANCE OF LEPTIN AND LIPIDS IN SHEEP'S MILK FOR HUMAN HEALTH

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Chronic metabolic disorders, referred to as „civilization diseases", such as diabetes, obesity or cancer are major public health problems. In recent years, people are becoming more aware that the cause of these diseases is an inappropriate lifestyle and diet. In the conditions of epidemiological threats and living in a polluted environment, the consumption of natural products, such as sheep's milk and its products, may support the functioning of the body. A measure of the high pro-health value of sheep's milk is i.a. lower cholesterol content, more favorable fatty acid composition, such as conjugated linoleic acid (CLA) and higher polar lipid content. CLA is one of the most important antioxidants of milk fat and has anti-carcinogenic and antimutagenic properties. Metabolic hormones, in particular leptin, are also crucial bioactive factor in sheep's milk. Leptin is involved in the control of the reproductive and endocrine systems, blood pressure, hematopoiesis and angiogenesis. The aim of the research was to determine the content of CLA and leptin in sheep's milk. The conducted research shows, that with the progress of lactation and the shortening of the day, the content of leptin in milk increases. Leptin content in the first two months of milking was (May 36.7 ± 6.2 ng/ml; June 36.7 ± 5.3 ng/ml), while in the last month it increased significantly ($P \leq 0.01$) and was (September 47.7 ± 6.2 ng/ml). Additionally, the content of CLA in the tested milk changed. In May, the content of CLA was (2.529 ± 0.01%), and in September (2.674 ± 0.01%). The obtained research results may allow the production of medicinal food from sheep's milk, which can be used in the prevention of many human diseases, including civilization diseases.

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S8.P4

SINGLE NUCLEOTIDE POLYMORPHISM OF THE PROMOTER OF *TNFRSF1A* GENE (-610T<G, RS4149570) AS A USEFUL PREDICTOR OF MALNUTRITION IN PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY DUE TO HEAD AND NECK CANCER

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Head and neck cancers (HNCs) are 7th for the prevalence among malignancies in the world. In this group of patients malnutrition, at the moment of diagnosis, is observed even in 52%. Malnutrition in patients with cancer is associated with a higher risk of morbidity and mortality. It is usually related to a higher rate of toxicities associated with treatment (chemotherapy or radiotherapy) and decreased quality of life. Defining risk factors of developing moderate and severe malnutrition would enable the introduction of greater individualization of treatment of HNC patients. Available studies suggest that inflammation caused by abnormalities levels of pro-inflammatory cytokines, e.g. tumor necrosis factor-α or alterations in their receptors, e.g. tumor necrosis factor receptor superfamily member 1A (TNFRSF1A) may promote the development of malnutrition. The study included 74 patients with advanced HNC (III and IV stage according to VII edition of TNM) treated with intensity modulated radiation therapy (IMRT). Nutritional status was determined using BMI, subjective global assessment (SGA), and nutritional risk score (NRS-2002) scales and laboratory tests. Single nucleotide polymorphism (SNP) (-610T>G; rs4149570) in the *TNFRSF1A* gene was determined by mini-sequencing. The occurrence of the GG genotype of TNFRSF1A gene significantly increased (over 5.5 times) the risk of severe (C) malnutrition according to the SGA scale (53.12% vs.16.67%; OR = 5.67; p=0.0015). On the other hand, GT heterozygote carriers had a significantly lower (more than 4-fold) risk of severe (C) malnutrition according to the SGA scale (17.14% vs. 46.15%; OR=0.24; p=0.0100). Based on the multivariate analysis, it was found that M1 feature (HR=9.46; p=0.0308), stage IV according to TNM classification (HR=3.76; p=0.0168) and the GG genotype of the *TNFRSF1A* gene (HR=2.18; p=0.0419) were independent, unfavorable prognostic factors. Conclusion: assessment of the *TNFRSF1A* SNP could be a useful tool in assessing the risk of disturbances in nutritional status and body composition in patients treated with IMRT due to HNC. Moreover, studied SNP in this group of patients may serve as an independent prognostic factor.

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S8.P5

REGULATORY EFFECT OF IRISIN ON CARDIAC FIBROBLASTS PROLIFERATION IS DEPENDENT ON GLUCOSE CONCENTRATION

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Irisin, (the myokine derived from precursor of fibronectin III) is secreted by skeletal muscle, heart and adipose cells. The myokine increases glucose uptake by muscle cells. Irisin upregulates expression of glucose transporters genes in adipose and muscle cells. Irisin involvement in induction of heart fibrosis in diabetics is supposed. The study is aimed at: 1) Verification of hypothesis suggesting that irisin may be involved in regulation of cardiac fibroblast proliferation, 2) Explanation, whether concentration of glucose in medium may influence on the final effect of the myokine, 3) Clarification, whether irisin may influence on the glucose transporter (GLUT) density on cardiac fibroblast membrane. The experiments were performed on cardiac fibroblasts, cultured in different concentrations of glucose: 1 M (hypoglycemia), 5 M (normoglycemia) and 25 M (hyperglycemia). Proliferation of fibroblasts was evaluated by BrdU method. Expression of GLUT was confirmed by flow cytometry. Different concentration of glucose did not influence on cardiac fibroblasts proliferation. Irisin treatment in hypoglycemic conditions was ineffective. The myokine applied at concentration 10^{-8} M, in normoglycemic as well as 10^{-8} M and 10^{-9} M in hyperglycemic conditions, increased proliferation of cardiac fibroblasts. Moreover, the expression of GLUT1, GLUT3 and GLUT4 on cardiac fibroblasts membrane was proved. The blockade of all three glucose transporters by application of WZB 117 markedly decreased proliferation of tested fibroblasts. However, irisin did not modified density of glucose transporters on fibroblasts membrane. We conclude that irisin stimulates the cardiac fibroblasts proliferation. The effect is dependent on glucose concentration in medium. Irisin did not modify density of glucose transporters (GLUT1, 3 and 4) on cellular membrane of cardiac fibroblasts.

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S8.P6

EFFECT OF N-ACETYLCYSTEINE SUPPLEMENTATION ON FATTY ACID TRANSPORTERS IN ADIPOSE TISSUE

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Obesity is a systemic, multifactorial, and largely preventable disease, affecting, along with overweight, over a third of the world's population in the XXI century. Chronically elevated body mass index (BMI) is linked to the occurrence of a broad range of diseases, namely cardiovascular diseases, diabetes, musculoskeletal disorders, and cancers. The adipose tissue is a critical regulator of systemic energy homeostasis by acting as a caloric reservoir. Augmented oxidative stress in adipose tissue of obese subjects leads to insulin resistance, dysregulated adipokines secretion, inflammation, and increased protein carbonylation. Based on this, we aimed to check whether anti-oxidative agent - N-acetylcysteine (NAC) impacts fatty acid transporters expression in adipose tissue using a rodent model of a high-fat diet (HFD). Four-weeks old Wistar rats were randomly divided into four groups (n=10): normal diet, normal diet + NAC, HFD, and HFD + NAC. The mRNA levels and protein expression of FAT/CD36, FABPpm, FATP1, and FATP4 were assessed using real-time PCR and Western Blot analyses. The level of lipids abundance (FFA, DAG, TAG, and PL) was estimated by GLC. In visceral and subcutaneous adipose tissues statistically significant differences in the mRNA and protein levels of the long-chain fatty acid transporters have been found. Eight weeks of NAC treatment during the HFD regime resulted in a significant increase ($p > 0.05$) in FATP1, FATP4, and FABPpm proteins expression in visceral and subcutaneous adipose tissue compared to the respective HFD. On the other hand there were observed a significant decrease ($p > 0.05$) in FATP1, FATP4, FABPpm, and also in FAT/CD36 mRNA expressions in both adipose tissues. Interestingly, there were observed decrease in FFA, DAG, TAG and PL content in NAC+HFD groups compared to HFD, in visceral and subcutaneous adipose tissue. Our results revealed that NAC supplementation during the HFD regime promotes a decrease in the lipids pool in adipose tissue compared to HFD. Currently, studies are underway to identify the mechanisms involved in the observed phenomena.

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SESSION IX

NEW INSIGHTS INTO CELLULAR FUNCTIONS

Wednesday (September 15, 2021; 14:15 – 17:45)
Thursday (September 16, 2021; 15:30 – 16:10)

Chair:

Prof. Mariusz Ratajczak
Stem Cell Institute at James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA
Department of Regenerative Medicine, Center for Preclinical Research and Technology, Medical University of Warsaw, Warszawa, Poland

Prof. Jakub Wlodarczyk
Laboratory of Cell Biophysics, Nencki Institute of Experimental Biology, Polish Academy of Science, Warsaw, Poland.

DETAILED SESSION IX SCHEDULE

Opening lectures (Wednesday; September 15, 2021; 14:15 – 16:15; *virtual stream B*)

S9.L1 EXTRACELLULAR MEMBRANE VESICLES-MEDIATED ANGIOGENESIS. **G. Camussi** (Department of Medical Sciences, University of Torino, Torino, Italy).

S9.L2 VERY SMALL EMBRYONIC-LIKE STEM CELLS (VSELS) - AN UPDATE AND FUTURE DIRECTIONS. **M. Kucia** (Medical University of Warsaw, Warsaw, Poland).

S9.L3 CONTROL OF NEURAL STEM CELL FATE DETERMINATION IN HUNTINGTON'S DISEASE BY ADENOSINE TRIPHOSPHATE (ATP) AND SPONTANEOUS CALCIUM OSCILLATIONS. **T. Glaser[1], H. Shimojo[2], D. Elisa Ribeiro[1], J. Correa-Velloso[1], A. Oliveira-Giacomelli[1], C. Lameu[1], Y.D. Teng[2], R. Kageyama[3], H. Ulrich[1].** ([1]Department of Biochemistry, IQ, University of Sao Paulo, Sao Paulo, Brazil, [2]Department of Neurosurgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, Division of SCI Research, Veterans Affairs Boston Healthcare System, Boston, MA, USA, [3]Institute for Virus Research, Kyoto University, Kyoto, Japan).

S9.L4 AN OVERVIEW OF NOVEL UNCONVENTIONAL MECHANISMS OF HEMATOPOIETIC DEVELOPMENT AND REGULATORS OF HEMATOPOIESIS – A ROADMAP FOR FUTURE INVESTIGATIONS. **M.Z. Ratajczak** (Medical University of Warsaw, Warsaw, Poland).

Oral presentations (Wednesday; September 15, 2021; 16:35 – 17:45; *virtual stream B*)

S9.L5 THE ROLE OF P2X4 PURINERGIC RECEPTOR IN HEMATOPOIETIC STEM/PROGENITOR CELLS TRAFFICKING. **M. Adamiak[1], M. Kucia[1,2], M.Z. Ratajczak[1,2]** ([1]Department of Regenerative Medicine Medical University of Warsaw, Poland, [2]Stem Cell Institute at James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA).

S9.L6 THE ROLE OF NOX2-ROS-NLRP3 INFLAMMASOME AXIS IN HEMATOPOIETIC STEM AND PROGENITOR CELLS (HSPCS) TRAFFICKING. **M. Kucia[1,2], K. Bujko[1], M. Adamiak[1], V. Chumak[1], J. Ratajczak[2], M.Z. Ratajczak[1]** ([1]Department of Regenerative Medicine, Center for Preclinical Research and Technology, Medical University of Warsaw, Warsaw, Poland, [2]Stem Cell Institute, University of Louisville Brown Cancer Center, Louisville, KY, USA).

S9.L7 BONE MARROW-DERIVED VSELS ENGRAFT AS LUNG PROGENITORS AFTER BLEOMYCIN-INDUCED LUNG INJURY. **A.K. Ciechanowicz[1], K. Sielatycka[2], M. Cymer[1], M.S. Uszynska[3], K. Bujko[1], M.Z. Ratajczak[1,3], D.S. Krause[4], M. Kucia[1,3]** ([1]Department of Regenerative Medicine, Center for Preclinical Research and Technology, Medical University of Warsaw, Warsaw, Poland, [2]Institute of Biology, Faculty of Exact and Natural Sciences, University of Szczecin, Szczecin, Poland, [3]Stem Cell Institute at James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA, [4]Department of Laboratory Medicine, Cell Biology and Pathology and the Yale Stem Cell Center, Yale University School of Medicine, New Haven, USA).

S9.L8 EXENDIN-4 AFFECTS METABOLIC AND SECRETORY ACTIVITIES OF HUMAN DERMAL FIBROBLASTS CULTURED IN A HYPERGLYCEMIC ENVIRONMENT. **M. Wolak[1], E. Bojanowska[1]** ([1]Department of Behavioral Pathophysiology, Medical University of Lodz, Lodz, Poland).

Session summary

Poster session (Thursday, September 16, 2021; 15:30 – 16:10; *virtual stream D*)

S9.P1 DIRECT EFFECT OF VITAMIN C ON CELL CYCLE AND APOPTOSIS GENE AND PROTEIN EXPRESSION IN CANCER CELLS. **N. Respekta, E.L Gregoraszczuk** (Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research , Jagiellonian University in Krakow, Krakow, Poland).

S9.P2 RELEASE OF INTERLEUKIN-6 IS DEPENDENT ON $\alpha 2\beta 1$ INTEGRIN. **M. Galdyszynska, P. Radwanska J. Drobnik** (Department of Pathophysiology, Medical University of Lodz, Lodz, Poland).

S9.P3 miR-138-5p AS A PREDICTIVE FACTOR OF SEVERE ORAL MUCOSITIS IN PATIENTS WITH HEAD AND NECK CANCER UNDERGOING INTENSITY-MODULATED RADIATION THERAPY. **R. Mlak[1], I. Homa-Mlak[1], T. Powrozek[1], M. Mazurek[1], A. Brzozowska[2], T. Malecka-Massalska[1]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]II Department of Radiotherapy, Center of Oncology of the Lublin Region St. John of Dukla, Lublin, Poland).

S9.P4 THE ASSESSMENT OF THE PROLIFERATIVE POTENTIAL OF BRONCHOALVEOLAR STEM CELLS AND ALVEOLAR TYPE 2 CELLS ISOLATED AT VARIOUS STAGES OF BLEOMYCIN-INDUCED LUNG INJURY. **A.K. Ciechanowicz[1], E. Suchocki[1], S. Leszczak[1], W.X. Lay[1], J. Prado Paulino[1], C. Leszczak[1], M. Kucia[1,2], D.S. Krause[3]** ([1]Department of Regenerative Medicine, Center for Preclinical Research and Technology, Medical University of Warsaw, Warsaw, Poland, [2]Stem Cell Institute at James Graham Brown Cancer Center, University of Louisville, Louisville, KY, USA, [3]Departments of Laboratory Medicine, Cell Biology and Pathology and the Yale Stem Cell Center, Yale University School of Medicine, New Haven, USA).

S9.L1

EXTRACELLULAR MEMBRANE VESICLES-MEDIATED ANGIOGENESIS

G. CAMUSSI

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Growing evidence indicates that membrane vesicles actively released from cells may act as autocrine and paracrine mediators in the angiogenic processes. These vesicles which include exosomes and microvesicles, can interact with neighboring cells and/or with distant cells and activate the angiogenic process through the transfer of encapsulated transcriptional regulators that may induce epigenetic changes in the recipient cells. These membrane vesicles gained a place amongst the vast group of angiogenic mediators and have been involved in physiological and pathological conditions of angiogenesis. The basic mechanism involved is the activation of an angiogenic program in quiescent endothelial cells. Many types of cells release angiogenic membrane vesicles such as stem/progenitor cells, inflammatory cells, activated endothelial cells and tumor cells. The angiogenic pathways activated in the recipient cells depend on the cell of origin, on the cargo of vesicles and on the state in which the vesicles are secreted. We recently investigated the mechanisms of action and the angiogenic capability of membrane vesicles derived from serum and their possible therapeutic use in regenerative medicine.

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S9.L2

VERY SMALL EMBRYONIC-LIKE STEM CELLS (VSELS) - AN UPDATE AND FUTURE DIRECTIONS

M. KUCIA

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Regenerative medicine is looking for a pluripotent/multipotent stem cell able to differentiate across germ layers and be safely employed in therapy. Unfortunately, with the exception of hematopoietic stem cells (HSCs) for hematological applications, the current clinical results with stem cells are somewhat disappointing. The potential clinical applications of the more primitive embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs) have so far been discouraging, as both have exhibited several problems, including genomic instability, a risk of teratoma formation, and the possibility of rejection. Therefore, the only safe stem cells that have so far been employed in regenerative medicine are monopotent stem cells, such as the abovementioned HSCs or mesenchymal stem cells (MSCs) isolated from postnatal tissues. However, their monopotency, and therefore limited differentiation potential, is a barrier to their broader application in the clinic. Interestingly, results have accumulated indicating that adult tissues contain rare, early-development stem cells known as very small embryonic-like stem cells (VSELs), which can differentiate into cells from more than one germ layer. Results from at least 40 independent laboratories indicate that adult tissues contain rare, early-development stem cells known as very small embryonic-like stem cells (VSELs), which can differentiate into cells from more than one germ layer. It has been proposed that VSELs originate from cells related to the germline, are deposited in developing organs during embryogenesis, and play a role as a backup population for monopotent tissue-committed stem cells. VSELs are quiescent but are activated during stress situations and mobilized into the circulation. The number of these cells decreases with age. Overall, the presence of these early-development cells in postnatal tissues challenges the accepted hierarchy within the adult stem cell compartment in bone marrow. Further research on these cells may provide a path forward to application of these cells in regenerative medicine that perhaps may solve several problems inherent in the use of controversial embryonic stem cells (ESCs) and somehow problematic induced pluripotent stem cells (iPSCs).

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S9.L3

CONTROL OF NEURAL STEM CELL FATE DETERMINATION IN HUNTINGTON'S DISEASE BY ADENOSINE TRIPHOSPHATE (ATP) AND SPONTANEOUS CALCIUM OSCILLATIONS

T. GLASER[1], H. SHIMOJO[2], D.E. RIBEIRO[1], J. CORREA-VELLOSO[1], A. OLIVEIRA-GIACOMELLI[1], C. LAMEU[1], Y.D. TENG[2], R. KAGEYAMA[3], HENNING ULRICH[1].

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Huntington's disease (HD) is an autosomal dominant inherited disease caused by at least 35 repetitions of the N-terminal CAG trinucleotide (glutamine) in the Huntington's gene (Htt). We used as *in vitro* disease models induced pluripotent iPS cells obtained from HD patients and Htt-gene edited embryonic stem cells, which were induced to neuronal differentiation into GABAergic neurons. Calcium oscillations were tracked by real-time fluorescence and luminescence microscopy to analyse the correlative relationship between calcium transient activity and rhythmic proneuronal transcription factor expression in embryonic stem cells after stable transfection with ASCL-1 or neurogenin-2 promoter-protein fused to the luciferase reporter gene. We show that pharmacological activity manipulation of P2Y2 and P2X7 purinergic receptors induced a two-step process of neuronal differentiation. *In vitro* models of Huntington's disease (HD) showed increased basal intracellular calcium concentration together with augmented apoptosis rates and lacked spike-like calcium oscillations and P2Y2 receptor activity, agreeing with deficiency of ASCL-1 expression activation and GABAergic differentiation. Our results suggest that HD may have developmental origins based on inefficient GABAergic differentiation, shedding new light on the mechanisms underlying neurogenesis of inhibitory neurons.

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S9.L4

AN OVERVIEW OF NOVEL UNCONVENTIONAL MECHANISMS OF HEMATOPOIETIC DEVELOPMENT AND REGULATORS OF HEMATOPOIESIS – A ROADMAP FOR FUTURE INVESTIGATIONS

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Hematopoietic stem cells (HSCs) are the best-characterized stem cells in adult tissues. Nevertheless, as of today, many open questions remain. First, what is the phenotype of the most primitive "pre-HSC" able to undergo asymmetric divisions during *ex vivo* expansion that gives rise to HSC for all hemato-lymphopoietic lineages. Next, most routine *in vitro* assays designed to study HSC specification into hematopoietic progenitor cells (HPCs) for major hematopoietic lineages are based on a limited number of peptide-based growth factors and cytokines, neglecting the involvement of several other regulators that are endowed with hematopoietic activity. Examples include many hormones, such as pituitary gonadotropins, gonadal sex hormones, IGF-1, and thyroid hormones, as well as bioactive phosphosphingolipids and extracellular nucleotides (EXNs). Moreover, in addition to regulation by stromal-derived factor 1 (SDF-1), trafficking of these cells during mobilization or homing after transplantation is also regulated by bioactive phosphosphingolipids, EXNs, and three ancient proteolytic cascades, the complement cascade (ComC), the coagulation cascade (CoA), and the fibrinolytic cascade (FibC). Finally, it has emerged that bone marrow responds by "sterile inflammation" to signals sent from damaged organs and tissues, systemic stress, strenuous exercise, gut microbiota, and the administration of certain drugs. This review will address the involvement of these unconventional regulators and present a broader picture of hematopoiesis and address a novel proposed stem cell hierarchy in BM microenvironment including presence of very small embryonic like stem cells (VSELs). These cells can differentiate into cells from more than one germ layer and results from at least 40 independent laboratories confirmed a presence of these cells in postnatal tissues including BM.

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S9.L5

THE ROLE OF P2X4 PURINERGIC RECEPTOR IN HEMATOPOIETIC STEM/PROGENITOR CELLS TRAFFICKING

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Our previous work we demonstrated that eATP activates P2X7 ion channel receptor in HSPCs and its deficiency impairs stem cell trafficking. Evidence suggest that P2X4 receptor in addition to P2X7, are also highly expressed on hematopoietic stem progenitor cells among P2X family and also is more sensitive to eATP and signals much faster. We have hypothesized that extracellular ATP activity on BM homing of HSPCs are dependent on P2X4 receptor. *In vivo* transplantations were performed with normal BM cells into irradiated mice or cells exposed to PSB12054–P2X4 receptor antagonist. Homing was evaluated by enumerating 24 hours after transplantation labeled cells, 12 days CFU-S and CFU-GM and hematological recovery. Results: Inhibition of P2X4 receptor both *in vivo* and *in vitro* negatively affected homing of HSPCs. HSPCs from control mice engrafted better than WT cells treated with PSB12054 what indicates involvement of P2X4 receptor in transplanted HSPCs. We noticed that P2X4 receptor similarly as P2X7 promotes trafficking of HSPCs, as its deficiency leads defective homing and engraftment of HSPCs after transplantation into myeloablated hosts. Moreover, the perturbation of P2X4 expression in BM of recipient mice also resulted in impaired homing, what corroborated with decrease of SDF-1 expression in BM microenvironment. Thus, our data sheds more light and confirm postulated cooperative dependence of both receptors in response to eATP signaling.

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S9.L6

THE ROLE OF NOX2-ROS-NLRP3 INFLAMMASOME AXIS IN HEMATOPOIETIC STEM/PROGENITOR CELLS TRAFFICKING

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Nox2 or nicotinamide adenine dinucleotide phosphate (NADPH) oxidase forms reactive oxygen species (ROS) are involved in several physiological and pathological processes of hematopoiesis. To support this, it has been reported that ROS are involved in mobilization of hematopoietic stem/progenitor cells (HSPCs) from bone marrow (BM) into peripheral blood (PB). Based on this and to learn more on the role of Nox2 in this process, we performed mobilization studies in Nox2-KO mice and noticed that these animals are poor G-CSF and AMD3100 mobilizers. Moreover, Nox-2 deficient BMMNC show defective homing and engraftment after transplantation into normal syngeneic recipients. To explain this, Nox2 as a source of ROS is involved in the activation of NLR family pyrin domain containing 3 (Nlrp3) inflammasome that by the release of extracellular adenosine triphosophate (eATP) promotes recruitment of CXCR4 receptor into membrane lipid rafts (MLRs) to enhance the responsiveness of HSPCs to stromal-derived factor-1 (SDF-1) gradient. Nox2 also sensitizes these cells responsiveness to other BM chemoattractants such as sphingosine-1 phosphate (S1P) and extracellular adenosine triphosphate (eATP). We report that Nox2 deficient HSPCs show defective migration to chemoattractants and do not form MLRs efficiently. This confirms the role of Nox2 as the ROS source that in Nlrp3 inflammasome-dependent manner enhances cell migration by promoting the formation of MLRs.

S9.L7

BONE MARROW-DERIVED VSELS ENGRAFT AS LUNG PROGENITORS AFTER BLEOMYCIN-INDUCED LUNG INJURY

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Alveolar type 2 (AT2) cells and bronchioalveolar stem cells (BASC) perform critical regenerative functions in response to lung injury. Published data show that non-hematopoietic bone marrow-derived very small embryonic-like stem cells (VSELs), can differentiate *in vivo* into surfactant protein C (SPC)-producing AT2 cells in the lung. Here we test directly whether VSEL derived BASC and AT2 cells function to produce differentiated progeny. With the use of a reporter mice in which the H2B-GFP fusion protein is driven from the murine SPC promoter, we tested whether bone marrow-derived VSELs or non-VSEL/non-hematopoietic stem cells (n-VSEL/n-HSCs) are capable of engrafting into BASCs and AT2 cells that function as lung progenitor cells. Immediately following bleomycin administration, WT recipient mice underwent intravenous administration of VSELs or n-VSEL/n-HSCs from SPC-H2B-GFP mice. GFP+ AT2 and BASC were isolated and tested for progenitor activity using *in vitro* organoid assays. After 21 days *in vivo*, we observed differentiation of VSELs but not n-VSEL/n-HSCs into phenotypic AT2 and BASC consistent with previous data in irradiated recipients. Subsequent *in vitro* organoid assays revealed that VSEL-derived AT2 and BASC maintained physiological potential for differentiation and self-renewal. These findings prove that VSELs produce functional BASC and AT2 cells, and may open new avenues using VSELs to develop effective cell therapy approaches for patients with lung injury.

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S9.L8

EXENDIN-4 AFFECTS METABOLIC AND SECRETORY ACTIVITIES OF HUMAN DERMAL FIBROBLASTS CULTURED IN A HYPERGLYCEMIC ENVIRONMENT

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Treatment of hard-healing wounds in diabetic individuals still remains a challenging medical problem. Exendin-4, a glucagon-like peptide-1 receptor agonist with antidiabetic properties, was found to have beneficial effects on wound healing in rodents but, to date, there have been no reports on the possible exendin-4 effects on human dermal fibroblasts. Therefore, we have examined the effects of this drug on the metabolic and secretory activities of human skin fibroblasts. We used a commercial human fibroblast cell line CLTH Dermal Fibroblasts incubated in the high-glucose (5 g/l, i.e., 25 mmol/l) Dulbecco's Modified Eagle's Medium (DMEM) in a humidified atmosphere with 5% CO_2 at 37°C in the presence of 0–100 nmol exendin-4 for 3 days. The fibroblast metabolic activity was measured using MTT method. The secretory activity was assessed regarding the matrix metalloproteinase-9 (MMP-9) and tissue inhibitor of metalloproteinase-1 (TIMP-1) secretion and gene expression by immunoenzymatic methods and a real-time PCR reaction, respectively. Collagen type I and glycosaminoglycan (GAG) contents in fibroblast colonies were examined using ELISA method. At a concentration of 20 nmol, exendin-4 inhibited the fibroblast metabolic activity but had no effects when used at higher concentrations. The drug did not affect significantly the MMP-9 content and MMP-9 gene expression in fibroblast colonies. On the other hand, it increased both TIMP-1 content and gene expression when used at lower concentrations. Also, at the same doses, exendin-4 markedly increased GAG content without affecting collagen production. To conclude, exendin-4 augmented the production of TIMP-1, an important pro-healing protein, and GAG, a basic constituent of the extracellular matrix. Hence, the drug has a potential to improve wound healing process in diabetic human subjects.

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S9.P1

DIRECT EFFECT OF VITAMIN C ON CELL CYCLE AND APOPTOSIS GENE AND PROTEIN EXPRESSION IN CANCER CELLS

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Vitamin C regulates many physiological processes. Protects against immune system deficiencies, cardiovascular disease, prenatal health problems, and eye disease. It is also scavenger of free radicals in biological systems participating in the first line of antioxidant defence, protecting lipid membranes, and proteins from oxidative damage. Vitamin C has a controversial history in cancer treatment; however, there are reports described that ascorbate, given in pharmacologic doses as effective in treating some cancers and in improving patient well-being. In the present study, we determined the effect of high physiological or pharmacological dose of vitamin C on selected parameters in ovarian cancer. Ovarian epithelial (OVCAR-3) and granulosa (KGN) cancer cells were incubated for 1 hour with vitamin C in high physiological (0.1 mM) or pharmacologic concentrations (0.5, 1, 10, 20 mM). Cells proliferation, membrane cell permeability, caspase-3 activity, cell morphology, UCP-2, CYCS as marker of oncosis, and BECN1, ATG5/7 gene expressions as markers of autophagy were measured. In both types of cells, an inhibitory effect of vitamin C on cell proliferation corresponding with inhibitory effect on cyclin A and CDK2 protein expression and stimulatory effect on membrane cell permeability was noted. A stimulatory effect on caspase-3 activity in KGN cells, while no effect on caspase-3 activity in OVCAR-3 cells suggested cell-specific apoptotic action of vitamin C. Morphological observations and data concerning oncosis and autophagy gene expression showed various types of cell deaths, including autophagy, oncosis and apoptosis in OVCAR-3 cells, and near-entirely apoptosis in KGN cells. Our study filling the gap in research on the mechanism of vitamin C action in ovarian cancer suggesting direct effect on cell cycle and apoptosis. Moreover, points to action of vitamin C as PARP inhibitor.

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S9.P2

RELEASE OF INTERLEUKIN-6 IS DEPENDENT ON A2B1 INTEGRIN

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Cardiac fibrosis, which determines stiffness of the heart wall, is a complex phenomenon. Cardiac fibroblasts constitute about 70% of cardiac cells and determine extracellular matrix metabolism. Moreover, cardiac fibroblast sense not only the biochemical stimuli but also the physical changes in the environment which may lead to release of cytokines, interleukin-6 (IL-6) including. The aim of the present study was to examine whether the stiffness of the environment of cardiac fibroblasts can influence the release of IL-6 and soluble IL-6 receptor (sIL-6). Moreover, it verify the role of integrin $\alpha 2\beta 1$ activation and its intracellular signaling in these processes. The research was conducted using stable cardiac fibroblast cell line, cultured on the polyacrylamide gels with different stiffness (soft gel elasticity 2.23 ± 0.8 kPa and stiff gel elasticity 8.28 ± 1.06 kPa), as well as on integrin $\alpha 2\beta 1$ knockout animals (homozygous Itga2tm1.1Tkun/tm1.1Tkun) and wild-type mice. Cardiac fibroblasts settled on the soft gel demonstrated increase in expression of the $\alpha 2$ integrin subunit on both gene and protein level and subsequent higher release of IL-6 and sIL-6 in those cells. The inhibition of $\alpha 2$ integrin subunit by means of siRNA or administration of TC-I 15 ($\alpha 2\beta 1$ integrin inhibitor) decreased the release of IL-6. Administration of Src inhibitor increase release of IL-6 in cells cultured on soft gel. Both heart and serum of integrin $\alpha 2\beta 1$ knockout animals exhibit markedly lower levels of IL-6 in comparison to wild type animals. No changes in sIL-6 level were observed in animals. Our data suggest that release of IL-6 and sIL-6 in cardiac fibroblast is related to changes in physical properties of the cell environment. Moreover, integrin $\alpha 2\beta 1$ exerts a regulatory effect on IL-6 release *via* Src signaling.

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S9.P3

MIR-138-5P AS A PREDICTIVE FACTOR OF SEVERE ORAL MUCOSITIS IN PATIENTS WITH HEAD AND NECK CANCER UNDERGOING INTENSITY - MODULATED RADIATION THERAPY

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Globally, the incidence of head and neck cancers (HNCs) is on the 6th location across all malignant neoplasms. Radiotherapy (RT), widely used in the treatment of HNCs, causes numerous troublesome side effects. The most common and most serious complication of RT is oral mucositis (OM). Severe OM (grade ≥3) often forces the reduction of radiation doses or leads to treatment discontinuation, which significantly reduces its effectiveness. Despite, that the introduction of the intensity-modulated radiation therapy (IMRT) technique led to the significant reduction of radiation reactions, most patients still develop OM. Interestingly, it was observed, that even patients receiving the same dose of radiation may develop various degrees of OM severity (probably due to patient variability at the molecular level). miR-138 belongs to the group of small, non-coding RNAs responsible for the regulation of many different genes, including this involved in DNA repair mechanisms (e.g. *ERCC1*, *ERCC2*, *PARP2*). The study material was peripheral blood serum obtained from 36 patients with pathomorphological diagnoses of HNC, subjected to IMRT. The expression level of miR-138-5p was assessed by the RT-PCR method and commercially available probes. The study group was dominated by men (86%). The median age of the patients was 63 years. According to the 7th edition of TNM, the dominant features were: T3 (53%), N + (67%) and M0 (100%). We noted, that patients with severe OM (>grade 3) after 4, 5, 6, and 7 weeks of RT had significantly higher levels of pre-treatment expression of miR-138-5p. Pre-treatment miR-138-5p expression demonstrated to have a significant predictive value for weeks 4th to 7th of OM evaluation. The sensitivity and specificity of this biomarker were, respectively, in the 4th week: 100% and 86% ($p < 0.0001$), in the 5th week: 86% and 79% ($p = 0.0012$), in the 6th week: 100% and 86% ($p < 0.0001$) and in the 7th week: 83% and 92% ($p < 0.0001$). miR-138-5p is a promising biomarker, that may serve as a useful tool in the prediction of more severe OM in patients with HNCs undergoing IMRT.

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S9.P4

THE ASSESSMENT OF THE PROLIFERATIVE POTENTIAL OF BRONCHOALVEOLAR STEM CELLS AND ALVEOLAR TYPE 2 CELLS ISOLATED AT VARIOUS STAGES OF BLEOMYCIN-INDUCED LUNG INJURY

A.K. CIECHANOWICZ[1], E. SUCHOCKI[1], S. LESZCZAK[1], W.X. LAY[1], J. PRADO PAULINO[1], C. LESZCZAK[1], M. KUCIA[1,2], D.S. KRAUSE[3]

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Alveolar type 2 (AT2) and bronchoalveolar stem cells (BASC) are rare subpopulations of lung cells that are directly responsible for the regeneration of small airways and alveoli, which are vulnerable to injury. The aim of the experiment is to assess the physiological ability of AT2 cells and BASCs to proliferate and self-renew in response to bleomycin-induced lung injury. Studies were conducted on healthy 6-8 week old C57BL/6J mice. Animals were administrated intratracheally with bleomycin (2.5 mg per kg. b.w.) suspended in 50 µl of saline. On 0, 3, 5, 7, 10, 12 and 14 days after bleomycin administration animals were sacrificed. To evaluate our hypothesis we conducted flow cytometry analysis, AT2 and BASC FACS sorting, organoid assay, western blot analysis (WB) and full proteome analysis. FACS analysis showed a significant increase on the 5th day of the amount of AT2 and BASCs sorted. This indicates that cells up to day 4 from lung injury have the highest proliferative potential. To confirm this hypothesis, organoid cultures were established. Flow cytometric analysis confirmed the hypothesis that AT2 cells and BASCs isolated on the 3rd day from injury have the highest proliferative potential. WB analysis showed an increase in expression of TTF1 and pro-SPC proteins in group from day 7. The literature states that the newly formed AT2 and BASC cells begin to present characteristic TTF1 and pro-SPC proteins only from 2–3 days, what confirms our results. In proteome analysis we identified 5739 proteins, and observed up-regulation of proteins responsible for cell proliferation and differentiation process in 3rd day after injury what confirms our hypothesis.

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SESSION X

AGING

Friday (September 17, 2021; 10:45 – 13:55)

Chair:

Prof. Zbigniew Kmiec
Department of Histology, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland

DETAILED SESSION X SCHEDULE

Opening lectures (Friday, September 17, 2021; 11:10 – 12:15; *virtual stream A/B*)

S10.L1 AGE-RELATED CHANGES IN THE REGULATION OF ENERGY BALANCE: THE ROLE OF ALTERED HYPOTHALAMIC NEUROPEPTIDE ACTIVITY IN THE DEVELOPMENT OF MIDDLE-AGED OBESITY AND AGING ANOREXIA. **M. Balasko, M. Szekely, E. Petervari** (Institute for Translational Medicine, Medical School, University of Pecs, Pecs, Hungary).

S10.L2 NK CELLS AT THE CROSSROADS OF INNATE AND ADAPTIVE IMMUNITY IN THE PROCESS OF AGING. **L. Kaszubowska** (Medical University of Gdansk, Gdansk, Poland).

Oral presentations (Friday, September 17, 2021; 12:15 – 13:55; *virtual stream A/B*)

S10.L3 THE POSITIVE EFFECT OF 12 WEEKS OF DANCE TRAINING ON THE AMYLOID PRECURSOR PROTEIN, SEROTONIN CONCENTRATION AND PHYSICAL PERFORMANCE IN ELDERLY WOMEN. **E. Rodziewicz-Flis[1], M. Kawa[1], W. Skrobot[2], D.J. Flis[3], J.J. Kaczor[3]** ([1]Departments of Manual and Physical Therapy, Gdansk University of Physical Education and Sport, Gdansk, Poland, [2]Functional Diagnostic and Kinesiology, Gdansk University of Physical Education and Sport, Gdansk, Poland, [3]Physiology and Biochemistry, Gdansk University of Physical Education and Sport, Gdansk, Poland).

S10.L4 DIFFERENT MOVEMENT CADENCES INDUCES PSYCHOPHYSIOLOGICAL CHANGES IN ELDERLY MEN. **W. Barbosa[1], P. Zovico, C. Reis[1], R. Rica[2], D. Bocalini[1]** ([1]Laboratorio de Fisiologia e Bioquimica Experimental, Universidade Estacio de Sa, Vitoria, ES, Brasil, [2]Centro de Educacao Fisica e Desporto, Universidade Federal do Espirito Santo (UFES), Vitoria, ES, Brasil).

S10.L5 POTENTIAL ROLE OF SEX HORMONE-BINDING GLOBULIN IN THE DEVELOPMENT OF ENDOTHELIAL DYSFUNCTION IN OLDER MEN. **M. Grandys[1], J. Majerczak[2], M. Frolow[3], R. Nizankowski[3], S. Chlopicki[4,5], J.A. Zoladz[1]** ([1]Department of Muscle Physiology, Chair of Physiology and Biochemistry, University School of Physical Education, Krakow, Poland, [2]Department of Neurobiology, Poznan University of Physical Education, Poznan, Poland, [3]Laboratory of Clinical Pharmacology of Endothelium, Jagiellonian Centre for Experimental Therapeutics (JCET), Jagiellonian University, Krakow, Poland, [4] Jagiellonian Centre for Experimental Therapeutics, Jagiellonian University, Krakow, Poland, [5]Department of Experimental Pharmacology, Chair of Pharmacology, Jagiellonian University Medical College, Krakow, Poland).

S10.L6 OXI-INFLAMMATORY RESPONSE IN AGEING. **E. Wacka, B. Morawin, A. Tylutka, A. Zembron-Lacny** (Department of Applied and Clinical Physiology, Collegium Medicum University of Zielona Gora, Zielona Gora, Poland).

S10.L7 INFLUENCE OF DEHYDRATION ON LIPID METABOLISM OF AGED MALE RATS. **S.Q.Cognuck[1], W.L. Reis[2], M.S. Silva[1], S.V. Zorro[3], G. Almeida-Pereira[1], L.K. de Barba[1], L.L.K. Elias[1], J. Antunes-Rodrigues[1]** ([1]Physiology Department, Ribeirao Preto Medicine School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil, [2]Department of Physiological Science, Center of Biological Sciences, Federal University of Santa Catarina, Florianopolis, Brazil, [3]Medical Clinic Department, Ribeirao Preto Medicine School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil).

S10.L8 FENOFIBRATE-INDUCED WHITE ADIPOSE TISSUE BROWNING IS REDUCED IN OLD AGE. **A. Wronska, A. Zubrzycki, Z. Kmiec** (Department of Histology, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland).

Session summary

Poster session ((Friday, September 17, 2021; 10:45 – 11:05; *virtual stream C*)

S10.P1 ELASTASES IN THE DEVELOPMENT OF CHRONIC INFLAMMATION WITH AGE. **L.M. Samokhina[1], V.V. Lomako[2]** ([1]GD National Institute of Therapy of L.T. Malaya name of National Academy of Medical Sciences of Ukraine, Laboratory of Immuno-biochemical and Molecular Genetic Studies, Kharkiv, Ukraine, [2]Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine, Department of Cryophysiology, Kharkiv, Ukraine).

S10.P2 AGE ASPECTS OF VASOCONSTRICTION DEVELOPMENT IN RATS **L.M. Samokhina[1], V.V. Lomako[2]** ([1]GD National Institute of Therapy of L.T. Malaya name of National Academy of Medical Sciences of Ukraine, Laboratory of Immuno-biochemical and Molecular Genetic Studies, Kharkiv, Ukraine, [2]Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine, Department of Cryophysiology, Kharkiv, Ukraine).

S10.L1

AGE-RELATED CHANGES IN THE REGULATION OF ENERGY BALANCE: THE ROLE OF ALTERED HYPOTHALAMIC NEUROPEPTIDE ACTIVITY IN THE DEVELOPMENT OF MIDDLE-AGED OBESITY AND AGING ANOREXIA

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The number of people aged 65 or older is projected to grow to nearly 1.5 billion by 2050. Long-term regulation of body weight (BW) and body composition shows two different trends: obesity develops typically in the middle-aged, whereas old age is characterized by anorexia, weight loss and sarcopenia. Both trends imply world-wide public health burdens. As most mammals also show similar trends in their long-term BW development, a dysregulation of energy homeostasis may also contribute to these phenomena. Therefore, the investigation of regulatory alterations in energy balance during the course of aging, are of outstanding importance. Earlier studies demonstrated the potential role of age-related shifts in the responsiveness to such peripherally administered anorexigenic and hypermetabolic (catabolic) mediators as cholecystokinin in the development of the above mentioned BW trends. The present work summarizes the outcomes of studies carried out in the Laboratories of Energy Balance and Experimental Gerontology of the Institute for Translational Medicine of the Medical School, University of Pecs Hungary, with regard to the age-related changes in key central catabolic mediator systems, such as leptin, alpha-melanocyte stimulating hormone (alpha-MSH) and corticotropin-releasing peptide (CRF). Age-related changes in the anorexigenic and hypermetabolic responsiveness to intracerebroventricular leptin, alpha-MSH and CRF administrations were recorded in different age-groups of normally fed male Wistar rats (from young adult to old groups, from 3 to 24 months of age, respectively). The expressions of the long form of the leptin receptor (Ob-Rb) in the arcuate nucleus and those of CRF in the paraventricular nucleus of the hypothalamus (PVN) were assessed by quantitative RT-PCR along with immunohistochemical detection of type 4 melanocortin receptors in the PVN. The anorexigenic responsiveness to all these central mediators showed a common pattern, diminished efficacy in the middle-aged and increased efficacy in the aging/old groups. The hypermetabolic responsiveness changed similarly in case of leptin and alpha-MSH. The hypothalamic receptor mRNA expressions for leptin and alpha-MSH and those for mRNA of CRF showed a similar pattern. Age-related changes in major central catabolic neuropeptide systems promote the development of middle-aged obesity and aging anorexia and cachexia. Future research needs to investigate the underlying causes and identify preventive measures.

S10.L2

NATURAL KILLER CELLS AT THE CROSSROADS OF INNATE AND ADAPTIVE IMMUNITY IN THE PROCESS OF AGING

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Aging is associated with many physiological changes, which include both innate and adaptive arms of the immune system. These age-related alterations occur at the cellular as well as humoral level of the immunity. However, they reflect rather age-related remodeling of the immune system at multiple structural and functional levels instead of a complete, unidirectional decline of the immune system functions. Natural killer (NK) cells are key effector lymphocytes of innate immunity provided with cytotoxic activity involved in antiviral and anticancer response. These lymphocytes reveal also some regulatory properties as they are capable of activating other cells of both innate and adaptive immunity by secretion of cytokines and chemokines. They appeared also to reveal both adaptive and memory-like phenotypes. The process of aging observed in immune system usually corresponds to chronic increase in proinflammatory status. In healthy aging this process is followed by anti-inflammatory response to maintain homeostasis. This phenomenon is associated with a general trend of raising the basal levels of cellular protective proteins to cope with stressors that accompany aging. It was also observed in NK cells of the oldest seniors and concerned increased expression of cellular protective proteins SIRT1, HSP70 and SOD2 which expression level corresponded to longevity. Moreover, the oldest seniors seem to reveal well-developed adaptive stress response in NK cells as they present increased, constant level of SIRT1 and intracellular HSP70. However, the age of participants was positively associated with sensitivity of SOD2 to stimulation indicating its distinct role in cellular stress response. Interestingly, T-lymphocytes represented slightly different pattern of cellular protective proteins expression, i.e. SIRT1, HSP70 and SOD2 as compared with NK cells and NKT-like cells. Thus, the specific pattern of cellular protective proteins' expression in NK cells of the oldest seniors may suggest an important role of these cells in the process of aging and their involvement in maintaining immune homeostasis to cope with higher levels of chronic stress compared to younger counterparts.

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S10.L3

THE POSITIVE EFFECT OF 12 WEEKS OF DANCE TRAINING ON THE AMYLOID PRECURSOR PROTEIN, SEROTONIN CONCENTRATION AND PHYSICAL PERFORMANCE IN ELDERLY WOMEN

E. RODZIEWICZ-FLIS[1], M. KAWA[1], W. SKROBOT[2], D.J. FLIS[3], J.J. KACZOR[3]

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A sedentary lifestyle is a risk factor for deterioration of physical functions, higher fall risk and may lead to the development of neurodegenerative diseases. One of the best known factor, that could contribute to healthy aging is physical activity. Its' beneficial effect on age-related changes in cognitive processes, neurodegenerative diseases and physical performance may be associated with modifying circulating protein and/or hormone concentrations. The aim of the study was to examine if 12 weeks of dance training could attenuate the risk of falls, improve physical functions and modify the circulating concentration of amyloid precursor protein and serotonin in serum of elderly women. 20 older women (aged 73.3 ± 1.5) were randomly assigned into two groups: dance training (DG; n=10) and control group (CG; n=10). The training was performed 3 times a week for 12 weeks. To assess the study aims Time up and go test (TUG), 6 minutes walk test (6MWT), plasma amyloid precursor protein (APP) and serum serotonin (5-HT) concentration were performed. Women in the DG improved distance performed during the walking test as well as TUG test time. The improvement in physical functions in the training group was associated with an increase in APP and a decrease in 5-HT concentrations. No changes in the above parameters were observed among the CG. Results indicate that the training intervention could have a beneficial effect on physical functions among older women. Moreover, physical training may be an important factor in modifying the concentration of circulating proteins associated with neurodegenerative disorders.

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S10.L4

DIFFERENT MOVEMENT CADENCES INDUCES PSYCHOPHYSIOLOGICAL CHANGES IN ELDERLY MEN

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Although the effectiveness of Brazilian Public Gyms (BPG) is a consolidated public health program to promote and facilitate active behavior, the program still lacks information on changes in training load parameters elderly using BPG devices. Fifteen physically independent elderly men participated voluntarily in this study. Three 30-minute exercise sessions were randomly distributed with low (L: 1 movement every 2 seconds), medium (M: 1 movement per second) and high (H: 2 movements per second) cadence with 30“ of stimulus and 30“ of recovery using the following devices: elliptical, rower, surf and leg press. Heart rate (HR), perceived exertion (PE) and recovery (PR), pleasure (PP), number of movements (NM) were evaluated before and immediately after the three sessions. The difference between the parameters were analyzed by analysis of variance and t test with significance level $p < 0.05$. Results: Differences ($p < 0.0001$) were found to absolute (L: 107 ± 12 <M: 130 ± 9 <H: 149 ± 5; bpm) and relative heart rate ($F=49.49$; $p < 0.0001$). The B (60 ± 9%) cadence presented values lower than M (75 ± 3%) and H (91 ± 3%) that also differed from each other. Significant differences ($p < 0.01$) to area under curve of PE (L: 75 ± 26, M: 115 ± 16, H: 154 ± 4) and PR (L: 173 ± 16, M: 139 ± 12, H: 97 ± 6; UA) were identified around cadences. Statistical differences ($p < 0.01$) were found in NM (L: 435 ± 13 < M: 883 ± 191 <H: 1726 ± 53), PE after 30 min of the session (L: 4.2 ± 0.7 <M: 5.7 ± 0.7 <H: 7.4 ± 0.5). In relation to PP, the M (–4.29 ± 0.38%) cadence provided a smaller ($p < 0.01$) reduction compared to cadences L (–21.43 ± 0.49%) and H (–48.81 ± 0.90%) cadency that differed from each other. Conclusion: the performance of different cadences induced different responses in training load indicators in proportion to their speed of execution in the elderly submitted to the exercise session in BPG. However, the moderate cadence provided an increase in HR with values considered safe to perform the exercise.

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S10.L5

POTENTIAL ROLE OF SEX HORMONE-BINDING GLOBULIN IN THE DEVELOPMENT OF ENDOTHELIAL DYSFUNCTION IN OLDER MEN

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Sex hormone-binding globulin (SHBG) is a transport plasma glycoprotein for sex steroid hormones that regulates their biological activity and metabolic clearance. However, it has been also postulated that SHBG level may be related to increased risk of cardiovascular diseases, but this association is far from being fully understood. In this study we have determined serum SHBG concentration in relation to markers of arterial stiffness and early atherosclerosis in young (22.2 ± 2.6 years, n=12) and older, physically non-active subjects (61.0 ± 7.9 years, n=11). Serum SHBG concentration was assessed by electrochemiluminescence immunoassay and markers of arterial stiffness and atherosclerosis were determined noninvasively using applanation tonometry (pulse wave velocity (PWV), arterial stiffness (AI)), infrared photoplethysmography (stiffness index (SI)) and ultrasound technique (carotid intima-media thickness (cIMT)). We demonstrated that serum SHBG concentration was almost 2 fold higher in older men (27.90 ± 9.62 vs. 50.53 ± 17.54 nmol/L in young and older men respectively, $p < 0.001$), what was accompanied by higher level of PWV, AI, SI and cIMT in older men ($p < 0.001$). Moreover, serum SHBG concentration was significantly positively correlated to all markers of arterial stiffness (PWV, AI, SI, $p < 0.001$) as well as to cIMT ($p < 0.03$). We have concluded that elevated serum SHBG concentration may be a valuable biomarker of arterial stiffness and cardiovascular risk in ageing men.

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S10.L6

OXI-INFLAMMATORY RESPONSE IN AGEING

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Aging is a process caused by many factors, such as lifestyle, malnutrition, decreased synthesis of anabolic hormones and growth factors, intensification of inflammatory processes, oxidative stress, etc. In recent years, special attention has been paid to chronic low-grade inflammation as one of the factors enhancing senescence of vascular endothelial cells. The study was designed to demonstrate the impact of chronic low-grade inflammation on the regenerative potential of blood vessels in older adults. Blood samples were collected from 60 individuals (females n=42, males n=18) aged 70.4 ± 5.5 years. Serum oxi-inflammatory markers such as C-reactive protein (CRP), oxidised LDL (oxLDL) and 3-nitrotyrosine (3NT) as well as conventional atherogenic markers such as triglycerides (TG), total cholesterol (TC), high-density lipoproteins (HDL) and low-density lipoproteins (LDL) were determined. Moreover, the numbers of endothelial progenitor cells (EPC) as well as CD34 and CD38 hematopoietic cells were measured by using ELISE kits. Statistical analyses were performed by the software Statistica 13.1 (StatSoft Inc., Tulsa, OK, USA). The protocol of the study was approved by the ethics committee at Medical University of Poznan, Poland (No 550/11), in accordance with the Helsinki Declaration. We obtained high levels of TC >150 mg/dL, LDL >130 mg/dL and non-HDL >130 mg/dL were found in 50% of subjects from taking the hypolipidemic drugs (only 10% of group). Despite dyslipidaemia, oxLDL and 3NT demonstrated the low concentrations 319 ± 284 ng/mL and 1.29 ± 0.81 nmol/mL possibly due to subjects' daily physical activity which improves nitro-oxidative metabolism; approx. 60% of them achieved the result of gait speed above 1.3 m/s. Interestingly, female demonstrated significantly higher concentration of oxLDL (404 ± 290 ng/mL) than male (119 ± 130 ng/mL). This confirms that female sex increases the risk of LDL oxidation thus atherogenesis in old age. However, the opposite tendency was observed for CD34 and CD38 (female 22.43 ± 11.16 ng/mL and 1.28 ± 0.90 ng/mL; male 18.36 ± 8.05 ng/mL and 0.72 ± 0.12 ng/mL). High levels of CRP >5 mg/L was found in 20% of individuals. These findings demonstrate that oxi-inflammation impairs the recovery of blood vessels, and an assessment of CD34 and CD38 hematopoietic cells can be a useful tool for monitoring of the vascular regenerative potential. However, the role of progenitor cells in vascular diseases needs to be part of further studies including relatively high number of subjects.

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S10.L7

INFLUENCE OF DEHYDRATION ON LIPID METABOLISM OF AGED MALE RATS

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Dehydration produces energy metabolism alterations. Our objective was to determinate the effect of dehydration in the lipid metabolism of old male rats. Male rats of 3- and 18-month-old were submitted to water deprivation (WD) for 48 hours. Retroperitoneal white adipose tissue (R-WAT) weight, lipidogram assay, plasma palmitic acid, glycerol, and the relative expression of proliferator-activated receptor alpha (*P-para*), hormone-sensitive lipase (*HSL*), and aquaporin 7 (*Aqp7*) mRNA in R-WAT were determined. Rats showed no difference in glycerol level, *P-para*, and *HSL* expression. The 18-month-old WD rats had lower weight of R-WAT, total cholesterol, and palmitic acid than respective control. The 3-month-old WD rats showed less expression of *Aqp7* mRNA than their respective controls. Both 3- and 18-month-old WD rats showed lower plasma triglyceride. We concluded that age influence lipid metabolism of dehydrated rat.

Acknowledgements: We thank Maria Valci dos Santos and Milene Mantovani for their excellent technical assistance. This work was supported by the Coordenacao de Aperfeicoamento de Pessoal de Nivel Superior (CAPES), Conselho Nacional de Desenvolvimento Cientifico e Tecnologico (CNPq), and Fundacao de Amparo a Pesquisa do Estado de Sao Paulo, Brazil (FAPESP # 2013/09799-1).

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S10.L8

FENOFIBRATE-INDUCED WHITE ADIPOSE TISSUE BROWNING IS REDUCED IN OLD AGE

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The hypolipemic drug fenofibrate (FN) is known to act through peroxisome proliferator-activated receptor alpha (PPARα) which may stimulate mitochondrial oxidative metabolism. The aim of this study was to examine whether FN affects the thermogenic activity of brown adipose tissue (BAT) as well as browning of white adipose tissue (WAT), and whether these effects depend on age. Young adult (4-month-old) and old (24-month-old) Wistar rats were fed with either standard rodent chow (control animals) or the same chow supplemented with FN in two doses: 0.5% and 0.1% by weight, for 30 days (n=8–10 young or old animals in every group). Snap-frozen samples of epididymal WAT (eWAT) and intarscapular BAT were analysed for gene expression (qPCR) and protein content (Western blotting). In BAT of young rats, treatment with 0.5% FN increased the protein content of CITED1, a transcription factor involved in thermogenic activation and a marker of adipocyte browning. However, neither UCP1 nor PGC-1α proteins were significantly upregulated. The mRNA expression of Ucp1, Pgc-1α, and PGC-1α downstream targets Cpt1b and Acadm decreased after 0.5% FN. In BAT of old rats, the treatment affected neither the studied proteins' content nor mRNA levels. In eWAT of young rats, UCP1 and CITED1 tended to increase after FN, with Pgc-1α, Cpt1b, and Acadm mRNA levels likewise increased. In eWAT of old rats, similar changes in mRNA were observed. We concluded that fenofibrate did not activate the thermogenic function of brown adipose tissue, but modestly stimulated mitochondrial oxidative metabolism and "browning" of white adipose tissue in young adult rats. Aging blunted both these effects.

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S10.P1

ELASTASES IN THE DEVELOPMENT OF CHRONIC INFLAMMATION WITH AGE

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Chronic inflammation develops with age, and this condition is a strong risk factor for multiple organ pathology. The development of inflammation is associated with the functioning of elastases: serine (EC 3.4.21.37) of neutrophilic origin (El), cysteine or thiol (EC 3.4.22) of endothelial (EEl) origin, and metalloelastase (MEl) or matrix metalloprotease 12 (EC 3.4.24.65) of macrophage origin. The aim was to investigate the activity of elastases of various origins and the elastase inhibitory activity of α-1-proteinase inhibitor (EIA α-1-PI) in the tissues of male rats of different ages. The work was performed on white outbred rats (Rattus norvegicus) 3, 6, and 24 months old according to the bioethics rules (n=6 in each group). The elastases activity and EIA α-1-PI were determined in the nuclear-free fractions of 10% homogenates of tissues of the cerebral cortex (CC), lungs, heart, liver and kidneys by highly sensitive (10^{-10} g) enzymatic methods (Samokhina L.M., 2014, 2015; ISBN: 978-3-659-63483-3; ISBN 978–3–659–33949–3). It was noted that El activity decreases with age at 6 and 24 months in the tissues of internal organs, which may be the result of a loss of compensatory reserve, but increases in CC at 6 and 24 months and in the kidneys at 24 months, which may be due to a decrease in antioxidant protection and lead to the inflammation, as well as destruction and vasoconstriction. An increase EEl, EIA α-1-PI at 6 months and a decrease at 24 months was shown, which can be considered as links of the body's compensatory response. The MEl activity increased in CC at 24 months, decreased in the lungs, which may be a consequence of oxidative stress and the participation of MEl in the pathological changes.

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S10.P2

AGE ASPECTS OF VASOCONSTRICTION DEVELOPMENT IN RATS

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Angiotensin II (AII) plays a key role in the regulation of blood pressure and vascular tone. In tissues of rats, rabbits, mice, AII is formed with the chymase participation at a high concentration of AI. Tonin forms AII directly from angiotensinogen. The calpains activity promotes an increase in AII-induced left ventricular hypertrophy and vascular remodeling. The aim of this work is to study the activity of chymase, tonin, and calpains in the tissues of male rats of different ages. The work was performed with using white rats (Rattus norvegicus) 3, 6, 24 months, n=6 in each group. The activity of chymase, tonin and calpains was determined in blood serum and non-nuclear fractions of 10% homogenates of tissues of the cerebral cortex (CC), lungs, heart, liver and kidneys by highly sensitive enzymatic methods (ISBN: 978-3-659-63483-3); (ISBN 978-3-659-33949-3). It was noted that the chymase activity is higher at 24 months in blood serum, CC and liver, which may indicate the chymase release by mast cells, and (given the species specificity of rat chymase to degrade AII) promote vasodilation, at least in CC; in the kidneys the chymase activity decreases in 24 months, suggesting the development of local vasoconstriction. The tonin activity in 6 months is higher than at 3 months, indicating also the vasoconstriction development, and decreases at 24 months (except for CC). The calpains activity increases at 6 months (in the lungs, heart, liver, and kidneys) and 24 months (in all tissues except the heart), maximum - in the lungs. The calpains activation promotes endothelial dysfunction, cardiovascular diseases, structural and functional changes in the kidneys, inflammation, etc. The high calpains activity in the lungs at 24 months can be induced by increased respiration, is associated with the development of tissue inflammation and edema, and an increase in pulmonary vascular permeability.

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SESSION XI

PHYSIOLOGY OF REPRODUCTION

Thursday (September 16, 2021; 9:00 – 15:25)

Chair:

Prof. Anita Franczak
Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology,
University of Warmia and Mazury in Olsztyn, Olsztyn, Poland

Prof. Urszula Kosior-Korzecka
Sub-Department of Pathophysiology, Department of Preclinical Veterinary Sciences,
Faculty of Veterinary Medicine, University of Life Sciences in Lublin, Lublin, Poland

DETAILED SESSION XI SCHEDULE

Opening lecture (Thursday, September 16, 2021; 9:00 – 9:40; *virtual stream B*)

S11.L1 EPIGENETIC MECHANISMS AND BIO-MECHANICAL CUES DRIVE CELL DIFFERENTIATION. **T.A.L. Brevini, G. Pennarossa, R. Pasquariello, F. Gandolfi** (Laboratory of Biomedical Embryology, Centre for Stem Cell Research, UniStem, Universita degli Studi di Milano, Milano, Italy).

Oral presentations (Thursday, September 16, 2021; 9:40 – 13:25; *virtual stream B*)

S11.L2 PRESENCE OF LACTOBACILLI WITHIN THE BOVINE FEMALE REPRODUCTIVE TRACT AND THEIR POSSIBLE ROLE DURING REPRODUCTIVE EVENTS. **C. Gabler** (Institute of Veterinary Biochemistry, Department of Veterinary Medicine, Freie Universitaet Berlin, Berlin, Germany).

S11.L3 THE IMPACT OF ENERGY METABOLISM CHANGE IN PORCINE CUMULUS-OOCYTE COMPLEX DURING IN VITRO MATURATION. **G. Gorczyca[1], K. Wartalski[2], M. Duda[1]** ([1]Department of Endocrinology, Institute of Zoology and Biomedical Research, Jagiellonian University, Krakow, Poland, [2]Department of Histology, Jagiellonian University Medical College, Krakow, Poland).

S11.L4 SEX STEROID RECEPTOR AGONISTS AND ANTAGONISTS AFFECT THE EXPRESSION OF TRANSCRIPTION FACTOR FORKHEAD L2 (FOXL2) IN THE NEONATAL PORCINE OVARY. **P. Witek, N. Marek, M. Grzesiak, M. Slomczynska, K. Knapczyk-Stwora** (Department of Endocrinology, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland).

S11.L5 PRO- APOPTOTIC EFFECT OF VASPIN ON HUMAN PLACENTA BeWo CELLS. **M. Dawid, E. Mlyczynska, P. Kurowska, M. Jurek, A. Rak** (Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland).

S11.L6 RELATIVE ABUNDANCE OF APELIN RECEPTOR TRANSCRIPT IN THE PORCINE PITUITARY DURING THE ESTROUS CYCLE AND EARLY PREGNANCY. **K. Kisielewska, E. Rytelewska, M. Gudelska, M. Kiezun, K. Dobrzyn, E. Zaobidna, K. Bors, G. Kopij, K. Szymanska, B. Kaminska, N. Smolinska, T. Kaminski** (University of Warmia and Mazury, Olsztyn, Poland).

S11.L7 VISFATIN/NICOTINAMIDE PHOSPHORIBOSYLTRANSFERASE (NAMPT) EXPRESSION IN PORCINE CORPUS LUTEUM DURING THE OESTROUS CYCLE AND EARLY PREGNANCY. EFFECT OF LUTEINIZING HORMONE (LH) AND P_4 ON VISFATIN PROTEIN LEVEL. **E. Mlyczynska[1], E. Zaobidna[2], E. Rytelewska[2], M. Kiezun[2], K. Dobrzyn[2], N. Smolinska[2], T. Kaminski[2], A. Rak[1]** ([1]Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland, [2]Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn, Olsztyn-Kortowo, Poland).

S11.L8 CHEMERIN AS A HORMONE MODULATING ENDOMETRIAL REMODELING IN PIGS DURING THE PERI-IMPLANTATION PERIOD: AN *IN VITRO* STUDY. **E. Rytelewska, M. Kiezun, K. Dobrzyn, E. Zaobidna, M. Gudelska, K. Kisielewska, K. Bors, G. Kopij, K. Szymanska, B. Kaminska, T. Kaminski, N. Smolinska** (University of Warmia and Mazury, Olsztyn, Poland).

S11.L9 DECORIN AND DERMATOPONTIN DIFFERENTIALLY AFFECT CARUNCULAR EPITHELIAL CELL ADHESION IN PREGNANT COWS. **M. Jamiol[1], J. Wawrzykowski[1], M. Kankofer[1]** ([1]Department of Biochemistry, Faculty of Veterinary Medicine, University of Life Science in Lublin, Lublin, Poland).

S11.L10 THE ELECTROMAGNETIC FIELD (EMF) RADIATION INDUCES TRANSCRIPTOMIC ALTERATIONS IN PIG MYOMETRIUM DURING THE PERI-IMPLANTATION PERIOD. **E.M. Drzewiecka[1], W. Kozlowska[1], L.P. Paukszto[2], A.Z. Zmijewska[1], P.J. Wydorski[1], J.P. Jastrzebski[2], A. Franczak[1]** ([1]Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn, Poland, [2]Department of Plant Physiology, Genetics and Biotechnology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland).

S11.L11 PPARγ REGULATES THE EXPRESSION OF GENES IN THE PORCINE INFLAMED ENDOMETRIUM DURING FOLLICULAR PHASE OF THE ESTROUS CYCLE. **K. Mierzejewski[1], L. Paukszto[2], A. Kurzynska[1], Z. Kunicka[1], J.P. Jastrzebski[2], M. Golubska[1], I. Bogacka[1]** ([1]University of Warmia and Mazury in Olsztyn, Faculty of Biology and Biotechnology, Department of Animal Anatomy and Physiology; Olsztyn, Poland, [2]University of Warmia and Mazury in Olsztyn, Faculty of Biology and Biotechnology, Department of Plant Physiology, Genetics and Biotechnology, Olsztyn, Poland).

S11.L12 KISS-1/GPR54 mRNA EXPRESSION AND THE RELATIONSHIP BETWEEN KISS-10 AND LUTEINIZING HORMONE SECRETION IN PITUITARY GLAND OF CYCLIC AND PCOS - AFFECTED SOWS. **U. Kosior-Korzecka[1], V. Longo[2], C. Della Croce[2], N. Szysiak[1], A. Furmanczyk-Gnyp[1], A. Nowakiewicz[1], I. Puzio[3], B. Surowka[1], N. Minakow[1], B. Szymczak[1]** ([1]Department of Preclinical Veterinary Sciences, Faculty of Veterinary Medicine, University of Life Sciences in Lublin, Lublin, Poland, [2]National Research Council, Institute of Agricultural Biology and Biotechnology, Pisa, Italy, [3]Department of Animal Physiology, Faculty of Veterinary Medicine, University of Life Sciences in Lublin, Lublin, Poland).

S11.L13 KISS-INDUCED ALTERNATIONS IN PRL mRNA TRANSCRIPT ABUNDANCE IN PORCINE PITUITARY CELLS DURING THE ESTROUS CYCLE. **A. Zmijewska[1], W. Czelejewska[1,2], E.M. Drzewiecka[1], S. Okrasa[1], A. Franczak[1]** ([1]Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland, [2]Department of Neurosurgery Laboratory of Regenerative Medicine, School of Medicine, Collegium Medicum, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland).

S11.L14 EFFECTS OF LONG-TERM CHANGES IN BODY WEIGHT ON THE ABILITY OF RESISTIN TO MODULATE REPRODUCTIVE HORMONES IN SHEEP. **M. Szczesna, W. Biernat, K. Kirsz, D.A. Zieba** (Department of Animal Nutrition and Biotechnology, and Fisheries, Faculty of Animal Sciences, University of Agriculture in Krakow, Krakow, Poland).

S11.L15 VASPIN ENHANCED PORCINE OOCYTES *IN VITRO* MATURATION *VIA* MAP3/1 AND PRKAA1 KINASES PATHWAYS. **P. Kurowska[1], M. Mlyczynska[1], A. Estienne[2], A. Barbe[2], I. Rajska[3], K. Sobol[3], K. Poniedzialek-Kempny[3], J. Dupont[2], A. Rak[1]** ([1]Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Jagiellonian University, Krakow, Poland, [2]INRAE, UMR85, Unite Physiologie de la Reproduction et des Comportements, Nouzilly, France, 3 Department of Reproductive Biotechnology and Cryopreservation, National Research Institute of Animal Production, Balice, Poland).

Session summary

Poster session (Thursday, September 16, 2021; 13:30 – 15:25; *virtual stream C*)

S11.P1 ELECTROMAGNETIC FIELD OF EXTREMELY LOW FREQUENCY INDUCES CHANGES IN THE RELATIVE ABUNDANCE OF *HSD17B2* AND *VDR* IN THE ENDOMETRIUM OF PIGS DURING THE PERI-IMPLANTATION PERIOD. **W. Kozlowska, E.M. Drzewiecka, A. Zmijewska, P.J. Wydorski, A. Franczak** (Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland).

S11.P2 EFFECT OF VITAMIN D3 ADMINISTRATION ON GLUCOSE AND INSULIN LEVEL, AND HOMA-IR INDEX IN RATS WITH LETROZOLE-INDUCED PCOS. **M. Grzesiak[1], K. Kaminska[1], O. Fraczek[1], A. Szlaga[2], A. Maslanka[3], D. Klimczyk[3], P. Sambak[2], P. Dziurowicz[1], K. Knapczyk-Stwora[1], A. Blasiak[2], A. Rak[3]** ([1]Department of Endocrinology, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland, [2]Department of Neurophysiology and Chronobiology, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland; [3]Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland).

S11.P3 PROTEIN EXPRESSION AND IMMUNOLOCALISATION OF VASPIN AND GRP78 RECEPTOR IN HUMAN PLACENTA OF INTRAUTERINE GROWTH RESTRICTION. PRELIMINARY DATA. **M. Jurek[1], M. Dawid[1], T. Milewicz[2], P. Pawlicki[3], M. Kotula-Balak[4], A. Rak[1]** ([1]Laboratory of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland, [2]Department of Gynecological Endocrinology, Jagiellonian University Medical College, Krakow, Poland, [3]Center for Experimental and Innovative Medicine, University of Agriculture in Krakow, Krakow, Poland, [4]University Centre of Veterinary Medicine JU-UA, University of Agriculture in Krakow, Krakow, Poland).

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S11.P5 TRANSCRIPTOMIC PROFILE OF OVIDUCTAL ISTHMUS IN PIGS ON DAYS 2 TO 3 OF PREGNANCY. **M. Martyniak, E. Waszkiewicz, A. Franczak, G. Kotwica** (Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury, Olsztyn, Olsztyn, Poland).

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S11.P7 DIETARY SUPPLEMENTATION WITH NETTLE INDUCES APOPTOSIS AND AFFECTED FOLLICULOGENESIS IN THE RABBIT OVARY **K. Kaminska[1], K. Kapusta[1], S. Palka[2], M. Kmiecik[2], J. Zubel-Lojek[3], M. Grzesiak[1]** ([1]Department of Endocrinology, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland, [2]Department of Genetics, Animal Breeding and Ethology, University of Agriculture in Krakow, Krakow, Poland, [3]Department of Animal Physiology and Endocrinology, University of Agriculture in Krakow, Krakow, Poland).

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S11.P9 THE EFFECT OF TYPE 1 DIABETES AND HIGH FAT DIET ON THE EXPRESSION OF RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS (RAGE) IN UTERUS. **K. Zglejc-Waszak[1], A. Korytko[1], J. Wojtkiewicz[1], K. Wasowicz[2], J.K. Juranek[1]** ([1]University of Warmia and Mazury in Olsztyn, School of Medicine, Collegium Medicum, Department of Human Physiology and Pathophysiology, Olsztyn, Poland, [2]University of Warmia and Mazury in Olsztyn, Faculty of Veterinary Medicine, Department of Pathophysiology, Olsztyn, Poland).

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S11.P11 IMPACT OF FETAL NUMBER ON ACUTE PHASE PROTEINS, CORTISOL AND HEMATOLOGICAL PARAMETERS IN EWES DURING THE PERIPARTURIENT PERIOD. **M. Gregula-Kania[1], U. Kosior-Korzecka[2], K. Kania[3], A. Hahaj-Siembida[1]** ([1]Institute of Animal Breeding and Biodiversity Conservation, Faculty of Animal Sciences and Bioeconomy, University of Life Sciences in Lublin, Lublin, Poland, [2]Sub-Department of Pathophysiology, Department of Preclinical Veterinary Sciences, Faculty of Veterinary Medicine, University of Life Sciences in Lublin, Lublin, Poland, [3]Department of BioPhysics, Faculty of Environmental Biology, University of Life Sciences in Lublin, Lublin, Poland).

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S11.P13 THE IMPACT OF CHEMERIN ON THE SECRETION OF CYTOKINES (IL-1β, IL-6) AND THE EXPRESSION OF CYTOKINE RECEPTORS (IL1R1, IL6R) BY THE PORCINE ENDOMETRIUM DURING THE OESTROUS CYCLE AND EARLY PREGNANCY. **G. Kopij, M. Kiezun, E. Zaobidna, K. Dobrzyn, K. Kisielewska, E. Rytelewska, M. Gudelska, K. Bors, K. Szymanska, B. Kaminska, T. Kaminski, N. Smolinska** (University of Warmia and Mazury in Olsztyn, Olsztyn, Poland).

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S11.P15 THE INFLUENCE OF KETOGENIC DIET ON THE COURSE OF GESTATIONAND BIOCHEMICAL COMPOSITION OF HIPPOCAMPAL FORMATION OF PREGNANT RATS. **Z. Rauk[1], P. Szulc[2], W. Kosiek[1], Z. Setkowicz-Janeczko[1]** ([1]Laboratory of Experimental Neuropathology, Institute of Zoology and Biomedical Research, Faculty of Biology, Jagiellonian University, Krakow, Poland, [2]Faculty of Biochemistry, Biophysics and Biotechnology, Krakow, Poland).

S11.P16 VISFATIN GENE EXPRESSION IN THE PORCINE PITUITARY GLAND DURING THE ESTROUS CYCLE AND EARLY PREGNANCY. **K. Szymanska[1], M. Kiezun[1], E. Zaobidna[1], K. Dobrzyn[1], E. Mlyczynska[2] , E. Rytelewska[1], K. Kisielewska[1], M. Gudelska[1], K. Bors[1], G. Kopij[1], B. Kaminska[1], A. Rak[2], N. Smolinska[1], T. Kaminski[1]** ([1]Department of Animal Anatomy and Physiology, Faculty of Biology and Biotechnology, University of Warmia and Mazury in Olsztyn, Olsztyn, Poland, [2]Department of Physiology and Toxicology of Reproduction, Institute of Zoology and Biomedical Research, Jagiellonian University in Krakow, Krakow, Poland).

S11.L1

EPIGENETIC MECHANISMS AND BIO-MECHANICAL CUES DRIVE CELL DIFFERENTIATION

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Multiple regulatory mechanisms interact and orchestrate a proper regulation of gene expression and spatial restriction, to allow cells to adopt distinct differentiation traits and a terminal phenotype. Changes in methylation, for instance, are among the main actors of pluripotency, and under the control of methyltransferases and Ten-eleven Translocation (TET) enzymes, add/or erase phenotype distinct methylation changes along embryo development as well as during mesenchymal to epithelial transition (MET). On the other hand, extracellular factors such as small molecules have the ability to interact with cell plasticity and to induce a transient pluripotent state that allows the direct conversion of an adult mature cell into another differentiated cell type. In addition, mechanical properties of the cellular microenvironment and 3-D rearrangement can affect both cell potency and differentiation, through dramatic effects on cytoskeleton remodelling and with the involvement of specific mechano-sensing-related pathways, such as the Hippo and the RhoGTPase, that are finely able to tune oocyte quality and developmental competence as well as plasticity and differentiation of somatic cells. Here we will discuss the involvement of epigenetic cues and bio-mechanical effector in driving cell potency and differentiation as well as in terminal cell phenotype specification.

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S11.L2

PRESENCE OF LACTOBACILLI WITHIN THE BOVINE FEMALE REPRODUCTIVE TRACT AND THEIR POSSIBLE ROLE DURING REPRODUCTIVE EVENTS

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Uterine diseases in cattle are mainly caused by pathogenic bacteria and these bacterial species have been in the focus of research and treatment over the last decades. However, commensal bacteria were also identified in the bovine reproductive tract of healthy cows by cultivation as well as by sequencing of 16S rRNA with mainly Lactobacillus spp. found in vagina and uterus. Significant changes have been observed within the uterine commensal bacterial composition during the first weeks after calving. Higher abundance of Lactobacillus spp. in healthy animals indicates an influence on reproductive events. Therefore, such strains have become of particular interest to improving the uterine health status for better fertility rates. There are several characteristics awarded to Lactobacillus spp. that explain the potential positive influence on the health of their host. Lactobacillus spp. can represent a barrier to infection by suppressing the population of bacterial pathogens through competition for nutrients and production of organic acids, hydrogen peroxide and bacteriocins lethal to pathogens. They can also protect their host from the detrimental effects of pathogens through competition for adherence to epithelial cells and the production of a protective biofilm on the epithelial cell surface. *In vitro* co-culture experiments of Lactobacillus spp. with endometrial epithelial cells have demonstrated that several Lactobacillus spp. do not affect viability of epithelial cells nor provoke a pro-inflammatory reaction by up to 96 h. Intrauterine applied Lactobacillus spp. provoke a weak immune response with a low number of immune cells invading for a short time, as well as an increased mRNA expression of some pro-inflammatory factors after 7 days. Intrauterine administered *L. buchneri* to cows with subclinical endometritis led to improved fertility rates, decreasing the number of days open or insemination attempts. Three weeks after administration, endometrial mRNA expression of several pro-inflammatory factors was lower in the *L. buchneri* group compared to the placebo group. A mixture of Lactobacillus spp. were applied intravaginal around the time of calving leading to a decreased number of cases of uterine diseases and/or better fertility rates by decreased days open. The presence of Lactobacillus spp. also did not affect sperm viability parameters. In conclusion, the data show that an intact commensal bacterial composition seems to be necessary for improved fertility rates in cattle.

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S11.L3

THE IMPACT OF ENERGY METABOLISM CHANGE IN PORCINE CUMULUS-OOCYTE COMPLEX DURING *IN VITRO* MATURATION

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In the past decade, extensive observations demonstrated that the mitochondria (MT) play a crucial role in the oocyte cytoplasm maturation, since they provide adenosine triphosphate (ATP) for fertilization and preimplantation embryo development. In turn, intracellular lipids, in both oocyte and cumulus cells, are stored mainly in lipid droplets (LD) providing energy for their normal growth and development. Thus, alterations in ovarian lipid profile can impact the cumulus-oocyte complex (COC) during its maturation. The increasing human exposure to agents capable of inducing changes in the genetic material, accumulation of endocrine active compounds (EACs) in the environment might adversely modulate mitochondrial and lipid content. Therefore, the main purpose of this research was to elucidate whether exposure of porcine COCs to selected EACs affects their energy metabolism. The COCs were isolated from healthy, medium-sized porcine follicles (4–6 mm in diameter), encapsulated in alginate beads and then cultured (3D) in the presence of vinclozolin (Vnz; a fungicide), nandrolone (Ndn; an anabolic steroid), and cyclosporin A (CsA; an immunosuppressant). After termination of culture (96 h) COCs were prepared for TEM analysis, Nile Red (NR) staining and Aligent Seahorse XFp Cell Mito Stress Test. The results demonstrated that ATP production in all experimental groups was lower compare to control. Proton leak was highest in COCs cultured with addition of Vnz. Moreover, Vnz induced non-mitochondrial respiration. TEM analysis showed modified distribution and shape of MT in COCs exposed to Ndn and Vnz - changing them from diffuse to aggregate and from spherical to elongated, respectively. It was also observed that LDs in Ndn and Vnz treated COCs were accumulated and solidified. The results of the NR analysis were consistent with the results of the TEM analyses. Concluding, the obtained results indicate a disrupting effect of Ndn and Vnz to COCs energy metabolism, which may adversely affects regulatory mechanisms of maturation and hence in porcine oocyte competence acquisition.

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S11.L4

SEX STEROID RECEPTOR AGONISTS AND ANTAGONISTS AFFECT THE EXPRESSION OF TRANSCRIPTION FACTOR FORKHEAD L2 (FOXL2) IN THE NEONATAL PORCINE OVARY

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In many mammals the formation of primordial ovarian follicles begins during fetal development and involves the breakdown of egg nests, and subsequent recruitment of pregranulosa cells. In pigs, the formation of the primordial follicle pool is completed around post-partum day 25. Once formed, some primordial follicles are recruited into the primary follicle pool. This process is characterized by differentiation of the flattened pregranulosa cells into cuboidal granulosa cells. Ovarian folliculogenesis is governed by many factors and hormones. Previously, we have demonstrated that neonatal exposure to endocrine active chemicals influenced the number of primordial and primary follicles in piglets. The main factor responsible for the regulation of granulosa cell function is the transcription factor forkhead L2 (FOXL2), which is necessary for the proper formation and activation of ovarian follicles. Thus, the objective of this study was to determine whether exposure of the neonatal pigs to testosterone propionate (TP, an androgen), flutamide (FLU, an antiandrogen), 4-*tert*-octylphenol (OP, compound with estrogenic activity), ICI 182,780 (ICI, an antiestrogen), and methoxychlor (MXC, compound with estrogenic, antiestrogenic and antiandrogenic properties) influenced ovarian *FOXL2* expression as well as the expression of its target genes, *AMH* and *CYP19A1*. Piglets were injected with TP, FLU, OP, ICI, MXC, or corn oil (control) between postnatal days 1 and 10 (n=4/each group). Ovaries were excised from the 11-day-old pigs and to assess FOXL2, AMH, and CYP19A1 expression immunohistochemistry and/or real-time PCR and Western blot were performed. FOXL2 protein was localized in stroma cells surrounding egg nests and in both pregranulosa and granulosa cells. TP, OP, and MXC increased *FOXL2* and *AMH* mRNAs, while FLU and ICI decreased *CYP19A1* mRNA. The FOXL2 protein abundance was increased in all examined groups. TP, OP, ICI, and MXC increased AMH protein abundance, while TP, FLU and OP decreased CYP19A1 protein abundance. In summary, we showed that the exposure to compounds affecting androgen and estrogen action during the neonatal window of porcine development altered *FOXL2* expression. This may, in part, explain the impaired folliculogenesis in those animals, as we previously described.

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S11.L5

PRO-APOPTOTIC EFFECT OF VASPIN ON HUMAN PLACENTA BEWO CELLS

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Vaspin, a member of adipokines was first isolated in 2005 from the visceral adipose tissue of the rat abdominal obesity model (OLETF). It belongs to the serine protease inhibitors and acts through a protein G-coupled receptor - GRP78. The expression of vaspin has been described in many tissues and organs, where it plays a pleiotropic function. Interstingly, recent literature data indicate an anti- apoptotic effect of vaspin in ovarian cells, while its role in placenta has not been explored. The aim of this study was to invastigate the effect of vaspin on placental apoptosis by studing Bcl-2, BAX, p53, caspase-8, caspase-9, caspase-3 protein expression in placental BeWo cells. Apoptosis is an essential feature of normal placental development but is exaggerated in association with placental disease. In normal pregnancy, trophoblast apoptosis increases with placental growth and advancing gestation. However, apoptosis is notably exaggerated in the pregnancy complications, hydatidiform mole, pre-eclampsia, and intra-uterine growth restriction (IUGR). Human placenta choriocarcinoma cell line BeWo (ATCC®CCL-98™) were cultured in DMEM/F12 medium with 1% FBS and vaspin at doses: 0.1, 1, 10 ng/ml for 24, 48, 72 h of apoptotic factors: Bcl-2, BAX, p53, caspase-8, caspase-9 and caspase-3 by Western blot. Statistical analysis were performed using GraphPad Prism 5 and a one-way ANOVA test ($p < 0.05$). We examined that vaspin at various doses and after different incubation times increased the expression of pro-apoptotic proteins such as: BAX, p53, caspase-8, caspase-9, caspase-3. On the other hand, with regard to the expression of the anti- apoptotic protein Bcl2, it demonstrate the opposite effect. In conclusion, our preliminary studies indicated pro- apoptotic effect of vaspin on BeWo cells. Presented data suggest that adipokine may be an important regulator of the apoptosis process, but also play crucial role as a marker and initiator of numerous pregnancy pathologies, such as preeclampsia or IUGR.

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S11.L6

RELATIVE ABUNDANCE OF APELIN RECEPTOR TRANSCRIPT IN THE PORCINE PITUITARY DURING THE ESTROUS CYCLE AND EARLY PREGNANCY

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The current knowledge on role of the adipose tissue suggests that it is also an endocrine organ. It secretes biologically active compounds, named adipokines. Previous research demonstrated an involvement of some adipokines in the proper functioning of the female reproductive system in pigs by acting at all branches of the hypothalamic-pituitary-ovarian axis. Apelin also seems to be a hormone involved in the regulation of both, the reproduction and energy homeostasis. The aim of this study was to investigate apelin receptor (*APLNR*) mRNA expression in the porcine anterior (AP) and posterior (PP) pituitary on days 2–3, 10–12, 14–16 and 17–19 of the estrous cycle, as well as on days 10–11, 12–13, 15–16 and 27–28 of gestation. Expression of *APLNR* mRNA was evaluated using real-time PCR method. Data were analysed using one-way ANOVA. In the AP, during the estrous cycle, the relative abundance of *APLNR* mRNA transcript was higher on days 2–3, when compared to days 14–16. During early pregnancy, the higher mRNA content was observed on days 15–16, whereas lower on days 27–28. Comparing early gestation stages and days 10–12 of the estrous cycle, there were no significant changes in *APLNR* mRNA content between the cycle and early pregnancy. In the case of PP, relative abundance of *APLNR* mRNA was higher on days 10–12 and 17–19, when compared to days 2–3 of the estrous cycle. During early pregnancy period, the highest relative abundance of *APLNR* transcript was observed on days 27–28. Comparison of the cycle and early pregnancy revealed increased *APLNR* mRNA level on days 27–28 of pregnancy, when compared to days 10–12 of the cycle. Our studies demonstrated the presence of *APLNR* mRNA in the both porcine pituitary lobes. Moreover, the provided data showed that the level of *APLNR* transcript fluctuates during the estrous cycle and early pregnancy, which suggests that porcine pituitary may show various sensitivity to the apelin action throughout the estrous cycle and early pregnancy.

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S11.L7

VISFATIN/NAMPT EXPRESSION IN PORCINE CORPUS LUTEUM DURING THE OESTROUS CYCLE AND EARLY PREGNANCY. EFFECT OF LUTEINIZING HORMONE AND PROGESTERONE ON VISFATIN PROTEIN LEVEL

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Visfatin, also termed nicotinamide phosphoribosyltransferase (NAMPT), is the adipose tissue derived hormone with a mimetic effect to insulin, responsible for maintaining energy homeostasis, regulation of angiogenesis and inflammation. Last studies documented visfatin effect on female reproduction both at central and gonadal level; its expression was noted in the human, mouse, chicken, bovine, and hen ovarian follicular cells. Moreover, it was shown that visfatin enhanced basal and IGF1-induced steroid hormone secretion by the bovine granulosa cells, however the data on its role in the porcine reproduction are still limited. The aim of the study was to determine the expression of visfatin in the porcine corpus luteum (CL) during the oestrous cycle and early pregnancy, and then examine the direct effect of luteinizing hormone (LH) and progesterone (P_4) on visfatin protein expression in luteal cells. Luteal tissue samples were harvested from gilts on days 2–3, 10–12, and 14–16 of the oestrous cycle, and days 10–11, 12–13, 15–16, 27–28 of pregnancy (n=6 per group). The expression of the visfatin gene (NAMPT) was measured by quantitative real time PCR, while the protein level by Western blot. Next, the ovaries of the gilts (n=5 per group) on days 2–3, 10–12 and 14–16 of the oestrous cycle were used to determine the impact of hormones: LH (100 ng/ml) and P_4 (10, 100, 1000 nM) on visfatin protein abundance. Differences between groups were analysed by one-way ANOVA followed by Tukey's *post hoc* test. We observed the highest expression of NAMPT in CL collected on days 2–3 and 14–16 of the oestrous cycle, and days 12–13 to 15–16 of pregnancy. Conversely, at the protein level, the greatest expression of visfatin was found on days 10–12 of the oestrous cycle and on days 15–16 to 27–28 of pregnancy. Additionally, we noticed that both LH and P4 increased significantly visfatin protein abundance: LH on days 2–3 and 14–16, P_4 on days 2–3 and 10–12 of the oestrous cycle. Our results indicates that visfatin expression in luteal cells changed during the oestrous cycle and early pregnancy; moreover both LH and P_4 increased luteal expression of visfatin. In conclusion, our preliminary study indicates that visfatin is the adipokine which can be a new potential regulator of CL function in pigs.

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S11.L8

CHEMERIN AS A HORMONE MODULATING ENDOMETRIAL REMODELING IN PIGS DURING THE PERI-IMPLANTATION PERIOD: AN *IN VITRO* STUDY

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The implantation in pigs is superficial and non-invasive, including phases of apposition, adhesion and attachment of conceptuses to the endometrial surface. This process is related to the remodeling of connective tissue and the extracellular matrix. Matrix metalloproteinases (MMPs) are the proteolytic enzymes that degrade the extracellular matrix and are essential for the tissue remodeling processes. In turn, the tissue inhibitors of metalloproteinases (TIMPs) are important regulators of MMPs activity. According to our recent studies, chemerin - a hormone which participates in the regulation of energy homeostasis and the immune response - may also be involved in the regulation of porcine uterus functioning. Hence, the aim of this study was to investigate the *in vitro* effect of chemerin, at the physiological concentrations, on the protein abundance of crucial metalloproteinases (matrix metallopeptidase 2 (MMP-2); matrix metallopeptidase 9 (MMP-9)) and tissue inhibitors of metalloproteinases (tissue inhibitor of metalloproteinases 1 (TIMP-1); tissue inhibitor of metalloproteinases 2, (TIMP-2)) in the porcine endometrium during the peri-implantation period. Endometrial tissue explants (n=5 per period) were harvested from sows during the beginning of implantation (days 15 to 16 of pregnancy) and the end of implantation (days 27 to 28 of pregnancy). Tissue explants were preincubated for 2 h and then incubated for 24 h with chemerin (at the doses of 100 and 200 ng/mL) or medium without any treatment (controls). The protein abundance of the target proteins was determined by Western Blot. The results were analyzed by one-way analysis of variance followed by Duncan's post hoc test. The study revealed that chemerin (at both studied doses) enhanced the protein abundance of TIMP-1 and TIMP-2, and decreased the abundance of MMP-2 and MMP-9 during the beginning of implantation. In turn, the opposite results were obtained during the end of implantation, when chemerin (100 and 200 ng/mL) enhanced the protein abundance of MMPs, and decreased the abundance of TIMPs. Therefore, the obtained results confirm that chemerin, at physiological concentrations, may affect endometrial remodeling in pigs during the peri-implantation period.

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S11.L9

DECORIN AND DERMATOPONTIN DIFFERENTIALLY AFFECT CARUNCULAR EPITHELIAL CELL ADHESION IN PREGNANT COWS

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Proper placental development and maturation depend on cell-cell and cell-ECM interactions mediated by ECM proteins, which include glycoproteins and proteoglycans. Biological properties of ECM proteins, whose profiles dynamically change during pregnancy, allow them to play a key role in the processes of cell adhesion and invasion into the endometrium during placentation and separation of fetal membranes postpartum. Among them decorin (DCN) and dermatopontin (DPT) seem to play a significant role in the functioning of the placenta. They interact with each other and their presence was confirmed in placental tissues of cows during pregnancy. Both DCN and DPT are small protein molecules considered to have a role in the formation of the extracellular matrix and cell adhesion. The aim of the study was to evaluate the effect of DCN and DPT on the adhesion of caruncular epithelial cells derived from cows during early-mid pregnancy. Caruncular epithelial cells were isolated from pregnant cows (2^{nd}, n=2; 4^{th} month, n=2) and used for the examination of the influence of DCN 10 (μg/mL) and DPT (5, 50 and 100 ng/mL) on cell adhesion. The adhesion of cells to fibronectin was measured spectrophotometrically. The MTT assay was used to evaluate the effect of selected proteins on the viability of placental cells. DCN limited the adhesion of cells in the 2^{nd} month of pregnancy, whereas DPT was shown to have pro-adhesive activity both in the 2^{nd} and 4^{th} month of pregnancy. The results obtained here indicate that both proteins, showing the opposite effect, may influence cell adhesion during attachment and most probably also detachment of bovine placenta. Further studies on mechanisms of action of DPT and DCN in bovine placenta are necessary.

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S11.L10

THE ELECTROMAGNETIC FIELD (EMF) RADIATION INDUCES TRANSCRIPTOMIC ALTERATIONS IN PIG MYOMETRIUM DURING THE PERI-IMPLANTATION PERIOD

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There are documented effects of the electromagnetic field (EMF) radiation on physiological processes in mammals including gametes production and regulation of reproductive cycle, the function of the uterus, and pregnancy outcome. However, the molecular background of the EMF-induced alterations remains not sufficiently established. In this study, the myometrial slices obtained from pigs during the peri-implantation period (days 15–16 of pregnancy, n=5) were exposed to an EMF at a frequency of 50 Hz within a short-term duration (2 h) for further transcriptomic profiling using a next-generation sequencing (NGS) method followed by validation procedure using real-time PCR. As result, the EMF radiation affected the expression of 215 transcript active regions (TARs), and among them, the assigned gene name possessed 90 ones (differentially expressed genes, DEGs). Among the evaluated DEGs there were genes encoding interleukin-15 (IL15), tumor necrosis factor (TNF), prodynorphin (PDYN), homeobox-D13 (HOXD13), signal transducer and activator of transcription-5A (STAT5A), vascular cell adhesion molecule-1 (VCAM1), and early growth response protein-2 (EGR2). The evaluated DEGs are categorized mostly to gene ontology biological processes terms connected with defense and immune responses, and secretion and export. Mostly enriched KEGG pathways were TNF signaling pathway, and regulation of IFNA signaling, and there was found REACTOME interferon alpha/beta signaling pathway. In conclusion, the EMF within a short duration of treatment mostly affects genes involved in defense and immune responses to different factors in the myometrium, which can affect the proper course of molecular events accompanying the peri-implantation period.

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S11.L11

PPAR-GAMMA REGULATES THE EXPRESSION OF GENES IN THE PORCINE INFLAMED ENDOMETRIUM DURING FOLLICULAR PHASE OF THE ESTROUS CYCLE

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Peroxisome proliferator-activated receptors (PPARs) belong to a ligand-dependent nuclear receptor family. Numerous studies have revealed the presence and significance of different PPAR isoforms in the reproductive system. In this study, we determine the effect of PPAR gamma ligands - agonists: 15d-prostaglandin J2 (PGJ_2) or pioglitazone (P) and antagonist: T0070907 (T) on a global transcriptome profile in the porcine LPS-stimulated endometrium, incubated *in vitro*. To identify expression profiles of endometrial genes the RNA-Seq was performed on the NovaSeq 6000 Illumina platform. To identify differentially expressed genes (DEGs) we applied 74 Cufflinks method. The final results constituted DEGs, significantly confirmed by statistical test (adjusted p-value <0.05). Enrichment gene ontology and pathway analysis were performed with use of gProfileR based on Gene Ontology (GO), and Kyoto Encyclopaedia of Genes and Genomes (KEGG) databases. Within all experimental comparisons we detected 187, 476, 557 and 230 DEGs for PGJ_2 vs. LPS, P vs. LPS, T vs. LPS and LPS vs. control, respectively. The results revealed the engagement of PPARγ ligands in various immunological processes, including IL-1β production, IL-17 signalling pathway, defence response. Most of the described DEGs have been assigned to p53 signalling pathway. Moreover, the study provide relevant finding related to the ability of pioglitazone to regulate the expression of genes (GADD45β, CDK1, CCNG1, CCNA1) controlling DNA damage repair upon stress-triggered conditions. These numerous results provide a basis for further studies on PPARγ mechanisms controlling reproductive functions during inflammation.

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S11.L12

KISS-1/GPR54 MRNA EXPRESSION AND THE RELATIONSHIP BETWEEN KISS-10 AND LUTEINIZING HORMONE SECRETION IN PITUITARY GLAND OF CYCLIC AND POLYCYSTIC OVARY SYNDROME-AFFECTED SOWS

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The aim of study was to compare the effect of kisspeptin-10 (KiSS-10) on *in vitro* luteinizing hormone (LH) secretion by pituitary cells of cyclic sows (n=10) and sows with follicular cysts (n=12). In addition, the concentration of KiSS-10 in the blood plasma and pituitary *kiss-1/gpr54* mRNA expression in both groups of animals were determined. Pituitary cells were cultured in McCoy 5A medium without hormones (the negative control), with GnRH (4×10^{-9} M; the positive control), with KISS-10 (10^{-11}–10^{-7} M) or with both GnRH (4×10^{-9} M) and KISS-10 (10^{-11}–10^{-7} M). After 2, 6, 12, 18, 24 and 30 hours of the experiment, the media for LH analysis were collected and the proliferation index (PI) of the control cells and those treated with KISS-10 (10^{-11}–10^{-7} M) or both GnRH (4×10^{-9} M) and KiSS-10 (10^{-11}–10^{-7} M) was determined. KiSS-10 in the blood plasma and LH in the culture medium were determined by ELISA assays using species-specific antibodies. The obtained results show that plasma KiSS-10 concentration was higher in cyclic sows compared to those polycystic ovary syndrome (PCOS)-affected. Pituitary *kiss-1 mRNA* expression was lower whereas *gpr54* mRNA expression was higher in sows with follicular cysts than in cyclic sows. The *in vitro* effect of KiSS-10 on pituitary cells isolated from cyclic sows and sows with follicular cysts depended on the KiSS-10 concentration used. In the 10^{-9}–10^{-7} M concentration, KiSS-10 exerted a stimulatory effect on LH secretion *in vitro* in both groups, with the highest LH secretion observed under the influence of 10^{-8} M of KiSS-10. Despite of high positive correlation between the concentration of KiSS-10 and LH secretion both in cultures without GnRH and with GnRH, the level of KiSS-10-stimulated LH secretion was significantly lower in cells isolated from PCOS-affected sows than from cyclic sows.

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S11.L13

KISS-INDUCED ALTERNATIONS IN *PRL* MRNA TRANSCRIPT ABUNDANCE IN PORCINE PITUITARY CELLS DURING THE ESTROUS CYCLE

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Kisspeptins (KISS) affect the synthesis and secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) and act as the principal positive regulators of female reproductive axis. The question arises if KISS may also contribute to the regulation of prolactin (PRL) synthesis in the pituitary gland. The study aims to determine the *in vitro* effect of KISS on *PRL* mRNA transcript abundance in pituitary glands collected from pigs on days 2–3, 10–12, 15–16, and 19–20 of the estrous cycle. The pituitary cells were cultured *in vitro* and treated with KISS (10^{-6} M, 10^{-7} M) for four hours. The abundance of the *PRL* mRNA transcript was examined by real-time PCR. The expression of the *PRL* mRNA was elevated by the KISS at doses 10^{-6} M and 10^{-7} M in porcine pituitary cells collected during the early-luteal (days 2–3) and mid-luteal (days 10–12) phase of the estrous cycle. Moreover, the stimulatory effect of the KISS at a dose 10^{-6} M on PRL mRNA transcript abundance was observed during luteolysis and follicular phase of the estrous cycle. In conclusion, KISS may be recognized as a modulator of PRL synthesis in porcine pituitary cells during the estrous cycle.

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S11.L14

EFFECTS OF LONG-TERM CHANGES IN BODY WEIGHT ON THE ABILITY OF RESISTIN TO MODULATE REPRODUCTIVE HORMONES IN SHEEP

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Adipokines are hormones that are mainly produced by white adipose tissue, an endocrine organ involved in energy homeostasis. They play important roles in the regulation of lipid and glucose metabolism, inflammation and immune disorders. New roles for adipokines have recently emerged in the field of fertility and reproduction, particularly since leptin was described. Indeed, the adipokine resistin (RSTN) is able to regulate the functions of male and female gonads and of the hypothalamic-pituitary axis in primates. Fertility is strongly dependent on metabolic status of the organism; thus, matching reproductive activity to nutritional reserves is fundamental to the survival of a species. Both, long-term undernutrition and overnutrition influence reproductive potential and this linkage is mediated in part through the action of two important adipokines, leptin and resistin. In the current study, we manipulated the diet of ewes over 4 months to produce either a thin (Lean) or fat (Fat) body condition and investigated how resistin affects reproductive and metabolic status under low (thin sheep) or high (fat sheep) circulating levels of leptin. Twenty ovariectomized ewes with estrogen replacement were assigned to one of four groups (n=5 per group): Lean-S (n=5) and Fat-S (n=5) groups which were treated with saline and Lean-R (n=5) and Fat-R (n=5) groups treated intravenously one time with recombinant bovine resistin (rbresistin; 5.0 µg/kg BW). Jugular blood samples (5 mL) were collected at 10-min intervals over 4 h *via* indwelling catheters to establish reproductive hormone status before and after resistin challenge. Plasma was assayed for LH, FSH, PRL. Resistin decreased ($P < 0.001$) plasma LH in both Lean and Fat groups relative to saline controls, with effects on both amplitude and frequency of pulses. Varying effects of resistin were also observed on both plasma FSH and prolactin and were dependent upon nutritional status. Results demonstrate that resistin is intimately involved in the regulation of reproductive hormone secretion in the female and these effects are modulated by extremes in metabolic status (lean vs fat) that can contribute to ovarian pathophysiology. RSTN appears to be another adipokine, in addition to leptin, that is involved in the regulation of reproductive processes in sheep. RSTN regulates the release of reproductive hormones from the pituitary. The study needs further investigation since resistin is able to modulate LH pulse characteristics, it can be speculated that RSTN can work on hypothalamus level in sheep.

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S11.L15

VASPIN (VISCERAL ADIPOSE TISSUE-DERIVED SERINE PROTEASE INHIBITOR) ENHANCED PORCINE OOCYTES *IN VITRO* MATURATION *VIA* MAP3/1 AND PRKAA1 KINASES PATHWAYS

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Oocyte maturation is a critical stage of embryo production in mammals. Adipokines, hormones produced by adipose tissues, are important regulators of whole-body physiology including reproduction. Our previous research showed that adipokine vaspin regulates porcine ovarian follicle's function e.g., stimulates steroidogenesis, proliferation and inhibits apoptosis. Hence, in the present study, we measured porcine cumulus-oocyte complexes (COCs) mRNA and protein expression of vaspin and its receptor 78-kDa glucose-regulated (GRP78) before and after oocytes *in vitro* maturation (IVM) by real-time PCR and Western blot. Moreover, we investigated vaspin/GRP78 localization in COCs by immunofluorescence and the effects of vaspin on oocyte IVM, as well as the molecular mechanism of its action. Porcine COCs were matured in vitro for 22 h or 44 h with vaspin (1 ng/mL) and then nuclear maturation assessed by Hoechst 33342 or DAPI staining and additionally by the measurement of progesterone (P4) level in the maturation medium and mitogen activated kinase (MAP3/1), as well as AMP activated kinase (PRKAA1) phosphorylation. As first, we demonstrated that vaspin and GRP78 protein expression increased in oocytes and cumulus cells after IVM. Furthermore, vaspin stimulated porcine oocyte IVM and P4 concentration, as well as MAP3/1 phosphorylation, with opposite effects on PRKAA1. Molecular mechanism was studied using pharmacological inhibitors of MAP3/1 (PD98059) and PRKAA1 (compound C); we investigated, that the effect of vaspin was reversed to the control level in all studied parameters. To conclude, vaspin, by improving *in vitro* oocyte maturation *via* MAP3/1 and PRKAA1 kinase pathways, can be a new factor to accomplish in vitro fertilization protocols and production of farm animals.

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S11.P1

ELECTROMAGNETIC FIELD OF EXTREMELY LOW FREQUENCY INDUCES CHANGES IN THE RELATIVE ABUNDANCE OF *HSD17B2* AND *VDR* IN THE ENDOMETRIUM OF PIGS DURING THE PERI-IMPLANTATION PERIOD

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The extremely low-frequency electromagnetic field (EMF) originating from human-made sources becomes a part of the environment that may influence female reproduction. Our past studies indicate that the EMF affects the synthesis of androgens and estrogens in the uterus during the peri-implantation period. The goal of this study was to determine if the EMF (50 Hz, 2 h treatment duration) induces changes in the expression of hydroxysteroid 17β dehydrogenase 2 (*HSD17B2*) that metabolizes potent estradiol-17β (E_2) to weakly estrogenic estrone (E_1). It was also documented that vitamin D acting *via* vitamin D receptor (*VDR*) affects the synthesis of estrogen in the uterus. For this reason, this study aimed also to determine the effect of the EMF radiation on *VDR* mRNA transcript abundance in endometrial slices of pigs during the peri-implantation period (n=5). The next-generation sequencing (NGS) provided evidences that the expression of endometrial *HSD17B2* and *VDR* mRNA transcripts alter in the response to EMF radiation. To confirm the NGS results, the *HSD17B2 and VDR* mRNA transcript abundances were determined with one-step real-time PCR with TaqMan probes. The results of this study confirmed that endometrial slices exposed *in vitro* to the short-term duration of EMF treatment express an increased abundance of *VDR* and a decreased *HSD17B2* mRNA transcript abundance. The observed alterations in *HSD17B2* and *VDR* expression in the endometrium may lead to hyper-concentration of estrogens in the intra-uterine environment and induce cytotoxic effects on embryos during the peri-implantation period. These results could become a basis for further studies explaining the consequences of EMF treatment in the reproductive system.

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S11.P2

EFFECT OF VITAMIN D_3 ADMINISTRATION ON GLUCOSE AND INSULIN LEVEL, AND HOMA-IR INDEX IN RATS WITH LETROZOLE-INDUCED POLYCYSTIC OVARY SYNDROME

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Polycystic ovary syndrome (PCOS) is one of the most common endocrinopathies in women of reproductive age. It is characterized by hyperandrogenism, anovulation, ovarian cysts, and metabolic disorders, such as insulin resistance and hyperinsulinemia. Decreased vitamin D_3 (VD) level was also found among PCOS patients and beneficial effects of VD in PCOS treatment were reported. The aim of the present study was to examine the effect of VD administration on plasma glucose and insulin concentration, and homeostatic model assessment for insulin resistance (HOMA-IR) in PCOS-induced rats. The research was conducted on rats divided into four experimental groups (n=8 per each group): 1) control (C); 2) supplemented with VD (VD; 500IU daily); 3) treated with letrozole (L; 1 mg/kg body weight/daily) and 4) treated with letrozole and VD together (L+VD). After blood collection, total plasma VD, fasting glucose (FG) and insulin (FINS) concentrations were assessed and HOMA-IR was calculated as follow: FG (mmol/l) × FINS (μU/ml)/22.5. VD level was significantly higher in VD-supplemented group, while lower in the group with induced PCOS, when compared to the C group. In the L+VD group, the VD concentration markedly increased in comparison to the L group. Glucose and insulin concentrations were the highest in rats with PCOS, whereas VD supplementation (L+VD group) showed the tendency to decreased them. Similarly, HOMA-IR was significantly greater in the L group when compared to the C group with tendency to decreasing in the L+VD group. Our results obtained on rat PCOS model indicate that VD supplementation has a promising potential to improve metabolic parameters in PCOS, including insulin sensitivity. However, further studies on adequate VD dose are required.

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S11.P3

PROTEIN EXPRESSION AND IMMUNOLOCALISATION OF VASPIN AND GRP78 RECEPTOR IN HUMAN PLACENTA OF INTRAUTERINE GROWTH RESTRICTION. PRELIMINARY DATA

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Intrauterine growth restriction (IUGR) is a serious pathological complication associated with compromised fetal development during pregnancy. IUGR is often linked with impaired placental development, structure and morphology, which in turn alter placental function and capacity of delivering nutrients to the fetus. Various factors including adipokines influence transfer of substances between maternal and fetal circulations. Vaspin (visceral adipose tissue-derived serine protease inhibitor) is known regulator of energy balance, it decreases food intake, promotes preadipocytes differentiation, improves insulin sensitivity and glucose tolerance, and plays an important role in female reproduction. The aim of the present study was to investigate protein expression and immunolocalisation of vaspin and its receptor GRP78 in the maternal and fetal parts of the human placenta of healthy pregnant women (control) and with IUGR. Placental tissue was collected in a gynaecological hospital in Krakow, Department of Gynecological Endocrinology, Jagiellonian University Medical College, Poland, where the clinical information on pregnancy outcomes was obtained. Western Blot and immunohistochemistry methods were used to analyze vaspin and GRP78 expression. Statistical analysis were carried out in GraphPad Prism 5 and a one-way ANOVA test ($p > 0.05$). We observed that protein expression of both vaspin and GRP78 significantly decreased in the fetal part of placenta with IUGR compared to control. Immunohistochemical localization of vaspin revealed its presence in both control and IGUR placenta. In control, positive signal of strong intensity was present in maternal plate, syncytiotrofoblast and fetal plate. In IGUR, the immunosignal was the weakest in fetal plate. Immunosignal for GRP78 was revealed in both control and IGUR placenta, however in control, GRP78 showed moderate signal intensity in all placenta parts when compared to IGUR placenta. In conclusion, our study for the first time showed the immunoexpression and immunolocalisation of vaspin and GRP78 in the maternal and fetal parts of placentas from healthy and complicated by IUGR pregnancies, indicating vaspin as a new regulator in placenta cells. Interesting, protein expression of vaspin/GRP78 was significantly lower in the placenta of IGUR. Future studies will be necessary for understanding the role of vaspin on placenta physiology providing new insights into the pathology of IUGR.

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S11.P4

PROTEOMIC ANALYSIS OF PORCINE CORPUS LUTEUM DURING THE ESTROUS CYCLE: EFFECTS OF PPAR-GAMMA LIGANDS

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The corpus luteum (CL) is an endocrine gland present in the ovary of mature females during the estrous cycle as well as pregnancy. There is evidence indicating the relationship between secretory function of the CL and peroxisome proliferator-activated receptors (PPARs). In this study, we investigate the impact of PPARγ ligands on the proteomic profile of the CL during the mid-luteal phase (days 10–12) and late-luteal phase (days 14–16) of the estrous cycle. The CL slices were incubated *in vitro* for 6 h in the presence of PPARγ ligands (agonist pioglitazone, antagonist T0070907) or without ligands (control; n=4 for each group). Global proteomic analysis was performed by TMT-based LC MS/MS method. We identified in total 586 proteins in the pig's corpus luteum. Comparative proteomics analysis indicated that 7 various proteins were differentially regulated (DRPs, significantly confirmed by Kruskal-Wallis one-way analysis of variance, adjusted p-value <0.05) in the CL tissue treated with PPAR ligands. In the mid-luteal phase one protein, CAND1, was downregulated after T0070907 treatment. In the group of the upregulated DRPs in the late-luteal phase of the CL treated with pioglitazone we identified: SPTAN1, GOLGB1, TP53BP1, MATR3, RRBP1 and SRRT. Three of them - SPTAN1, GOLGB1 and TP53BP1, were also upregulated in the CL in the late-luteal phase treated with T0070907. Interestingly, CAND1 and RRBP1 are a potential prognostic biomarkers in various types of cancers, due to their involvement in tumor formation and progression. Moreover, the mid-luteal phase control vs. late-luteal phase control comparison analysis showed that certain proteins constitute a specific proteomic signature for each of the examined phases, i.e., 23 and 28 proteins for the mid- and late-luteal phase, respectively. These results provide a basis for further research on the influence of PPARγ ligands on the expression of tumor biomarkers.

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S11.P5

TRANSCRIPTOMIC PROFILE OF OVIDUCTAL ISTHMUS IN PIGS ON DAYS 2 TO 3 OF PREGNANCY

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The proper activity of oviducts is crucial for fertilization, embryo development and its transfer to the uterus. It was hypothesized that the presence of embryos in the pig oviducts may evoke alterations in transcriptomic profile of oviductal isthmus. The transcriptomic profile of oviductal isthmus was determined in pigs on days 2–3 of pregnancy and compared with the transcriptome of the tissue during days 2–3 of the estrous cycle. The porcine (V2) expression microarrays 8×60K were used. The analysis indicated 1.91% differentially expressed genes (DEGs) (P ≤0.05; Fold-change ≥2.0) and 32.78% of them were up-regulated. Up-regulated DEGs were grouped to gene ontologies (GO) and categorized into functional pathways. Analysis of the relationships among DEGs in isthmus on days 2–3 of pregnancy showed that altered genes are mainly involved in the regulation of endocrine and immune functions, signal transduction and molecule interaction. The largest amount of DEGs was involved in environmental information processing. The presence of embryos in the oviduct induces alterations in transcriptomic profile of pigs oviductal isthmus.

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S11.P6

THE EFFECT OF SATURATED FATTY ACIDS ON GNRH-INDUCED GONADOTROPIN SECRETION FROM ANTERIOR PITUITARY CELLS OF PUBESCENT EWE LAMBS

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Recently we have shown that the pathologically changed pattern of gonadotropin secretion, responsible for ovulation disorders in fatty ewes, results from the prolonged increase in leptin concentration as well as from diminution of leptin receptors (OB-Rb and OB-Ra) mRNA expression in anterior pituitary cells. Leptin acting peripherally reduces the secretion of insulin - the potent inhibitor of lipolysis. Consequently, the increment in plasma fatty acids level is observed. We also found that in ewe lambs born to obese sheep carrying twins or triplets, high plasma level of saturated fatty acids (SFA) was in positive correlation with the delay in puberty. The relationship between SFA and gonadotropin secretion from the ovine pituitary cells in pubescent ewe lambs is not clear, we resolved to study the effect of SFA on LH and FSH secretion stimulated with GnRH. Moreover, leptin action on gonadotropin secretion in ewes is mediated by nitric oxide. In our study we analysed SFA effect on NO release and also the correlation between gonadotropins and NO under the influence of saturated fatty acid. Pituitary glands were isolated from 7 months old ewe lambs. Pituitary cells were cultured in McCoy 5A medium without GnRH and SFA (negative control), with GnRH only (positive control), with GnRH and 10^{-9}–10^{-3} M/l of the butyric (C4:0), caprylic (C8:0), lauric (C12:0), palmitic (C16:0) or stearic acid (C18:0), or with GnRH and 10^{-9}–10^{-3} M/l of the aforementioned SFA with L-arginine or L-NAME. After 2 or 6 hours of exposure to SFA followed by 2, 6, 12, 18, 24 or 30 h incubation, the media for LH and FSH analysis were collected. Concurrently, NO release and the proliferation index of control and treated cells were determined. There was found that all used SFA reduce GnRH-induced LH and FSH secretion from pituitary cells *in vitro*. The most significant ($P \leq 0.05$) suppressive effect was observed after 6 h exposure of cells to 10^{-3} M/l of caprylic acid, 10^{-4} M/l of palmitic acid and 10^{-4} M/l of stearic acid compared to positive control. SFA did not change significantly NO release. There was no correlation between gonadotropin secretion and NO release under the influence of SFA.

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S11.P7

DIETARY SUPPLEMENTATION WITH NETTLE INDUCES APOPTOSIS AND AFFECTED FOLLICULOGENESIS IN THE RABBIT OVARY

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There is a growing interest in the use of herbs as a part of complementary medicine in the treatment of reproductive disorders in women. Among a plethora of medical plants, special attention has been paid to nettle (*Urtica dioica L.*), which was found to regulate menstrual cycles in women with polycystic ovary syndrome. However, the cellular and molecular mechanism of its action in the ovary is still unclear. To gain insight into this, we examined the effect of nettle on follicle formation, ovarian cell proliferation and apoptosis, and steroid concentrations in the plasma of juvenile rabbits. Animals were divided into two groups (n=10 per each group) and fed with control or 1% nettle-supplemented pellets from 5 to 12 weeks of age. Just after slaughter, one ovary of each rabbit was fixed in 10% buffered formalin for histology, immunohistochemical localization of proliferating cell nuclear antigen (PCNA) and TUNEL assay, while contralateral ovaries were snap frozen for Western blot analysis of PCNA and caspases-9, -8 and -3 protein abundances. Blood samples were collected for the assessment of progesterone, testosterone and estradiol concentrations. The addition of nettle decreased the numbers of primordial (P=0.015) and early antral (P=0.02) follicles and increased the number of primary (P=0.04) ones when compared with the control group. Furthermore, dietary supplementation with nettle resulted in an increased (P=0.026) number of atretic follicles among the secondary follicles class that was also confirmed by TUNEL assay. Results from Western blot analysis showed the induction of apoptosis by nettle through activation of caspase-9 (P=0.047), caspase-8 (P = 0.022) and caspase-3 (P = 0.004), and no effect on proliferation marked by unchanged PCNA protein abundance. The addition of nettle to the diet did not affect plasma steroid concentrations. In conclusion, nettle affected follicle development in the juvenile rabbit ovary in a stage specific manner; it seems to accelerate the initial recruitment of primordial follicles to growth and increase the atresia of secondary follicles. These effects are probably related to changes at the cellular level due to induction of apoptosis through caspase-mediated routes.

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S11.P8

CHEMERIN IMPACT ON DIFFERENTIALLY EXPRESSED GENES IN THE ENDOMETRIAL TRANSCRIPTOME OF PIGS DURING PERIIMPLANTATION PERIOD

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Chemerin (CHEM) is one of many biologically active proteins secreted by the adipose tissue, involved in the regulation of the energy homeostasis of the organism. In the present study, RNA-Seq was performed to investigate the expression of protein-coding (mRNAs) transcripts in the *in vitro* cultured porcine endometrial slices collected during implantation (days 15 to 16 of gestation) exposed to CHEM (400 ng/ml). To identify the expression profiles of the treated tissues, the cDNA libraries were performed by TruSeq Stranded Total RNA with Ribo-Zero H/M/R Kit (Illumina, San Diego, USA) and the transcriptomes high-throughput sequencing was performed on the Illumina NovaSeq 6000 platform (Illumina, San Diego, USA). All reads were trimmed to equal length (120 bp) and mapped to the pig reference genome with ENSEMBL annotation (Sscrofa11.1.99) using the STAR mapper v. 2.7.1a. To identify the differentially expressed genes (DEGs), we applied the DESeq2 method with correction of batch effect using Surrogate Variable Analysis library. In the current study, among all 130 DEGs, 58 were up-regulated and 72 were down-regulated in the CHEM-treated group. DEGs were assigned to 73 functional annotations. The products of above genes take part in many processes, important for the implantation, such as intense tissue remodeling, cell adhesion, angiogenesis, immune response and steroidogenesis. CHEM affects the transcriptomic profile of the porcine endometrium, and in consequence, may influence a proper course of gestation and embryo development.

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S11.P9

THE EFFECT OF TYPE 1 DIABETES AND HIGH FAT DIET ON THE EXPRESSION OF RECEPTOR FOR ADVANCED GLYCATION END-PRODUCTS (RAGE) IN UTERUS

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The uterus is an essential organ for reproduction in mammals. A growing body of literature has shown that diabetes mellitus (DM) and high-fat diet (HFD) affect female reproductive function. Moreover, DM and HFD is associated with a chronic low-grade inflammatory state that is involved in the development of associated metabolic complications. We hypothetize that hyperglycemic and high fat milieu may active Advanced Glycation End-Products (AGEs) molecular pathway in mouse uterus. Receptor for Advanced Glycation End-products (RAGE) is involved in multiple processes related to host immunity, vascular regulation, and inflammatory damage in various disease states. Moreover, RAGE is expressed in nearly all tissues in mammals, with large quantities in lungs. The aim of the study was to determine the expression of RAGE protein in uterine tissues harvested from female mice with DM 1 (intraperitoneal injection of 50 mg/kg streptozotocin diluted in PBS for 5 days; n=5) and female mice fed HFD (ssniff EF R/M D12331 mod. - Surwit, ssniff Spezialdiaeten GmbH, Soest, Germany; n=5) or normal diet a*d libitum* for 32 weeks (Labofeed B, Morawski, Poland; n=5). The expression of RAGE was estimated using immunohistochemical (IHC) staining. The presence and intracellular localization of RAGE protein in luminal epithelial, stromal, glandular epithelium and myometrium cells was confirmed. The highest expression of RAGE was observed in uterine tissues of DM 1 mice ($P \leq 0.05$). Moreover, myometrial expression of RAGE was increased in HFD in comparison to control group ($P \leq 0.05$). These data suggest the presence of an altered uterine environment in females with DM 1 and HFD and indicate that elevated uterine level of RAGE may detrimentally impact endometrial and myometrial function during estrous cycle. We might speculate that DM 1 and HFD could modulate local immune system and activate the AGE-RAGE signaling pathway in uterine tissues during estrous cycle.

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S11.P10

AQUAPORINS EXPRESSION IN REPRODUCTIVE TRACT OF THE BULL (BOS TAURUS) CHANGES WITH SEXUAL MATURITY. PRELIMINARY STUDY

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Aquaporins (AQPs) also known as water channels (WCPs) are small (28-37 kDa), transmembrane, hydrophobic proteins, that facilitate the transport of water and other small molecules. To date, 13 aquaporins (AQP0-AQP12) have been discovered in mammals, and their presence has been found in a wide range of cell types that build the whole body. Almost all AQPs, except AQP6 and AQP12, are expressed in the male reproductive organs (testis, epididymis, vas deferens) and sperm. Numerous studies have suggested that these proteins are involved in a number of processes responsible for the proper functioning of the male reproductive system and the production of reproductive cells. Reproduction methods are associated with a constant need to search for new factors that not only significantly affect reproductive processes, but also create new possibilities in the assessment of male reproductive potential. Owing to the potential importance of AQPs in the development, maturation and function of male germ cells and in the production of high-quality semen, we have attempted to identify and analyze the expression of AQPs in the male reproductive system of cattle. The experiment is conducted on the Polish male Holstein-Friesian, black and white animals. The study is carried out on the bovine tissues of the male reproductive tract. The tissue samples are collected from three age groups of animals: (i) calves aged 5 to 7 weeks; (ii) young cattle aged 5 to 6 months and (iii) adult bulls aged 1–3 years. To determine the immunolocalization and immunoexpression of AQPs immunohistochemistry and Western blotting are used. So far, it has been revealed that in AQP1 is found in endothelial cells of blood vessels in the bovine testis. On the basis of our preliminary studies, it has been shown that AQP3, AQP7, AQP8 and AQP9 are located within the seminiferous tubules epithelium in cattle. Moreover, expression of AQP3 and AQP7 increase with the age in the bovine testis. The obtained preliminary results seem to be very promising and suggest that AQPs are involved in the proper development of organs and the course of reproductive processes in male cattle.

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S11.P11

IMPACT OF FETAL NUMBER ON ACUTE PHASE PROTEINS, CORTISOL AND HEMATOLOGICAL PARAMETERS IN EWES DURING THE PERIPARTURIENT PERIOD

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An optimal transition requires a comprehensive understanding of the physiological events that occur during the periparturient period. Thus, the appropriate range of maternal APP concentrations should be determined to reflect the response to changes in homeostasis or disease as well as to reduce perinatal mortality. The objective of the study was to compare the plasma concentrations of SAA, Hp, Fb, and cortisol in healthy single- and twin-bearing ewes from 2 weeks before to 2 weeks after parturition. Moreover, pregnancies with more than one fetus are often accompanied by hematological disorders compared to single pregnancies. Thus, we determined hematological parameters in peripheral blood during the periparturient period to assess whether anemia develops and whether twin-lambing sheep are more sensitive to anemia during late pregnancy. We selected only healthy sheep and enrolled a total of 40 ewes of the prolific meat line BCP. The blood samples were obtained by jugular venipuncture and collected in sterile vacuum tubes, with EDTA as an anticoagulant, 14 and 7 days before parturition, a few hours after parturition, and finally 7 and 14 days after parturition. The ewes were classified into two research groups: females with single and twin pregnancy. We measured SAA, fibrinogen, haptoglobin and cortisol concentrations as well as hematology was performed. We found a greater concentration of SAA, Hp, Fb, and cortisol in the periparturient period in twin- compared to single-bearing ewes. There were no differences between single- and twin-bearing ewes for any hematological parameters. The profile of APP changes was similar both in single- and twin-bearing females: an increase in SAA and Fb and a decrease in Hp concentrations. The cortisol concentration did not change significantly. With regard to hematological parameters, both single- and twin-bearing ewes exhibited trends typical for the periparturient period. The values of all parameters were within the physiological range.

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S11.P12

CHEMERIN EFFECT ON STEROIDOGENESIS IN THE PORCINE UTERUS: AN *IN VITRO* STUDY

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Steroidogenesis is one of the most important processes which occur in the female reproductive system during both the oestrous cycle and early gestation. In pigs, besides the ovaries and placenta, steroidogenesis process takes also place in the endometrial and myometrial tissues. Chemerin belongs to the family of adipokines - hormones secreted by the adipose tissue. Chemerin exerts pleiotropic effects. Its receptors have been found to be present in the porcine uterus, which suggests that this organ may be sensitive to the adipokine. Additionally, a growing body of evidence indicates the participation of chemerin in the regulation of reproductive system functions. The aim of this study was to determine the influence of chemerin (100 and 200 ng/mL) on steroidogenesis in the porcine endometrium, especially on the secretion of oestradiol (E_2), as well as on the expression of aromatase ($P450_{arom}$) and 3 beta-hydroxysteroid dehydrogenase (3βHSD) proteins during early gestation: on days 10 to 11 (transuterine migration of embryos) and 12 to 13 (maternal recognition of pregnancy). Concentrations of E_2 in media were defined by radioimmunoassay, whereas the expression of proteins was determined by Western blot method. To analyse statistical differences, one-way ANOVA, followed by Duncan's *post hoc* test, was used (n=5). Obtained results showed that chemerin affects production of E_2 in the porcine uterus. On days 10 to 11 of pregnancy, chemerin enhanced the expression of both steroidogenic enzymes and E_2 secretion. However, on days 12 to 13 of gestation, chemerin reduced $P450_{arom}$ and 3βHSD proteins concentrations in the *in vitro* incubated endometrial slices and E_2 levels in media. The presented data indicate that uterine steroidogenesis in pigs may be dependent on chemerin presence. Moreover, the adipokine influence on E_2 production during crucial stages of pregnancy indicates that chemerin may be an important link between energy homeostasis, immunological processes and reproductive functions in pigs.

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S11.P13

THE IMPACT OF CHEMERIN ON THE SECRETION OF CYTOKINES (INTERLEUKIN-1B, -6) AND THE EXPRESSION OF CYTOKINE RECEPTORS (IL1R1, IL6R) BY THE PORCINE ENDOMETRIUM DURING THE OESTROUS CYCLE AND EARLY PREGNANCY

G. KOPIJ, M. KIEZUN, E. ZAOBIDNA, K. DOBRZYN, K. KISIELEWSKA, E. RYTELEWSKA, M. GUDELSKA, K. BORS, K. SZYMANSKA, B. KAMINSKA, T. KAMINSKI, N. SMOLINSKA

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Chemerin belongs to the group of adipokines involved in the regulation of energy homeostasis. Recent studies have demonstrated that chemerin participates in the regulation of the uterus. In the period of uterine receptivity, the endometrium produces many factors, i.a. cytokines, which are crucial for the proper course of the implantation process. The aim of this study was to investigate the impact of chemerin on the protein expression patterns of cytokine receptors (IL1R1, IL6R). We also aimed to examine the secretion of cytokines (IL-1β, IL-6) by the porcine endometrium under the influence of chemerin (100, 200 ng/mL). On days 10 to 11 of the oestrous cycle, chemerin decreased the expression of IL1R1. On days 12 to 13 of pregnancy, chemerin at the dose of 200 ng/mL decreased the expression of IL1R1 protein. Moreover, chemerin at the dose of 100 ng/mL caused an increase in IL6R protein expression on days 10 to 11 of the oestrous cycle. The stimulatory influence on IL6R protein expression was observed on days 12 to 13 of pregnancy after treatment with the adipokine at the dose of 200 ng/mL. On days 10 to 11 of the oestrous cycle the adipokine (200 ng/mL) stimulated the secretion of IL-1β and IL-6. On days 12 to 13 of pregnancy, the adipokine of the dose of 100 ng/mL enhanced, while at the higher dose depressed IL-1β release. Secretion of IL-6 by the endometrial tissues explant was decreased by chemerin on days 12 to 13 of pregnancy. In conclusion, the influence of chemerin on IL1R1, IL6R protein expression as well as IL-1β, IL-6 secretion by endometrial explants was dependent on the dose of the adipokine and stage of the oestrous cycle or early pregnancy. Our results imply that chemerin may play an important role in the process of implantation in the pig.

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S11.P14

ADIPONECTIN AS A PROINFLAMMATORY FACTOR IN THE PORCINE ENDOMETRIUM DURING THE OESTROUS CYCLE AND IMPLANTATION: AN *IN VITRO* STUDY

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Adiponectin (ADPN) and its receptors are expressed in the human and porcine uterus. They play an important role in the regulation of reproductive processes. We have previously reported that the adipokine affects uterine steroidogenesis and prostaglandin secretion. These, with addition to the results of our preliminary studies of *in vitro* adiponectin effects on the porcine endometrial proteome with the use of mass spectrometry, prompt us to examine ADPN role in the regulation of immunological processes occurring in this tissue. We hypothesized that ADPN influences endometrial secretion of interleukins 1β (IL-1β) and 6 (IL-6), as well as their receptors, IL1R1 and IL-6R, protein expression. Porcine endometrial tissues were obtained from sows on days 10 to 12 of the oestrous cycle (mid-luteal phase, characterized by the highest secretion of progesterone by corpus luteum) and on days 15 to 16 of pregnancy (beginning of implantation). Endometrial explants were preincubated for 2 hours, and subsequently, incubated for another 24 h with ADPN (10 μg/mL) or without any treatment (control). Enzyme-linked immunosorbent assay (ELISA) method was used to evaluate the concentration of IL-1β and IL-6 in the culture media, whereas Western blot method was employed for examination of IL-1R1 and IL-6R protein content in the endometrial tissue. We have observed a stimulatory effect of ADPN on IL-1β and IL-6 secretion, as well as on IL1R1 and IL-6R protein content in all the examined tissues, except for endometrial explants from days 10 to 12 of the oestrous cycle in which ADPN caused a decrease in IL-1β release. The obtained results suggest that ADPN may be an important factor regulating immunological processes in the endometrium both during the oestrous cycle and at the stage of implantation. Proinflammatory action of ADPN in this tissue, especially at the window of implantation, may affect the embryo-maternal communication and, as a result, embryo adhesion and implantation.

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S11.P15

THE INFLUENCE OF KETOGENIC DIET ON THE COURSE OF GESTATION AND BIOCHEMICAL COMPOSITION OF HIPPOCAMPAL FORMATION OF PREGNANT RATS

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Ketogenic diet (KD) is a high-fat, low-carbohydrate diet, used in the treatment of drug-resistant epilepsy, both in children and in adults, including pregnant women. The main goal of this research was to determine the influence of KD application on the course of gestation and the biochemical composition of the brain of pregnant female rats. The animals were divided into 2 groups, obtaining normal or ketogenic diet. The body weight, blood level of glucose and ketone bodies and food consumption were monitored during the gestation period. After the delivery the number, sex and body weight of pups was assessed. The brain tissue of females was analyzed using FTIR method, in order to assess the biochemical composition of the hippocampal formation. The statistical analysis revealed a significantly higher ketone bodies blood level since the 4th day of gestation and a lower glucose level in 20th day of gestation in KD fed rats than in control group. Both groups presented a similar pattern of weight gaining during pregnancy, brain weight to body weight ratio in 2nd day postpartum, number of pups and the sex ratio of the brood. However, the pups' weight was significantly lower in KD fed group, despite the fact that KD fed rats appeared to consume significantly more calories per day. The pups' weight correlated negatively with mother's ketone bodies blood level and positively with glucose blood level in 20th day of gestation. The obtained results indicate a negative influence of ketosis on the birth weight and a greater importance of diet composition than caloricity in fetus development. The preliminary analysis of FTIR spectra for bands 1740cm^{-1}, 1360–1480 cm^{-1} and 2924 cm^{-1} (ketone bodies, unsaturated fatty acids, saturated fatty acids) revealed no differences between ketogenic and normal diet fed rats.

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S11.P16

VISFATIN GENE EXPRESSION IN THE PORCINE PITUITARY GLAND DURING THE OESTROUS CYCLE AND EARLY PREGNANCY

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Visfatin appears to be an energy sensor involved in the regulation of female fertility, which creates a hormonal link integrating the control of energy homeostasis and reproduction. Visfatin expression in adipocytes can be affected by hormonal factors such as steroid hormones, tumor necrosis factor-α, growth hormone and dexamethasone, while in the human granulosa cells by human chorionic gonadotropin and prostaglandin E_2. It is suggested that visfatin gene expression can be controlled by species-specific regulatory mechanism and the adipokine concentrations in human adipose tissue are affected by hormonal status related to pregnancy. We hypothesized that hormonal milieu connected with the specific phase of the oestrous cycle affects visfatin gene expression in the porcine pituitary. The gene expression was evaluated by RT-PCR method. Data were analysed based on one-way ANOVA and LSD *post hoc* test. During the oestrous cycle, the highest expression of visfatin gene was observed on days 10–12 and the lowest on days 17–19. During pregnancy, visfatin gene expression was the highest on days 12–13 and 27–28 in comparison to days 15–16. Comparing visfatin gene expression throughout the early pregnancy with days 10–12 of the oestrous cycle, visfatin mRNA content during all periods of pregnancy was significantly lower. The fluctuations in the expression levels of visfatin noticed during the oestrous cycle and early pregnancy may suggest its dependence on the hormonal milieu specific for the oestrous cycle and early pregnancy.

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SESSION XII

GASTROINTESTINAL PHYSIOLOGY AND PATHOPHYSIOLOGY PANCREAS AND LIVER

Wednesday (September 15, 2021; 10:50 – 13:20)
Thursday (September 16, 2021; 14:00 –15:30)

Chair:

Prof. Tomasz Brzozowski
Department of Physiology, Faculty of Medicine,
Jagiellonian University Medical College, Krakow, Poland

DETAILED SESSION XII SCHEDULE

Opening lectures (Wednesday, September 15, 2021; 10:50 – 11:55; *virtual stream B*)

S12.L1 ROLE OF MICROBIOTA-BRAIN-GUT AXIS IN PHYSIOLOGY AND PATHOPHYSIOLOGY OF GASTROINTESTINAL TRACT. **P.C. Konturek[1], W. Dieterich[2], Y. Zopf[2]** ([1]Thuringia Clinic Saalfeld, Teaching Hospital of the University of Jena, Saalfeld, Germany, [2]Department of Medicine I, Hector Center for Nutrition and Sport, University Erlangen-Nuremberg, Erlangen, Germany).

S12.L2 LIPIDS AND INFLAMMATORY BOWEL DISEASES - FRIENDS OR FOES? **J. Fichna** (Department of Biochemistry, Medical University of Lodz, Lodz, Poland).

S12.L3 THE INTERPLAY BETWEEN ENDOGENOUS GASEOUS MEDIATORS, CARBON MONOXIDE AND HYDROGEN SULFIDE IN PHYSIOLOGY AND PATHOPHYSIOLOGY OF GASTROINTESTINAL TRACT. **M. Magierowski** (Cellular Engineering and Isotope Diagnostics Laboratory, Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland).

Oral presentations (Wednesday, September 15, 2021; 11:55 – 13:20; *virtual stream B*)

S12.L4 ADMINISTRATION OF OBESTATIN ACCELERATES THE HEALING OF LINGUAL ULCERS IN RATS. **A. Stempniewicz[1], P. Ceranowicz[1], W. Macyk[2], J. Cieszkowski[1], G. Ginter[1], B. Kusnierz-Cabala[3], K. Galazka[4], M. Maraj[1], Z. Warzecha[1]** ([1]Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Inorganic Chemistry, Faculty of Chemistry, Jagiellonian University, Krakow, Poland, [3]Department of Diagnostics, Chair of Clinical Biochemistry, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [4]Department of Pathomorphology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland).

S12.L5 ANAEROBIC PHYSICAL TRAINING PREVENT GASTRIC EMPTYING DELAY AND ALTERATION IN FOOD BEHAVIOR IN RATS DEXAMETHASONE-TREATMENT. P.V.N. **Telles[1], L.C.S. Oliveira[1], J.F.R. Sousa[1], A.K.M. Cavalcante[2], A.A. Santos[2], M. Tolentino[1]** ([1]Laboratory of Exercise and Gastrointestinal Tract, Department of Physical Education, Federal University of Piaui, Teresina-PI, Brazil, [2]Department of Physiology and Pharmacology, School of Medicine, Federal University of Ceara, Fortaleza-CE, Brazil).

S12.L6 PROTECTIVE ADIPONECTIN ACTION AGAINST EXPERIMENTAL MUCOSAL DAMAGE IN THE GASTROINTESTINAL TRACT. **S. Kwiecien, A. Szlachcic, D. Wojcik, J. Majka, Z. Sliwowski, A. Danielak, A. Wojcik, K. Magierowska, M. Magierowski, T. Brzozowski** (Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland).

S12.L7 TIME-DEPENDENT MODULATING EFFECT OF SYSTEMIC INFLAMMATION ON THE SOMATOTROPIC AXIS SIGNAL TRANSDUCTION. **M. Wojcik, A. Krawczynska, W. Wiechetek, J. Bochenek, M. Tomczyk, A. Antushevich, A.P. Herman** (The Kielanowski Institute of Animal Physiology and Nutrition, Polish Academy of Sciences, Jablonna, Poland).

S12.L8 *HELICOBACTER PYLORI* INFECTION TRIGGERS ACTIVATION OF HUMAN FIBROBLASTS. A NEW TARGET OF GASTRIC CARCINOGENESIS? **G. Krzysiek-Maczka[1], A. Targosz[1], D. Wnuk[2], U. Szczyrk[1], M. Wierdak[3], M. Strzalka[1], T. Brzozowski[1], J. Czyz[2], A. Ptak-Belowska[1]** ([1]Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Cell Biology, the Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Krakow, Poland, [3]Department of Endoscopic, Metabolic and Soft Tissue Malignancies Surgery of University Hospital Jagiellonian University Medical College, Krakow, Poland).

Session summary

Poster session (Thursday, September 16, 2021; 14:00 –15:30; *virtual stream D*)

S12.P1 GASTROINTESTINAL (GI) SAFETY AND EFFICACY OF NOVEL HYDROGEN SULFIDE-RELEASING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS. **A. Danielak[1], U. Glowacka[1], K. Magierowska[1], D. Wojcik[1], J. Hankus[2], M. Szetela[1], J. Cieszkowski[1], E. Korbut[1], Z. Sliwowski[1], G. Ginter[1], J.L. Wallace[3], M. Magierowski[1]** ([1]Department of Physiology, Faculty of Madicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Pathomorphology, Faculty of Madicine, Jagiellonian University Medical College, Krakow, Poland, [3]Department of Physiology and Pharmacology, University of Calgary, Calgary, Canada).

S12.P2 OPIOID AND CHOLINERGIC RECEPTORS INTERACTION IN RAT INTESTINE. **K. Jaszcza, K. Pierzchala-Koziec** (Department of Animal Physiology and Endocrinology, University of Agriculture, Krakow, Poland).

S12.P3 SILVER NANOPARTICLES AS DRUG DELIVERY PLATFORMS IN EXPERIMENTAL MODEL OF PERIODONTITIS. **K.P. Steckiewicz, I. Inkielewicz-Stepniak** (Chair and Department of Pharmaceutical Pathophysiology, Medical University of Gdansk, Gdansk, Poland).

S12.P4 THE EFFECT OF INCREASED AND DECREASED H_2S BIOAVAILABILITY ON THE DEVELOPMENT OF BARRETT'S METAPLASIA. **E. Korbut[1], D. Wojcik[1], K. Magierowska[1], V. Janmaat[2], M. Wierdak[1], T. Brzozowski[1], M. Szetela[1], M. Whiteman[3], M. Magierowski[1]** ([1]Department of Physiology, Faculty of Madicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, Netherlands, [3]University of Exeter, Exeter, The United Kingdom).

S12.P5 THE EFFECT OF CARBON MONOXIDE (CO) RELEASED FROM PHARMACOLOGICAL DONORS ON THE DEVELOPMENT OF BARRETT'S ESOPHAGUS. **K. Krukowska[1], D. Bakalarz[1,2], D. Wojcik[1], M. Wierdak[1], K. Magierowska[1], E. Korbut[1], A. Danielak[1], T. Brzozowski[1], M. Magierowski[1]** ([1]Department of Physiology, Faculty of Madicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Forensic Toxicology, Institute of Forensic Research, Krakow, Poland).

S12.P6 MODULATION OF MITOCHONDRIAL ACTIVITY BY HYDROGEN SULFIDE-RELEASING AP-39 IN GASTROINTESTINAL PHYSIOLOGY AND PHARMACOLOGY. **K. Magierowska[1], D. Wojcik[1], D. Bakalarz[1,2], E. Korbut[1], Z. Sliwowski[1], S. Kwiecien[1], J. Cieszkowski[1], T. Brzozowski[1], M. Szetela[1], M. Whiteman[4], M. Magierowski[1]** ([1]Department of Physiology, Faculty of Madicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Forensic Toxicology, Institute of Forensic Research, Krakow, Poland, [3]University of Exeter, Exeter, The United Kingdom).

S12.P7 OPERATION OF TOTAL COLONIC AND SMALL BOWEL AGANGLIONOSIS (TCSA). **O. Dubarek[1], B. Filipiak[1], A. Noga[1], J. Tyrchniewicz[1]** ([1]Scientific Circle, Pediatric Surgery, Medical University, Zielona Gora, Poland).

S12.P8 INTESTINAL ALKALINE PHOSPHATASE ATTENUATES THE EXACERBATION OF MURINE COLITIS IN VOLUNTARY EXERCISING OBESE MICE. INVOLVEMENT OF INTESTINAL MICROBIOTA, OXIDATIVE STRESS AND CYTOKINES. **D. Wojcik[1], M. Hubalewska-Mazgaj[1], M. Surmiak[1], Z. Sliwowski[1], A. Wojcik[1], S. Kwiecien[1], A. Mazur-Bialy[2], J. Bilski[2], T. Brzozowski[1]** ([1]Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Ergonomics and Exercise Physiology, Faculty of Health Sciences, Jagiellonian University Medical College, Krakow, Poland).

S12.P9 SPEXIN AS A MODULATOR OF HEPATOCYTE METABOLISM - *IN VITRO* STUDY. **P.A Kolodziejski[1], M. Wojciechowska[2], N. Leciejewska[1], M. Sassek[1], L. Nogowski[1], K.W. Nowak[1], H. Krauss[3], E. Malek[4], K. Mielnik[1], E. Pruszynska-Oszmalek** ([1]Department of Animal Physiology, Biochemistry and Biostructure, Poznan University of Life Sciences, Poznan, Poland, [2]Department of Mother and Child Health, Poznan University of Medical Sciences, Poznan, Poland, [3]Department of Medicine, the President Stanislaw Wojciechowski State University of Applied Sciences in Kalisz, Kalisz, Poland, [4]Department of Preclinical Sciences and Infectious Diseases, Poznan University of Life Sciences, Poznan, Poland).

S12.P10 THE NEW SYNTHETIC OXIDOVANADIUM(IV) COMPLEX WITH PYRIDINE DERIVATIVE'S DISRUPTS MITOCHONDRIAL MEMBRANE POTENTIAL AND INDUCES APOPTOSIS IN PANCREATIC CANCER CELLS. **S. Kowalski[1], I. Inkielewicz-Stepniak[1]** ([1]Medical University of Gdansk, Department of Pharmaceutical Pathophysiology, Gdansk, Poland).

S12.P11 IMBALANCED DIET DURING PREGNANCY AFFECT GASTROINTESTINAL EXPRESSION OF THE ENZYMES INVOLVED IN ENDOGENOUS HYDROGEN SULFIDE (H_2S) BIOSYNTHESIS. **U. Glowacka[1], K.G. Gawlinska[2], D. Gawlinski[2], M. Szetela[1], T. Brzozowski[1], M. Filip[2], M. Magierowski[1]** ([1]Department of Physiology, Faculty of Madicine, Jagiellonian University Medical College, Krakow, Poland, [2]Maj Institute of Pharmacology Polish Academy of Sciences, Department of Drug Addiction Pharmacology, Krakow, Poland).

S12.P12 INFLUENCE OF THE IONIC AND ORGANIC COMPOSITION OF MICROELEMENTS ON THE PRESENCE OF HELICOBACTER PYLORI IN TAP WATER EVIDENCE FROM CRACOW. **A. Targosz[1], M. Plonka[1], W. Reczynski[2], M. Jakubowska[2], A. Ptak-Belowska[1], U. Szczyrk[1], M. Strzalka[1], T. Brzozowski** ([1]Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Analytical Chemistry, Faculty of Material Science and Ceramic, University of Science and Technology, Krakow, Poland).

S12.P13 ADMINISTRATION OF RIVAROXABAN IN THE COURSE OF ISCHEMIA/REPERFUSION-INDUCED ACUTE PANCREATATIS IN RATS ACCELERATES THE RECOVERY. **M. Maraj[1], P. Ceranowicz[1], W. Macyk[2], J. Cieszkowski[1], G. Ginter[1], B. Kusnierz-Cabala[3], K. Galazka[4], A. Stempniewicz[1], Z. Warzecha[1]** ([1]Department of Physiology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [2]Department of Inorganic Chemistry, Faculty of Chemistry, Jagiellonian University, Krakow, Poland, [3]Department of Diagnostics, Chair of Clinical Biochemistry, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland, [4]Department of Pathomorphology, Faculty of Medicine, Jagiellonian University Medical College, Krakow, Poland).

S12.L1

ROLE OF MICROBIOTA-BRAIN-GUT AXIS IN PHYSIOLOGY AND PATHOPHYSIOLOGY OF GASTROINTESTINAL TRACT

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Brain-gut axis (BGA) represents the bidirectional interaction between the central nervous system (CNS), enteric nervous system (ENS) and the gut. In the recent years, numerous studies have shown the importance of intestinal microbiota in the modulation of BGA. Multiple direct and indirect pathways exist through which the gut microbiota can modulate BGA. They include endocrine, immune (cytokines) and neural pathways. In addition, gut microbes produce metabolites (short chain fatty acids) or neurotransmitters (γ-aminobutyric acid-GABA; noradrenaline or dopamine) that may modulate the BGA. The dysfunction of BGA plays a central role in the functional and inflammatory disorders of gastrointestinal tract (irritable bowel disease, inflammatory bowel disease). The microbiota-based approach for treatment of these disorders includes the use of special diet (low FODMAP), prebiotics, probiotics, synbiotics and fecal microbiota transplantation (FMT). In the animal studies, the use of microbiota-based therapy (symbiotic) significantly ameliorated the negative effect of stress on microbiota-brain-gut-axis. In the clinical setting, studies on probiotics, including strains of Lactobacillus or Bifidobacterium have shown to improve symptoms severity in patients with IBS and IBD. Clinical studies on FMT remain limited and show contradictory results.

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S12.L2

LIPIDS AND INFLAMMATORY BOWEL DISEASES - FRIENDS OR FOES?

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Lipids and free fatty acids (FFAs) in particular have recently attracted much attention as possible modulators of the inflammatory state. In this context, novel findings (own and from literature) on FFAs actions through FFA receptors (FFARs) and FFAR-independent will be shared. A particular focus will be made on the translational aspect of the anti- and pro-inflammatory effect of selected FFAR ligands, especially in inflammatory bowel disease.

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S12.L3

THE INTERPLAY BETWEEN ENDOGENOUS GASEOUS MEDIATORS, CARBON MONOXIDE AND HYDROGEN SULFIDE IN PHYSIOLOGY AND PATHOPHYSIOLOGY OF GASTROINTESTINAL TRACT

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Endogenous gaseous mediators, carbon monoxide (CO) and hydrogen sulfide (H_2S) were reported to be the key components of gastrointestinal (GI) mucosa and to be involved in the maintenance of its integrity. CO and H_2S are produced by the enzymatic activity of heme oxygenase (HMOX) and cystathionine-γ-lyase (CTH) or cystathionine-β-synthase (CBS), respectively. Our studies reported that these molecules prevent gastric mucosa against the damage induced by the exposure to ischemia/reperfusion, stress or by the treatment with non-steroidal anti-inflammatory drugs (NSAIDs). CO- and H_2S-releasing pharmacological tools were also shown in our studies to accelerate gastric ulcer healing. Interestingly, H_2S-releasing derivatives of NSAIDs were reported to exert increased GI-safety as compared with the parent drugs. Additionally, we have observed that chronic treatment with H_2S-releasing or CO-releasing prodrugs prevent esophageal mucosa against the development of Barrett's metaplasia in experimental *in vivo* and *in vitro* models of gastroesophageal reflux disease (GERD). Importantly, among many complex molecular pathways being involved in gaseous mediators-mediated beneficial effects within GI tract, we reported that gastroprotective and therapeutic activity of H_2S is dependent on endogenous CO biosynthesis. To summarize, in majority of the investigated and above-mentioned GI pathologies we have observed the cross-talk between these gaseous molecules. Altogether, H_2S and CO seem to be the key targets for the further development of GI physiology, pathophysiology and pharmacology.

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S12.L4

ADMINISTRATION OF OBESTATIN ACCELERATES THE HEALING OF LINGUAL ULCERS IN RATS

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There are numerous strategies for the prevention or treatment of oral mucositis. However, their effectiveness is limited and does not correspond to expectations. Recent studies have shown that obestatin exhibits protective effect and accelerates the healing of gastrointestinal mucosa. The aim of present study was to examine the influence of obestatin administration on oral ulcers in rats. Lingual ulcers were induced by the use of acetic acid. Rats were treated intraperitoneally twice a day with saline or obestatin (4, 8 or 16 nmol/kg/dose) for six days. Study determined: oral mucosa morphology, cell proliferation, mucosal blood flow and mucosal pro-inflammatory interleukin-1β level (IL-1β). In animals with intact salivary glands without induction of oral ulcers, treatment with obestatin was without any effect. Obestatin administration in rats with lingual ulcers increased healing rate of these ulcers. Obestatin given at the dose of 8 or 16 nmol/kg/dose caused the strongest and similar therapeutic effect. This result was associated by a significant increase in blood flow and cell proliferation in gingival mucosa, as well as by a significant decrease in IL-1β level. We found that obestatin accelerated the healing of lingual ulcers in rats. This therapeutic effect was well-correlated with an increase in blood flow and cell proliferation in oral mucosa, as well as decrease of pro-inflammatory IL-1β level. Obestatin is potentially useful candidate for the prevention and treatment of oral mucositis.

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S12.L5

ANAEROBIC PHYSICAL TRAINING PREVENT GASTRIC EMPTYING DELAY AND ALTERATION IN FOOD BEHAVIOR IN RATS DEXAMETHASONE-TREATMENT

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Dexamethasone (Dexa) can trigger side effects, such as neuromuscular, cardiovascular, and gastric motility disorders. The chronic use of dexamethasone causes insulin resistance with a consequent increase in blood glucose. In addition, dexamethasone induces gastric changes, such as gastroparesis and increased stomach size. Exercise can improve gastrointestinal disorders. However, it is not clear how exercise can modulate the side effects of using Dexa on gastric motility. In this study, we investigate the role of anaerobic physical training on gastric motility and feeding behavior of rats treated with dexamethasone. Participants were divided into Control (Ctrl), Dexamethasone (Dexa), and Anaerobic Physical Training + Dexamethasone (AFTDexa) groups. The anaerobic physical training (AFT) protocol described by Krug *et al*., in *Muscle and Nerve* 2016. Initially, the rats went through an adaptation period of 5 days, where they made 4 climbs on a vertical ladder (110 cm high and 80° inclined), with a load corresponding to 30% body weight. Anaerobic physical training was performed 5 days/week of climbs on a vertical ladder (with an intensity of 8 × 50% to 100% of the maximum overload/8 weeks). At the end of the AFT or control, the rats received Dexamethasone (1 mg/kg, i.p /10 consecutive days). In the end, we evaluated anthropometric parameters and food behavior, heart rate, and gastric emptying in all groups. We observed a significant decrease ($p < 0.05$) in body weight and food consumption in the Dexa and AFTDexa groups compared to the control (–30.13 ± 10.32 and 24.22 ± 11.77 vs. 32.32 ± 8.03 g). Dexa treatment promoted significant tachycardia ($p < 0.05$) and a decrease ($p < 0.05$) in the r-r' interval. The exercise was able to significantly prevent ($p < 0.05$) cardiovascular effects. The Dexa group showed a significant decrease ($p < 0.05$) in gastric emptying of solids compared to the control group (24.58 ± 4.19 vs. 64.59 ± 6.16%). On the other hand, AFTDexa group, we observed that anaerobic physical training prevented ($p < 0.05$) the decrease in gastric emptying compared to Dexa (53.11 ± 8.33 vs. 24.58 ± 4.19%). Conclusion: the chronic use of Dexa causes tachycardia, decreased food consumption, and decreased gastric emptying. Anaerobic physical training modulates cardiovascular parameters, improving tachycardia. In addition, exercise prevented dysmotility induced by dexamethasone.

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S12.L6

PROTECTIVE ADIPONECTIN ACTION AGAINST EXPERIMENTAL MUCOSAL DAMAGE IN THE GASTROINTESTINAL TRACT

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Adiponectin is adipokine, exhibiting beneficial metabolic action through lipids and carbohydrates metabolism stimulation with accompanied anti-inflammatory action. We have established the role of adiponectin in healing of gastric lesions induced by ischemia - reperfusion (I/R) and TNBS-induced large bowel damage. The ischemia-reperfusion-induced acute damage exhibits a serious clinical problem. However the participation of reactive oxygen species (ROS) production, lipid peroxidation metabolites and involvement of sensory neurons, releasing NO, to the potential gastroprotective action of adiponectin remains unknown. We planned to determine the interplay between capsaicin-sensitive afferent nerves, NO/NOS system, lipid peroxidation products and the expression of proinflammatory and antioxidative factors in gastroprotective action of adiponectin against gastric I/R. Experiments were caried out on male Wistar rats and the area of gastric lesions was measured by planimetry. Colorimetric assays were employed to measure gastric mucosal levels of malondialdehyde (MDA) and 4-hydroxynonenal (4-HNE). High doses of capsaicin were administered to break sensory nerves. In separate group of animals with gastric fistula gastric acid production was determined. Adiponectin significantly reduced the gastric lesions induced by I/R or TNBS and this effect is accompanied by increase of gastric blood flow (GBF). Blockade of NO-synthase with L-NNA (20 mg/kg i.p.) reversed these effects, while additional application of L-arginine, added to L-NNA, restored the protective effect of adiponectin. Capsaicin denervation also impeded beneficial action of adiponectin in I/R model, restored by intraperitonel administration of CGRP, combined with this peptide. Adiponectin dose-dependently decreased gastric I/R lesions, as well as gastric acid secretion, the expression of mRNA for proinflammatory cytokines and MDA plus 4-HNE content while significantly increasing accompanied rise in gastrin, in I/R model. We concluded, that adiponectin, administered intravenously, exerted protective effect against ischemia/reperfusion-induced gastric lesions (I/R) and TNBS-induced large bowel lesions, through mechanism involving decrease of lipid peroxidation (MDA+4-HNE), gastric acid secretion, as well as *via* endogenous NO production and action capsaicin-sensitive afferent nerves.

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S12.L7

TIME-DEPENDENT MODULATING EFFECT OF SYSTEMIC INFLAMMATION ON THE SOMATOTROPIC AXIS SIGNAL TRANSDUCTION

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Systemic inflammation has a broad impact on the activity of neuroendocrine axes, including the somatotropic part (SA) of the hypothalamic-pituitary-somatotropic axis. So far, it was found that systemic inflammation inhibits the SA signal transduction inducing resistance to growth hormone (GH) - GHres. However, the direct mechanism of the GHres induction is still not fully elucidated. The GHres is characterized by an increased level of GH secretion, decreased level of IGF-1, and a lack of the physiological response to the exogenous GH administration. GHres is accompanied by a decreased GH receptor (*GHR*) and increased the suppressor of cytokine signaling 3 (*SOCS3*) expression. Moreover, many authors point to the critical role of the fibroblast growth factor 21 (FGF21), positively correlating with the GH level and negatively with the IGF-1. This study aimed to determine the SA signal transduction disturbances caused by systemic inflammation and whether there is a time-dependent relationship between the expression of genes responsible for the GHres development and the duration of inflammation. The experiment was conducted on 36 blackface ewes randomly divided into three groups that differ in time from the administration of lipopolysaccharide (LPS, 400 ng/kg) to euthanasia and liver tissue collection: 1.5, 3 and 9 h. The increased GH serum concentration was found 45 min after LPS injection and was sustained for the next 3 h and 45 min. Moreover, fast changes in *IL1β*, *TNFα*, and *IL6* gene expression in response to the LPS were determined. Increased *SOCS3*, *IGF-1,* and decreased *STAT5B* and *FGF21* expression in the 1.5 h group was observed. After 3 h, *GHR* and klotho beta (*KLB*) expression started to decline, while *IGF1* and *FGF21* equaled with the control group. After 9 h, *IGF1*, *GHR*, *STAT5B*, *IGF1*, and *KLB* expression decreased while *FGF21* increased markedly. The obtained results suggest the occurrence of inflammation-induced GHres on the level of the liver. In the present study, the role of FGF21 in evoking GHres seems marginal due to the inhibited signal transduction of FGF21 in the liver, which was indicated by changes in *KLB*, FGF21 cofactor, gene expression. A decrease in *STAT5B* expression combined with increased *SOCS3* mRNA level after 1.5 h may suggest this or another post-receptor mechanism of GH signal transduction inhibition in the initial phase of inflammation, which after 3 hours was strengthened by the decreased GHR expression.

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S12.L8

HELICOBACTER PYLORI INFECTION TRIGGERS ACTIVATION OF HUMAN FIBROBLASTS. A NEW TARGET OF GASTRIC CARCINOGENESIS?

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Gastric cancer (GC) remains the fourth most common cause of cancer-related death worldwide with 90% of all stomach tumors being malignant. Despite of the anti-GC therapies patients still suffer from cancer recurrence and metastasis due to the heterogeneity, high invasiveness, rapid proliferation and activity of anti-apoptotic systems in tumor cells resulting Molecular mechanisms leading to GC development are attributed to gastric infection with highly invasive bacteria *Helicobacter pylori* (*Hp*), however, the participation of *Hp*-infected gastric fibroblasts in pathogenesis of GC remains poorly understood. Herein, we explored the possibility that human gastric fibroblasts may constitute the direct target for *Hp* infection. Incubation of *Hp* with fibroblasts increased expression mRNA for TLR2,4, STAT3 and NFκB (relA) resulting in $Snail^{+}Twist^{+}$phenotype. Human *Hp*-activated gastric fibroblasts (*Hp*-AGFs) possessed cancer-associated fibroblasts (CAF) characteristics. Although control human fibroblasts were initially α-SMA positive, α-SMA became incorporated into stress fibers following *Hp*-infection and this effect was mimicked by co-incubation with TGFβ (5 ng/mL). TGFβ signaling inhibition by SB-431542 (ALK5/TGFβ type I receptor inhibitor, 10 μM/L) diminished expression of mRNA for most markers of fibroblast activation. The fast releasing hydrogen sulfide (H_2S) donor, NaHS downregulated pro-inflammatory pathway components: TLR2 and 4, STAT3 and NFκB (p65) in human *Hp*-AGFs (50 μM) and reduced expression Twist and Zeb but not that of Snail. We conclude that 1) *Hp* can activate human fibroblasts, and 2) H_2S donors can attenuate expression of CAF markers, thus deserving attention for its anti-inflammatory action in GC.

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S12.P1

GASTROINTESTINAL (GI) SAFETY AND EFFICACY OF NOVEL HYDROGEN SULFIDE-RELEASING NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

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Non-steroidal anti-inflammatory drugs (NSAIDs) represent one of the most commonly prescribed classes of drugs and play an important role in the therapy of numerous inflammatory diseases such as rheumatoid arthritis. However, these compounds are also known to evoke a range of gastrointestinal (GI) adverse effects including bleeding, hemorrhage and even perforation, which significantly limit their clinical implementation. Proton pump inhibitors (PPIs) are currently recommended as a co-therapy aiming at reducing NSAIDs-induced gastric damage. Nevertheless, they were not only shown to be ineffective in decreasing intestinal injury evoked by NSAIDs, but also to exacerbate it, possibly due to the alterations in intestinal microbiome profile (e.g. small intestinal bacterial overgrowth (SIBO)). On the other hand, hydrogen sulfide (H_2S) has been recognized as an anti-inflammatory, anti-oxidative and vasodilatory endogenous messenger contributing to GI protection. Additionally, H_2S released from chemical donors has been shown to protect gastric mucosa against the damage induced by ethanol, ischemia/reperfusion and NSAIDs. Based on these promising results, novel H_2S-releasing NSAIDs have been developed with improved anti-inflammatory activity and reduced GI-toxicity. We have demostrated in experimental animal models that H_2S-releasing derivatives of acetylsalicylic acid (ATB-340) or ketoprofen (ATB-352) did not affect ulcer healing and significantly reduced gastric and intestinal damage score as compared to classic aspirin or ketoprofen. Furthermore, ketoprofen combined with omeprazole (PPI) decreased GI damage down to the level of ATB-352 applied alone. Importantly, ketoprofen, but not ATB-352, administration was followed by significant alterations in intestinal microbiota, suggesting that GI safety of ATB-352 may be due to lower impact on intestinal microbiome profile. Therefore, novel H_2S-releasing NSAIDs including ATB-352 or ATB-340 should be considered as a safer alternative in future therapies of digestive system disorders.

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S12.P2

OPIOID AND CHOLINERGIC RECEPTORS INTERACTION IN RAT INTESTINE

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Enkephalins are short opioid peptides, which are also produced by the GI tract where they are formed in gastric and intestinal endocrine/nervous cells (ENS). Leu- and Met-enkephalin exist in the native, short form and total, extended proenkephalin (PENK) form. Both peptides are potent delta opioids receptor (DOR) agonists. Enterocytes and enteric nervous cells express muscarinic and cholinergic receptors as well as opioids receptors which may suggest that their interaction affects synthesis and release of many peptidergic hormones existing in GI tract. Ghrelin was found in the GI system and interaction with Met-enkephalin at the GI and CNS levels was suggested. Acetylcholine receptors (AChRs) in the gastrointestinal tract are represented by muscarinic and nicotinic receptors. Many anatomical and biochemical evidences indicate that opioidergic and cholinergic systems are co-localized and also act on the same neurons. Thus, the aim of the study was to evaluate the *in vivo* interaction of opioid and cholinergic receptors in the regulation of Met-enkephalin and ghrelin activity in the rat intestine. The experiment was carried out on male Wistar rats (n=24) kept in standard conditions with free access to feed and water. Rats were divided into 4 groups received a single (i.p.) injection of NaCl (control group) or receptor antagonists: 3 mg/kg BW of naltrexone (N group); 5 mg/kg BW of atropine (A group); and 5 mg/kg BW of hexamethonium (H group). Thirty min after receptor antagonists injection animals were euthanized, fragments of duodenum were taken for estimation of hormones concentration and for proenkephalin mRNA expression. Naltrexone decreased the native Met-enkephalin but increased PENK and ghrelin concentrations as well as PENK mRNA expression. Inhibition of muscarinic receptors (A group) also increased PENK concentration (by 72%) and PENK synthesis (by 133%) but decreased the ghrelin concentration in the duodenum (by 32%). Hexamethonium (H group) caused increase of PENK level (by 45%) and PENK mRNA expression by 75%. In summary, the present study showed strong evidence for a bidirectional link between opioid and cholinergic systems and the obtained results potentially have impact on the future research focused on delineating the relative contributions of immune, neural and endocrine pathways in the regulating of gastrointestinal milieu.

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S12.P3

SILVER NANOPARTICLES AS DRUG DELIVERY PLATFORMS IN EXPERIMENTAL MODEL OF PERIODONTITIS

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Periodontitis (PD) is inflammation of tissues surrounding the teeth, and it may be the cause of teeth loose. Currently treatment options for PD are limited thus novel therapeutic options are needed. Silver nanoparticles (AgNPs) may be interesting therapeutic agents in PD due to their synergistic anti-bacterial and anti-inflammatory properties. In this work we assessed AgNPs as drug delivery platforms in experimental model of periodontitis. AgNPs conjugated with chlorhexidine and AgNPs conjugated with metronidazole were examined. HGF1 (human gingival fibroblast), hFOB1.19 (human foetal osteoblast), RAW264.7 (murine macrophages) cell lines were used to determine anti-inflammatory properties and safety of AgNPs. MTT assay was used to determine viability of the cells, commercially available ELISA tests were used to determine levels of pro-inflammatory cytokines levels (TNF-α, IL-1β, IL-6, IL-8) and flow cytometry was used to measure reactive oxygen species and cell cycle distribution. Cytotoxicity of AgNPs depended on the type of the drug and AgNPs concentration. AgNPs conjugated with metronidazole were less toxic. In non-toxic concertation both types of AgNPs decreased production of pro-inflammatory cytokines by lipopolisacharyde stimulated murine macrophages. Also, AgNPs decreased intracellular level of metalloproteinase in human osteoblast cells, which may suggest that they will inhibit periodontal tissue degeneration. In tested concentration range AgNPs did not impact cell cycle distribution, thus it may suggest that they will not impact tissue regeneration processes. Silver nanoparticles may be safe and effective drug delivery platforms with anti-inflammatory properties to be used in periodontitis.

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S12.P4

THE EFFECT OF INCREASED AND DECREASED H_2S BIOAVAILABILITY ON THE DEVELOPMENT OF BARRETT'S METAPLASIA

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Barrett's esophagus (BE) is a pre-malignant condition characterized by the conversion of the normal esophageal squamous epithelium into metaplastic columnar epithelium. Hydrogen sulfide (H_2S), endogenously generated by cystathionine β-synthase (CBS) and cystathionine γ-lyase (CTH) contribute to the maintenance of gastrointestinal mucosa integrity. However, the role of H_2S-prodrugs in the pathogenesis of BE has not been elucidated. This study aimed to investigated the effect of chronic treatment with the slow-releasing H2S donor, GYY4137, on BE progression *in vivo* and *in vitro*. Human-derived esophageal keratinocytes (EPC2) with or without CRISPR/Cas9-induced CTH/CBS gene knock-outs (k/o) were treated with acidified bile mixture (BM), to induce clinically observed BE-like molecular profile and/or with GYY4137 (100 μM). Male Wistar rats with esophago-gastroduodenal anastomosis (EGDA) were treated i.g. for 8 weeks with vehicle, GYY4137 (0.5–50 mg/kg) or CTH inhibitor (PAG, 1–15 mg/kg). mRNA expression for BE-specific genes and proinflammatory targets was determined by real-time PCR. Serum content of 10 inflammatory-response markers and esophageal concentration of key modulators of important signaling pathways was determined by multiplex microbeads fluorescent assay. GYY4137 and CTH/CBS k/o did not affect EPC2 cell viability. BM treatment of CBS and CTH k/o EPC2 further enhanced molecular BE-specific alterations, similarly to the groups treated with PAG. In animal model, daily treatment with GYY4137 dose-dependently reversed while PAG increased BE-specific targets expression as compared with vehicle. Furthermore, we observed decreased proinflammatory markers serum concentration and altered levels of transcription factors and kinase activities (e.g. JNK, Akt, STAT3 or STAT5). We conclude that H_2S produced endogenously or released from pharmacological tools could be involved in the inhibition of BE metaplasia development and its further progression due to downregulation of dysplasia-accelerating pathway and molecular pro-inflammatory signaling.

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S12.P5

THE EFFECT OF CARBON MONOXIDE (CO) RELEASED FROM PHARMACOLOGICAL DONORS ON THE DEVELOPMENT OF BARRETT'S ESOPHAGUS

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CO (carbon monoxide) is a cellular gaseous mediator produced *via* enzymatic activity of heme oxygenase (HMOX). This molecule has been shown to exert cytoprotective effects within gastrointestinal (GI) mucosa in low concentrations. On the other hand, Barrett's esophagus (BE) predisposes GI mucosa to the development of esophageal adenocarcinoma (EAC). We aimed to evaluate if the chronic treatment with CO donors - CO releasing molecules (CORMs) affects BE development and progression base on experimental *in vitro* and *in vivo* models. Male Wistar rats with esophagogastroduodenal anastomosis (EGDA) were treated i.g. for 8 weeks with vehicle or with tricarbonyldichlororuthenium(II) dimer (CORM-2, 0.2–5.0 mg/kg). Next, the esophageal lesions/metaplasia index (ELMI) was evaluated micro- and macroscopically. Esophageal blood flow (EBF) was assessed by laser flowmetry. We determined the esophageal mRNA expression for BE-specific *KRT* genes family and for anti-inflammatory interleukin 1 receptor agonist (*IL-1RA*) and suppressor of cytokine signalling 3 (*SOCS3*) by real-time PCR. Within *in vitro* model human esophageal keratinocytes (EPC2) and human-derived EAC cell lines (OE33 and OE19) were treated for 3 days with sodium boranocarbonate (CORM-A1, 0.05–1000 μM). Cell viability was determined using thiazolyl blue tetrazolium bromide (MTT) assay. CORM-2 dose-dependently reduced the ELMI score and modulated the esophageal mRNA expression of *KRT1*, *KRT4*, *KRT8*, *KRT18* as compared to the vehicle. Moreover, CORM-2 elevated *SOCS3* and *IL1RA* expression. CORM-A1 dose-dependently inhibited EPC2 and OE19/OE33 proliferation but only in high doses (>500 μM). We conclude that CO released from its pharmacological donors might modulate BE esophagus development and its progression, possibly due to upregulation of anti-inflammatory response pathways within esophageal mucosa exposed to gastroesophageal reflux disease (GERD).

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S12.P6

MODULATION OF MITOCHONDRIAL ACTIVITY BY HYDROGEN SULFIDE-RELEASING AP-39 IN GASTROINTESTINAL PHYSIOLOGY AND PHARMACOLOGY

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Hydrogen sulfide (H_2S) is a physiological gaseous mediator, produced endogenously by L-cysteine metabolism. Interestingly, this molecule was observed to modulate mitochondrial activity. Moreover, H_2S-releasing compounds were reported to effectively maintain gastrointestinal (GI) mucosal barrier. Thus, we aimed to determine the impact of H_2S released from AP-39 on mitochondrial activity within gastric mucosa exposed to acetylsalicylic acid (ASA). Wistar rats were pretreated with vehicle, AP-39 (0.004–2.5 mg/kg i.g.) or NC-AP-39 as structural control without H_2S-releasing ability. Next, ASA was administered in a dose of 125 mg/kg i.g. Gastric damage score and gastric blood flow (GBF) were determined by planimetry, histology and laser flowmetry, respectively. Gastric mucosal mRNA expressions of annexin-A1 and TGF-β1 as well as serum concentration of TGF-β1, TGF-β2, and TGF-β3 were determined by real-time PCR or Luminex platform, respectively. PGE_2 content in gastric mucosa was determined by ELISA. Mitochondrial complex IV and V activity was determined by biochemical assays. AP-39 (0.02 mg/kg i.g.) decreased gastric lesions area induced by ASA and increased GBF level in parallel with modulation of complex IV and V activity. AP-39 maintained upregulated by ASA gastric mucosal annexin-A1 mRNA expression. AP-39 decreased serum content of TGF-β1 and TGF-β2 but did not affect decreased by ASA PGE_2 content in gastric mucosa. NC-AP-39 did not prevent gastric mucosa in tested experimental models. Taken together, we assume that direct targeting of mitochondria and modulation of mitochondrial complexes activity by H_2S released from AP-39 maintains gastric mucosal integrity. Furthermore, AP-39 seems to be promising pharmacological tool for the further studies related to the possible therapeutic role of H_2S-mediated mitochondrial activity modulation in the process of chronic gastric ulcer healing.

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S12.P7

OPERATION OF TOTAL COLONIC AND SMALL BOWEL AGANGLIONOSIS (TCSA)

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Hirschsprung disease (HD) is a birth defect characterised by the absence or malfunction of parasympathetic ganglionic cells within the distal intestine which causes gastrointestinal tract dysfunction. In the most common type, the disorder does not extend beyond the proximal part of the sigmoid colon. In the presented case, the patient admitted to our hospital shows a much less common type of disease. It exceeds beyond the entire large intestine and involves a part of the distal small intestine as well. Due to the extent of the disorder, in this type of HD, the entire segment responsible for water and electrolytes absorption is malfunctioning. That is why this form of the disease exhibits worse long-term outcomes and lower quality of life. During the procedure using a combination of Duhamel, Martin, Kalicinski methods, the patient underwent an anastomosis of the aganglionic rectum stump and the ganglionic segment of the small intestine. As the effect, there was formed the neorectum whose main function is to re-establish proper water and electrolytes absorption as well as the prevention of persistent diarrhea.

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S12.P8

INTESTINAL ALKALINE PHOSPHATASE ATTENUATES THE EXACERBATION OF MURINE COLITIS IN VOLUNTARY EXERCISING OBESE MICE. INVOLVEMENT OF INTESTINAL MICROBIOTA, OXIDATIVE STRESS AND CYTOKINES

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Inflammatory bowel diseases (IBD) are chronic inflammatory disorders of the colon and small intestine, commonly described as Crohn disease and ulcerative colitis. Most IBD patients suffer from undernutrition, but have a higher ratio of abdominal fat than healthy, lean people. Visceral fat is the main source of pro-inflammatory cytokines. Intestinal alkaline phosphatase (IAP) is considered as an important brush border enzyme that acts by dephosphorylation of bacterial LPS. Administration of IAP in conjunction with voluntary exercise has been shown led to resolution of experimental colitis, but the changes in the oxidation status of the intestinal mucosa as well as the alteration in intestinal microbiota in IAP-treated mice with colitis remain unknown. Animals fed a high-fat-diet (HFD) for 14-weeks were randomly assigned to exercise group maintained on in-cage spinning wheels (SW) for 7-weeks. Then mice were administered *i.g.* with IAP for 2-weeks followed by intrarectal administration of 2,4,6-trinitrobenzenesulfonic acid (TNBS). The macroscopic and microscopic changes in the colonic mucosa were expressed by disease activity index (DAI). The composition of intestinal microbiota was examined in stool samples by Next-Generation Sequencing (NGS) and proinflammatory markers in plasma were determined by Luminex. The intensity of colonic damage in sedentary TNBS mice was reduced when these mice had access to SW, and this effect in SW mice was potentiated by treatment with IAP. The lowest bacterial diversity was found in HFD fed mice with colitis but this effect was reversed by the combination of IAP and SW exercise. The combination of IAP administration and SW exercise reduced oxidative stress and plasma level of proinflammatory cytokines comparing to HFD sedentary mice. We conclude that the combination of IAP with voluntary exercise shows a beneficial effect on the course of experimental colitis, reducing inflammatory response, markers of oxidative stress and improving microbial diversity. Our data indicate a potential role of IAP and voluntary physical activity in the mechanism of resolution of intestinal disorders mediated by changes in colonic microbiota and attenuation of oxidative stress.

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S12.P9

SPEXIN AS A MODULATOR OF HEPATOCYTE METABOLISM - *IN VITRO* STUDY

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The Spexin is a novel highly conservative 14 amino acid peptide that was discovered in 2007 using bioinformatics methods (Mirabeau, *et al.*, *Genome Res* 2007). The biological activity of SPX is regulated via two isoforms of the galanin receptors - GALR2 and GALR3. To date, many positive effects of SPX on metabolism have been described. It was showed that SPX inhibits food intake, regulates fat tissue metabolism by effect on lipolysis and lipogenesis as well as regulates insulin secretion from pancreatic beta cells. In this study we decided to investigate the effect of SPX on hepatocyte metabolism *in vitro*. Using AML-12 and HepG2 cell lines we studied the effect of different doses of SPX on cell proliferation and viability, lipid accumulation and expression of genes involved in the development of non-alcoholic fatty liver disease (NAFLD). We noted that SPX stimulates proliferation and cell viability of AML-12 and HepG2 cells increasing phosphorylation of ERK1/2 kinases. We also noted that SPX has the inhibitory effect on lipogenesis and this effect depends on the type of fatty acids. We summarize that SPX is a strong regulator of proliferation and fat metabolism of hepatocytes.

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S12.P10

THE NEW SYNTHETIC OXIDOVANADIUM(IV) COMPLEX WITH PYRIDINE DERIVATIVE'S DISRUPTS MITOCHONDRIAL MEMBRANE POTENTIAL AND INDUCES APOPTOSIS IN PANCREATIC CANCER CELLS

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At the present time, there is a growing interest in metal-based anticancer agents. The modern bioinorganic chemistry can exploit the unique properties of metal ions by synthesis new metal complexes, which generate new conformations that can more effectively explore structure-activity relationship. It has been demonstrated that synthetic vanadium complexes exhibit many biological activities including anti-cancer properties, however, mechanisms still are not fully understood. In our research we examined the potential effects of three newly synthesized oxidovanadium(IV) complexes against pancreatic cancer cells. We measured cytotoxicity by using MTT assay, antiproliferative activity by bromodeoxyuridine assay and necrosis as well as late apoptosis by lactate dehydrogenase assay. Reactive oxygen species generation, apoptosis and mitochondrial membrane potential were determined by flow cytometry technique. Cells morphology was evaluated by using transmission electron microscope. Our results showed that oxidovanadium(IV) complexes with pyridine derivative's were cytotoxic on pancreatic cancer cells (PANC-1 and MIA PaCa2) over the concentration range of 12.5–200 μM, following 48 h incubation. Additionally, cellular mechanism of cytotoxic activity was dependent on ROS generation, induction apoptosis with simultaneous disruption of mitochondrial membrane potential. The results of our research will help to understand the cellular mechanisms of the cytotoxic activity of the vanadium complexes and will allow a more effective design structure of new vanadium-based compounds in the future.

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S12.P11

IMBALANCED DIET DURING PREGNANCY AFFECT GASTROINTESTINAL (GI) EXPRESSION OF THE ENZYMES INVOLVED IN ENDOGENOUS HYDROGEN SULFIDE (H_2S) BIOSYNTHESIS

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The placenta plays a key role in the mother-fetus relationship, ensuring fetal homeostasis by regulating the flow of nutrients. According to the theory and developmental origins of health and disease (DOHaD), exposure to the harmful environment during critical periods of development and growth can have a significant impact on the health of offspring. Unbalanced diet during pregnancy and lactation increases the predisposition of offspring to develop diseases such as obesity, metabolic syndrome, diabetes as well as mental illness and possibly to affect gastrointestinal (GI) mucosal barrier integrity. Epigenetic regulation plays an important role in the period of early embryogenesis in mammals and enables organisms to adjust gene expression and function in response to the environment. On the other hand, hydrogen sulfide (H_2S) is an endogenous gaseous mediator produced in GI tract by enzymatic activity of cystathionine-γ-lyase (CTH) or 3-mercaptopyruvate sulfurtransferase (MPST). This molecule exerts anti-inflammatory and vasodilatatory properties and its activity is important for the maintenance of gastric mucosal integrity. H_2S also regulates epigenetic processes through acetylation and methylation of histones. We investigated based on animal experimental model, the effects of the maternal high-fat (HFD), high-sugar (HCD) mixed diet (HMD; rich in carbohydrates and fats) during pregnancy and lactation on the expression of CTH and MPST within GI mucosa of offspring. We observed that HFD and HCD modulated mRNA expression for H_2S-producing enzymes in GI mucosa suggesting that possible dysregulation of physiological functions of GI mucosal barrier and its susceptibility to GI pathologies induced by imbalanced diet during pregnancy may involve altered activity of endogenous H_2S within GI tract.

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S12.P12

INFLUENCE OF THE IONIC AND ORGANIC COMPOSITION OF MICROELEMENTS ON THE PRESENCE OF HELICOBACTER PYLORI IN TAP WATER. EVIDENCE FROM CRACOW

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Although the natural niche for *H. pylori* (Hp) is the human stomach, for widespread infection to occur the organism may need to survive in the external environment. Using molecular techniques such as PCR, we traced the presence of Hp-DNA in the drinking water, indicating that this aqueous medium can act as a reservoir for this bacterium. We investigated the relationship between the twenty six selected elements including among others: total number of microorganisms at 22°C, color, pH, conductivity at 25°C, ionic and the organic composition of microelements and the presence of Hp DNA in the tested water samples. Three hundred seventy nine objects (water samples) from different municipal water distribution system from Cracow were collected. Samples of 1000 mL of water were concentrated by centrifugation and obtained pellet was resuspended in 1 ml of PBS used for DNA extraction. Water samples were subjected to PCR for the bacteria specific pathogenic cag-A gene encoding the cytotoxic protein Cag-A. VVariables were marked in accordance with polish standards (PN) and ISO. The strategy of multivariate data analysis was applied. Following algorithms were used: 1) Principal component analysis (PCA); 2) Linear discriminant analysis (LDA). The data obtained from the tests show that 212 (55.96%) objects were Hp DNA positive. LDA was built for classifying objects based on fifteen variables: color, pH, chlorides, nitrites, phosphates, chlorates, sulphates, free chlorine, sodium, magnesium, total organic carbon, trichloromethane, bromodichloromethane, dibromochloroethane, sum trihalogenometanes (ΣTMH) for which $p < 0.05$. This model correctly classified objects, i.e. 87.5% water samples. We believe that with these algorithms, we can distinguish objects with detection of DNA-Hp from those without detection of Hp-DNA- in water samples. Conclusions: the ionic and organic composition of the trace elements in the water can influence the presence of Hp-DNA. Thus, the assay of selected chemical micronutrients can indirectly indicate or sometimes predict the presence of Hp in drinking water.

S12.P13

ADMINISTRATION OF RIVAROXABAN IN THE COURSE OF ISCHEMIA/REPERFUSION-INDUCED ACUTE PANCREATATIS IN RATS ACCELERATES THE RECOVERY

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There is a close relationship between coagulation and inflammation. The aim of the study was to investigate if administration of rivaroxaban, direct Xa factor inhibitor in the coagulation cascade, alleviates the severity of ischemia-reperfusion induced acute pancreatitis in rats. AP was induced with 30 min ischemia and subsequent reperfusion in Wistar rats. Rivaroxaban in doses of 5, 20, 100 mg/kg was administered intragastrically once daily with the first dose 24 hours after the initiation of reperfusion. Histological, functional and biochemical examinations were conducted 2, 5, 9 and 14 days from AP induction. Administration of RXB in the dose of 5 and 20 mg/kg limited the morphological damage of the pancreas such as edema, vacuolization of acinar cells, necrosis or the number of hemorrhages. Also the improvement in the pancreatic blood flow was observed. It was accompanied by the reduction of pancreatic enzymes amylase and lipase. Additionally, treatment with rivaroxaban decreased the concentration of interleukin 1β in the serum, as well as the drop in the D-dimer level was recorded. Administration of rivaroxaban in the dose of 100 mg/kg led to the increased severity of damage of the pancreas and worse acute pancreatitis parameters as compared to lower doses. In some rats intestinal bleeding was observed.

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SESSION XIII

MULTI-OMICS PROSPECTIVES IN PHYSIOLOGY

Friday (September 17, 2021; (9:00 – 11:30)

Chair:

Prof. Maciej Kurpisz
Institute of Human Genetics, Polish Academy of Sciences, Poznan, Poland

DETAILED SESSION XIII SCHEDULE

Opening lectures (Friday, September 17, 2021; 9:00 – 10:49; *virtual stream B*)

S13.L1 TRANSCRIPTOMIC STUDIES FOR MALE INFERTILITY DIAGNOSIS AND THERAPY MONITORING. **M. Kurpisz[1], A. Malcher[1], N. Rozwadowska[1], P. Jedrzejczak[2]** ([1]Institute of Human Genetics, Polish Academy Sciences, Poznan, Poland, [2]Infertility and Reproductive Endocrinology Clinic of Gynaecological and Obstetric Hospital, University of Medical Sciences, Poznan, Poland).

S13.L2 MULTI-OMIC INSIGHT INTO THE PATHOMECHANISM OF CHRONIC KIDNEY DISEASE-RELATED ATHEROSCLEROSIS **J. Tracz[1], L. Handschuh[1], M. Lalowski[1,2], L. Marczak[1], K. Kostka-Jeziorny[3], B. Perek[3], M. Wanic-Kossowska[3], A. Podkowinska[4], A. Tykarski[3], D. Formanowicz[3], M. Luczak[1]** ([1]Institute of Bioorganic Chemistry, Polish Academy of Sciences, Poznan, Poland, [2]Department of Biochemistry and Developmental Biology, University of Helsinki, Finland, [3]Poznan University of Medical Sciences, Poznan, Poland, [4]Dialysis Station Dravis sp. z o.o., Poland).

S13.L3 MULTIMODAL ANALYSIS IN THE SEARCH FOR NEW BIOMARKERS OF DIABETIC KIDNEY DISEASE - microRNA AND EXTRACELLULAR VESICLES. **E.L. Stepien** (Department of Medical Physics, Marian Smoluchowski Institute of Physics, Jagiellonian University, Krakow, Poland).

S13.L4 MULTI-OMIC APPROACH FOR PREDICTING RESPONSE TO NEOADJUVANT RADIOTHERAPY OF COLORECTAL CANCER. **A. Wojakowska[1], U. Strybel[1], L. Marczak[1], M. Zeman[2], K. Polanski[3], L. Mielanczyk[4], M. Pietrowska[2]** ([1]Institute of Bioorganic Chemistry Polish Academy of Sciences, Poznan, Poland, [2]Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland, [3]Wellcome Sanger Institute, Wellcome Genome Campus, Hinxton, Cambridgeshire, United Kingdom, [4]Department of Histology and Cell Pathology, Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland).

Oral presentations (Friday, September 17, 2021; 10:50 – 11:30; *virtual stream B*)

S13.L5 DIETARY SUPPLEMENTATION WITH DIFFERENT SOURCES OF INULIN-TYPE FRUCTANS EVOKES CHANGES IN PROTEOMIC PROFILE OF PORCINE AORTA. **M. Marynowska[1], M. Ozgo[1], A. Herosimczyk, A. Lepczynski, J. Skomial, M. Barszcz, M. Taciak** ([1]Department of Physiology, Cytobiology and Proteomics, Faculty of Biotechnology and Animal Breeding, West Pomeranian University of Technology in Szczecin, Poland, [2]The Kielanowski Institute of Animal Physiology and Nutrition, Polish Academy of Sciences, Jablonna, Poland).

S13.L6 PROTEINS OF MARE'S COLOSTRUM ASSOCIATED WITH FOAL AND MAMMARY GLAND GROWTH AND DEVELOPMENT. **W. Medenska, A. Dratwa-Chalupnik, M. Ozgo, A. Cichy** (Department of Physiology, Cytobiology and Proteomics, West Pomeranian University of Technology in Szczecin, Szczecin, Poland).

Session summary

S13.L1

TRANSCRIPTOMIC STUDIES FOR MALE INFERTILITY DIAGNOSIS AND THERAPY MONITORING

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Transcriptomic libraries from specific organs may in future serve for molecular diagnosis, treatment and monitoring of disease more precisely than traditional histopathology. Male infertility seems to be dependent on genomic causes at least in 50% and identification of reason may provide a way for genetic correction of spermatogenesis. In order to obtain testicular library we have analyzed 20 testicular samples with Affymetrix Human Gene 1.0 ST microarrays, sixteen of them were obtained from patients with various types of non-obstructive azoospermia (NOA) syndrome and four were healthy donors with normal spermatogenesis. Six out of NOA syndrome patients were subjected to gonadotropin therapy (hCG+rFSH) and one positive therapy responder was re-analyzed in microarrays before and after successful treatment. Genes analyzed by microarrays were stratified in dendograms and were subsequently validated by qPCR or raw data validated from existing data bases. Then, Class II HLA DQB alleles were determined and sequenced. Thus all patients subjected to experimental therapy undergone histocompatibility genes expression evaluation. Among the 5000 significantly different (than background) gene expression analyzed in infertile vs. healthy individuals (gonads), 14 have been delineated with the highest range of expression from background average obtained for this organ. There were identified 7 genes most significantly downregulated (*AKAP-4*, *UBQLN3*, *CAPN11*, *GGN*, *SPACA4*, *SPATA3*, *FAM71F1*) and 7 significantly upregulated (*WBSCR28*, *ADCY10*, *TMEM225*, *SPATS1*, *FSCN3*, *GTSF1L*, *GSG1*) while differentiating between different severity of spermatogenic impairment. In respect to positive vs. negative responders of NOA patients to gonadotropins therapy, 5 transcripts were found to be significantly different. Among them was found Class II *HLA DQB1* gene which acquired statistical significance differentiating between successful and negative therapy. Thus, the microarray analysis performed demonstrated high utility prognostic value concerning negative correlation between Class II *HLA DQB1* expression in testis and successful therapy. This phenomenon could have an impact on male infertility diagnosis and treatment.

Acknowledgements: Supported by National Science Centre, Poland, grant no. 2020/37/B/NZ5/00549.

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S13.L2

MULTI-OMIC INSIGHT INTO THE PATHOMECHANISM OF CHRONIC KIDNEY DISEASE-RELATED ATHEROSCLEROSIS

J. TRACZ[1], L. HANDSCHUH[1], M. LALOWSKI[1,2], L. MARCZAK[1], K. KOSTKA-JEZIORNY[3], B. PEREK[3], M. WANIC-KOSSOWSKA[3], A. PODKOWINSKA[4], A. TYKARSKI[3], D. FORMANOWICZ[3], M. LUCZAK[1]

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A progressive loss of functional nephrons defines chronic kidney disease (CKD). Although cardiovascular disease (CVD) complications and atherosclerosis are the leading causes of morbidity and mortality in CKD, the mechanism by which the progression of CVD accelerates remains unclear. Our study used a complementary multi-omic approach to assess mild and advanced CKD patients with different atherosclerosis stages and two groups of patients with different classical CVD progression but without renal dysfunction. We utilized LC-MS/MS-based proteomics and MS-based shotgun lipidomics approach fortified with standard laboratory analytical methods and functional bioinformatic analyses to profile CKD and CVD leukocyte and plasma proteins. We revealed dysregulation of proteins involved in different phases of leukocytes' diapedesis process that is very pronounced in CKD's advanced stage. We also showed an upregulation of apoptosis-related proteins in CKD as compared to CVD. The lipidome profiling revealed the upregulation of triacylglycerols in CKD and downregulation of cholesterol/cholesteryl esters, sphingomyelins, phosphatidylcholines, phosphatidylethanolamines and ceramides as compared to CVD group and controls. The differential abundance of selected proteins was validated by multiple reaction monitoring, ELISA, Western blotting, and at the mRNA level by ddPCR. An increased rate of apoptosis was then functionally confirmed on the cellular level. Hence, we suggest that the disturbances in leukocyte extravasation proteins may alter cell integrity and trigger cell death. Our results also revealed the putative existence of a functional causative link - the low cholesterol level correlated with lower estimated glomerular filtration rate and kidney dysfunction that supports the postulated "reverse epidemiology" theory. Therefore, we suggest that the proteomic and lipidomic background of atherosclerosis-related to CKD is unique and might be associated with other factors, i.e., inflammation.

Acknowledgements: This work was supported by the National Science Centre,Poland, under grant no. 2015/19/B/NZ2/02450, to M. Luczak.

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S13.L3

MULTIMODAL ANALYSIS IN THE SEARCH FOR NEW BIOMARKERS OF DIABETIC KIDNEY DISEASE - microRNA AND EXTRACELLULAR VESICLES

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Among number of complications caused by T2DM, chronic kidney disease (CKD) is the most common complication treating more than the one third of diabetic patients and increases the mortality risk in patients with T2DM. Early biomarkers of kidney damage, including diabetic kidney disease (DKD), are still being required, mainly based on the results of proteomic and transcriptomic analyzes. The large amount of data, both qualitative and quantitative parameters, makes it difficult to select potential biomarkers. Statistical methods (canonical analysis, principal components analysis - PCA, correlation analysis) are a helpful tool, especially in cases of multivariate data matrices provided by omics techniques. Exemplary analyzes of miroRNA typing in urine extracellular vesicles (EVs) from CKD patients and metabolomic analyzes based on infrared and Raman spectroscopy data in urine EVs from patients with various degrees of severity of diabetic kidney disease, are presented. Such multimodal strategies are examples of typing the new CKD biomarkers and showing that not only upregulated, but also downregulated parameters are significant for disease recognition. As the result, the augmented or decreased microRNAs related with CKD and unique spectral signatures are presented.

Acknowledgements: All publications, collaborations and grants supporting these projects are mentioned in the webpage: http://mvs.if.uj.edu.pl/.

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S13.L4

MULTI-OMIC APPROACH FOR PREDICTING RESPONSE TO NEOADJUVANT RADIOTHERAPY OF COLORECTAL CANCER

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Radiotherapy (RT) is a common modality in colorectal cancer (CRC) treatment. Serum/plasma proteomics and metabolomics of CRC patients could provide valuable insight into the response to RT. Though small extracellular vesicles (sEVs) are an emerging type of liquid biopsy, metabolomic and proteomic changes in sEVs of cancer patients after RT have not been given as much attention. This study aimed to describe the correlation between specific molecular components of serum/plasma as well as sEVs and CRC patient's response to RT. Plasma and serum samples were collected from 40 CRC patients treated with RT before surgery. Samples were classified into two groups, depending on the response to the treatment: group A - patients whose responded (sensitive) to RT and group B - patients not responded (resistant) to RT. sEVs were isolated from serum/plasma using size-exclusion chromatography (SEC). LC-MS/MS-based approach was used for proteomic profiling of serum and serum-derived sEVs. Metabolites extracted from plasma and plasma-derived sEVs were analyzed by the GC-MS. Proteomic and metabolomic data were subjected to chemometric and functional analysis. LC-MS/MS approach allowed the identification of 276 proteins, of which 18 and 91 differentiating sensitive (group A) and resistant (group B) serum and serum-derived sEVs samples, respectively. An untargeted GC-MS-based approach allowed the identification of 110 and 50 metabolites in plasma and plasma-derived sEVs, respectively, of which 31 metabolites overlapped. Proteins that differentiated serum samples from patients with different response to RT were mainly associated with lipoprotein and cholesterol metabolism. Differentiating proteins isolated from serum-derived sEVs were connected with vesicle-mediated transport, immunological processes, complement activation, neutrophil degranulation and cholesterol metabolism. This study revealed a specific pattern of proteins and metabolites in serum/plasma and sEVs, which could distinguish CRC patients with different response to preoperative radiotherapy. Response to radiotherapy-related changes observed in the molecular pattern of sEVs was more significant than response-related changes detected in serum/plasma molecules.

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S13.L5

DIETARY SUPPLEMENTATION WITH DIFFERENT SOURCES OF INULIN-TYPE FRUCTANS EVOKES CHANGES IN PROTEOMIC PROFILE OF PORCINE AORTA

M. MARYNOWSKA, M. OZGO, A. HEROSIMCZYK, A. LEPCZYNSKI, J. SKOMIAL, M. BARSZCZ, M. TACIAK

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Diet has long been known to play a fundamental role in regulating host health status by modulating the composition of the gut microbiota. The use of feed supplements may also be considered as a means to improve animal production performances while maintaining health and welfare. Prebiotics, especially inulin have been established as one of the effective methods to increase the intestinal health of various animal species, including pigs. However, in the literature there are no reports on indirect effects of inulin-type fructans on the physiology of aorta. We hypothesised that inulin supplementation will modulate the protein profile of the aorta in growing pigs. The study was conducted on twenty four 50-day-old PIC x Penarlan P76 crossbred male piglets. Animals were divided into 3 groups (n=8), and fed: control diet (group I), experimental diet with 2% water extract of inulin (group II) and the diet with 4% dried chicory root (group III). The aortic proteins were separated using two-dimensional electrophoresis. The protein spots showing statistically significant changes were excised from the gels and subjected to protein identification by MALDI-TOF MS. Diet supplemented with 4% of chicory root triggered changes in the expression of 32 protein spots in the porcine aorta. 23 protein spots were differentially expressed in the group of pigs fed the diet supplemented with 2% of inulin compared with the control one. Both sources of inulin-type fructans had the potential to induce a substantial changes in the expression of proteins involved in the cellular stress response (TXNDC5, CALR, TCP1, PDIA3, HSPA8), suggesting that they may play an important role in antioxidant protection process in the aorta of growing piglets. Moreover, both experimental diets induced a positive changes in the expression of aortic proteins involved in mechanisms of blood pressure regulation (RCN2, ORM1, TXNDC5), vascular tone regulation (EFEMP1) and in the process of vascular development (ANXA2), as well as those playing a key role in actin cytoskeleton organisation (VIM, VCL, ACTR3).

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S13.L6

PROTEINS OF MARE'S COLOSTRUM ASSOCIATED WITH FOAL AND MAMMARY GLAND GROWTH AND DEVELOPMENT

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Colostrum is the first secretion of the mammary gland, which is the exclusive nourishment for the infant. Colostrum is a source of micro- and macronutrients and regulatory compounds, including bioactive proteins. All these compounds are essential for the foal's growth and development. Furthermore, in colostrum are present proteins associated with mammary gland organization and secretion of milk components. In the presented research using 2-DE coupled *via* MALDI-TOF MS, we identified 49 proteins representing 27 different gene products. Due to the epitheliochorial placenta prevents the transfer of immunoglobulins the foal is born defenseless against pathogens. It needs a supply of antibodies with the colostrum, as well as the bioactive proteins necessary to regulate the maturation of its immune system. In mare's colostrum, we identified proteins associated with supporting the immune system, such as interleukin-24 isoform × 1, immunoglobulins, complement C3 alpha chain-like. To provide immunomodulating proteins in unchanged form along with colostrum are deliver protease inhibitors. In the mare's colostrum samples were presented: alpha-1-antitrypsin and fetuin-B. The protein associated with nervous system development (ankyrin repeat domain-containing protein 6) was also present in the mare's colostrum. Furthermore, we identified proteins involved in various components transport, including iron, calcium, and vitamin D (albumin, serotransferrin, neuron-specific calcium-binding protein hippocalcin, vitamin D-binding protein). The development of the mare's mammary gland is a complex process that occurs during embryogenesis, puberty, pregnancy, and lactation. In mare's colostrum were identified proteins that are associated with the maturation of the mammary gland and the secretion of milk components: partitioning defective 3 protein homolog isoform X2 (PARD3/Par3) and FERM domain-containing protein 4B isoform X1 (FRM4B), rho GTPase-activating protein 39 (ARHGAP39), beta-lactoglobulin-1. Further analysis of mare's colostrum and milk will allow identified more proteins that are involved in the postnatal development of foals and proteins associated with synthesis and secretion of milk components. Determine the changes in the protein profile of mare's milk following days of lactation will allow a better understanding of the processes occurring in the mare's mammary gland and will clarify how changes in the composition of the bioactive proteins of the milk affect the growth and development of the foal.

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SESSION XIV

PHYSIOLOGY MEETS ENGINEERING

Friday (September 17, 2021; 9:00 – 11:55)

Chair:

Prof. Teresa Malecka-Massalska
Department of Human Physiology, Medical University in Lublin, Lublin, Poland

Assoc. Prof. Teodor Buchner
Faculty of Physics, Warsaw University of Technology, Warsaw, Poland

DETAILED SESSION XIV SCHEDULE

Opening lectures (Friday, September 17, 2021; 9:00 – 9:50; *virtual stream A*)

S14.L1 TISSUE ELECTRIC IMPEDANCE MEASUREMENTS: FROM PROPER UNDERSTANDING OF PHYSICS TONE TO NEW FUTURE IN CLINIC. **T. Buchner** (Faculty of Physics, Warsaw University of Technology, Warsaw, Poland).

S14.L2 ELECTRICAL PARAMETERS OF BIOLOGICAL SYSTEMS (ECIS TECHNIQUE) IN THE STUDY OF THE CHEMOPREVENTIVE AND THERAPEUTIC POTENTIAL OF SUBSTANCES OF BIOLOGICAL ORIGIN. **M. Prendecka-Wrobel[1], A. Kociubinski[2]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Faculty of Electrical Engineering and Computer Science, Department of Electronics and Information Technology, Lublin University of Technology, Lublin, Poland).

Oral presentations (Friday, September 17, 2021; 9:55 – 10:45; *virtual stream A*)

S14.L3 MACHINE LEARNING FOR PREDICTING THE OCCURRENCE OF SYMPATHETIC BURSTS BASED ON THE NONINVASIVE RECORDING OF CARDIOVASCULAR PARAMETERS. **B. Paleczny[1], R. Seredynski[1], A. Siennicka[1], A. Kotwica[2], R. Zygala[2], M. Pondel[2], M. Sinski[3], J. Lewandowski[3], B. Ponikowska[1]** ([1]Wroclaw Medical University, Wroclaw, Poland, [2]Wroclaw University of Economics and Business, Wroclaw, Poland, [3]Medical University of Warsaw, Warsaw, Poland).

S14.L4 MALE REPRODUCTIVE FUNCTION UNDER CONDITION OF TREATMENT WITH GOLD ANOCOMPOSITES. **O. Kaleinikova[1], S. Ukrainska[1], V. Sribna[1], Y. Kuziv[2], A. Vinogradova-Anyk[3], I. Karvatskiy[3], T. Voznesenskaya[1], T. Blashkiv[1], N. Kutsevol[2]** ([1]Bogomoletz Institute of Physiology, NAS of Ukraine, Kyiv, Ukraine, [2]Taras Shevchenko National University of Kyiv, Kyiv, Ukraine, [3]Bogomoletz National Medical University, Kyiv, Ukraine).

S14.L5 STABILIZATION OF PHYSIOLOGICAL FUNCTIONS OF CELLS IN THE ECIS ELECTRODE SYSTEM METALLIZED WITH CHROMONIKELIN AND COPPER. **M. Prendecka-Wrobel[1], A. Kociubinski[2], T. Malecka-Massalska[1]** (Department of Physiology, Medical University of Lublin, Poland; Lublin University of Technology, Faculty of Electrical Engineering and Computer Science, Lublin, Poland).

Session summary

Poster session (Friday, September 17, 2021; 11:05 – 11:55; *virtual stream C*)

S14.P1 ASYMMETRIC PROFILE OF SPONTANEOUS SEQUENTIAL CHANGES OF BLOOD PRESSURE COUPLED WITH MONOTONIC CHANGES OF SUCCESSIVE HEARTBEATS IN UNRESTRAINED NORMOTENSIVE RATS. **S. Zajaczkowski, T.H. Wierzba** (Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S14.P2 IMPAIRED BLOOD PRESSURE REGULATION IN SHR RATS ASSESSED BY DETAILED ANALYSIS OF MONOTONIC RUNS OF BLOOD PRESSURE AND HEART RATE. **T.H. Wierzba, K. Malinowski, G. Redlarski** (Department of Physiology, Medical University of Gdansk, Gdansk, Poland).

S14.P3 HOW DATA SCIENCE MAY SUPPORT PHYSIOLOGICAL EXPERIMENTS? A REVIEW OF EXAMPLES AND POSSIBILITIES. **A. Siennicka[1], B. Paleczny[1], R. Seredynski[1], M. Pondel[2], M. Wyciszkiewicz[1], T. Okupnik[1], B. Ponikowska[1]** ([1]Wroclaw Medical University, Wroclaw, Poland, [2]Wroclaw University of Economics and Business, Wroclaw, Poland).

S14.P4 CARDIAC AND NON-CARDIAC SOURCES OF T WAVE MORPHOLOGY. **K. Rams[1], M. Ozimek[1], M. Andrzejewska[1], T. Buchner[1]** ([1]Faculty of Physics, Warsaw University of Technology, Warsaw, Poland).

S14.P5 HEART RATE DYNAMICS IRREVERSIBILITY AND INFORMATION FLOW IN TYPE 1 LQTS PATIENTS UNDER BETA BLOCKER TREATMENT. **M. Andrzejewska, M. Ozimek, J.J. Zebrowski, K. Rams, T. Buchner** (Faculty of Physics, Warsaw University of Technology, Poland).

S14.L1

TISSUE ELECTRIC IMPEDANCE MEASUREMENTS: FROM PROPER UNDERSTANDING OF PHYSICS TO NEW FUTURE IN CLINIC

T. BUCHNER

Faculty of Physics, Warsaw University of Technology, Warsaw, Poland

Attempting to answer a seemingly simple question: how fast is the ECG signal? We ran at many interesting contradictions, concerning the physical nature of biopotential. What does actually change in tissue when the biopotential propagates to the electrode? This area, shared between clinicians, (electro)physiologists, neurophysiologists, bioengineers, electrochemists and biophysicists is a real Tower of Babel, where each specialty speaks its own language. Solving the riddle of biopotential by means of a new molecular biopotential theory seems to simplify our understanding of bioelectrical phenomena on systemic level. Basic phenomena, which constitute a foundation for propagation of biopotentials are outlined. The unequivocally believed volume conductor theory is opposed on anatomical basis. Relation between conductance an polarization is shown, with its crucial consequence: the relation between biopotential propagation and impedance spectrum. Some consequences concerning clinical applications are drawn: various patophysiological states have altered conductance response: from epilepsy, tumors (and other states of pronounced angiogenesis), arrhythmogenic myocardial scars to extravascular lung water and ventillation- perfusion ratio. Caveats, which also exist, include impedance cardiography and total body water measurements, which are very promising and quite widespread, but constantly suffer from poor measurement model. What is provoking in this theory is its simplicity, which allows its wide usage: from basic science to clinical intuition, which supplements the diagnosis. It is tempting to conclude, that if we change the paradigm, the full diagnostic power of impedance methods will be unleashed.

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S14.L2

ELECTRICAL PARAMETERS OF BIOLOGICAL SYSTEMS (ECIS TECHNIQUE) IN THE STUDY OF THE CHEMOPREVENTIVE AND THERAPEUTIC POTENTIAL OF SUBSTANCES OF BIOLOGICAL ORIGIN

M. PRENDECKA-WROBEL[1], A. KOCIUBINSKI[2]

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The thesis of the presentation is based on literature reports indicating possible therapeutic and chemopreventive activity of substances of biological origin and the probability of showing the character of these effects using selected electrical parameters, i.e. impedance, resistance and cell membrane capacity. Therapeutics and chemopreventive substances work in various ways including induction of apoptosis of pathologically altered cells. This group of biological substances includes antioxidants, vitamin A, fungal extracs and lycopene among others. Compared to other methods of for e.g. cancer prevention, chemoprevention is associated with lower costs, no invasiveness and utilization of easily accessible natural components, which is very important from both social and economic perspective. And the potential of medical fungi has not been fully used in chemoprevention yet. Literature reports say that medical fungi include a series of bioactive substances, which have been used mainly in textile and paper industry so far. In the face of new technical possibilities and assuming, that changes in the electrical properties of cells precede changes on the biochemical level, it would be very interesting to examine the character and dynamics of changes leading to desirable therapeutic or chemopreventive effects. It is possible with monitoring of selected electrical parameters i.e.: impedance, resistance and capacity of cell membrane in real time after application of chosen bioactive compounds to the examined cell lines. Resistance is a physical quantity describing relations between electric current voltage and strength in direct current circuits. It is commonly depicted with letter R and its SI unit is Ω (ohm). In direct current circuits resistance is directly proportional to voltage between the extremes of the conductor and inversely proportional to the strength of electric current but this correlation, known as the Ohm's Rule, is only valid in certain ranges of voltage value. Impedance is a quantity characterizing the correlation between electric current voltage and strength in alternate current circuits (opposite to resistance where direct current circuits are used). It is described as a complex function, which, for alternate current with frequency ω is expressed using the following formula:

$Z(\omega) = R(\omega) + iX(\omega)$, where $X(\omega)$ is reactance, which can be also transcribed as:

$Z(\omega) = |Z|e\text{-}j\varphi$, where φ is phase shift between current voltage and strength.

Electric capacity is considered, to be a physical quantity equal to the ratio of charge collected on the conductor to the potential of the conductor. Understanding the interaction of cells with biological substances and reflecting these changes in electrical parameters is a fascinating and hugely promising challenge.

S14.L3

MACHINE LEARNING FOR PREDICTING THE OCCURRENCE OF SYMPATHETIC BURSTS BASED ON THE NONINVASIVE RECORDING OF CARDIOVASCULAR PARAMETERS

B. PALECZNY[1], R. SEREDYNSKI[1], A. SIENNICKA[1], A. KOTWICA[2], R. ZYGALA[2], M. PONDEL[2], M. SINSKI[3], J. LEWANDOWSKI[3], B. PONIKOWSKA[1]

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The development of the microneurography technique in the 1960s was a milestone for autonomic neuroscience. Microneurography includes the percutaneous insertion of the needle-like microelectrode into the peripheral nerve, which enables direct intraneural recording of sympathetic outflow to the vasculature of the muscles (muscle sympathetic nerve activity, MSNA) in conscious humans. However, it is a technically demanding procedure characterized by a high ratio of failed attempts and prolonged recordings (>1 h) are contraindicated due to safety reasons. These limitations can be overcome by employing machine learning (ML) to retrieve the MSNA signal from physiological correlates of MSNA (i.e. total peripheral resistance) recorded simultaneously and noninvasively. We attempted to use ML to reconstruct the occurrence of MSNA bursts from the cardiovascular parameters recorded simultaneously and noninvasively. The 10-minute recording of the following signals: (1) multi-unit MSNA (raw and integrated), (2) arterial blood pressure waveform (recorded by the Nexfin monitor), (3) III-lead limb ECG, and (4) hemodynamic variables derived from the blood pressure waveform (systolic, diastolic, and mean blood pressure and total peripheral resistance), collected from a healthy volunteer was used. The Gradient Boosting (XGBoost) algorithm was employed for the prediction of the MSNA bursts occurrence. The recording was divided into two sets: the training set (60% of the whole recording), and the test set (40%). The Gradient Boosting algorithm accurately predicted the occurrence of 71.8% of the MSNA bursts in the test set. The preliminary results obtained with the non-optimized algorithm are encouraging and suggest that it is feasible to reconstruct the occurrence of the MSNA bursts from the simultaneous noninvasive recordings of the cardiovascular parameters, at least with moderate accuracy.

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S14.L4

MALE REPRODUCTIVE FUNCTION UNDER CONDITION OF TREATMENT WITH GOLD NANOCOMPOSITES

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Recently, it has been proved that polymers with a dextran core and grafted polyacrylamide chains dextran-polyacryl-amide (D-PAA) are effective in photodynamic chemotherapy, which gives confidence in the prospect of drug-nanosystem. This study aim is to evaluate the influence of a five-time treatment of polymers with a dextran core and grafted polyacrylamide chains dextran-polyacrylamide (D-PAA and D-PAA(PE)), as well as gold nanoparticles in the composition of such polymer matrices on the male reproductive function in mice. Experiments were carried out with the use of adult male albino Albino mice (weighing 25–30 g). We used an „uncharged" star-shaped polymeric matrices of D-PAA (dextran-polyacrylamide) and „charged" D-PAA(PE) (dextran-polyacrylamide polyelectrolyte). Hydrodynamic dimensions of both types of macromolecules are 70–80 nm. The size of the Au nanoparticles loaded in D-PAA, 2–5 nm, and the nanosized gold synthesized in D-PAA(PE) has sizes 4–11 and 16–20 nm. Au nanoparticles have a spherical shape. The obtained data indicate the disorder of the reproductive function of males under the conditions of five times intravenous treatment with gold nanoparticles in the polymer matrix D-PAA(PE), namely - there are significant changes in the viability and death of cells of different generations of spermatozoa and an increase in pre- and postimplantation embryonic mortality and a decrease in the number of live fetuses per female. Whereas, under the conditions of such administration, the introduction of D-PAA and D-PAA(PE), as well as AuD-PAA, no significant changes were observed in: 1) sperm and abnormal sperm forms (%); 2) spermatocytes (primary) and spermatids (%); 3) living, apoptotic and necrotic testicular cells (spermatocytes (primary)) and in the epididymis cells (spermatozoa); as well as in: 4) pre- and post-implantation mortality of embryos; and 5) the number of live newborns (pups).

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S14.L5

STABILIZATION OF PHYSIOLOGICAL FUNCTIONS OF CELLS IN THE ECIS ELECTRODE SYSTEM METALLIZED WITH CHROMONIKELIN AND COPPER

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Looking for an alternative to the currently used one gold, currently used in measuring plates for testing the electrical parameters of cells in the system ECIS. This work focuses on the interesting materials such as chrome nickel and copper. The aim of the conducted research was to determine the effect of chromonikelin and copper on the growth of cell culture during *in vitro* testing. In addition, specifying under what conditions the use of a given material will be sufficient and will open up new development paths. As part of the research work, chromonikelin and copper comb capacitors on biocompatible substrates were designed and manufactured. Metallization layers were deposited by magnetron sputtering on various materials. In the experiment cells from the mouse fibroblast line - NCTC clone 929 [L cell, L-929, strain L derivative] (ATCC® CCL-1™) from the American Type Culture Collection were used. During the cultivation, cell impedance measurements were performed and recorded. The best results were obtained on polycarbonate substrates, meeting all the defined requirements, incl. biocompatibility and resistance to chemical solutions used during technological works. The designed geometry of the comb capacitors was obtained by the photolithography process. Preliminary results of measurements on the plates have shown that it is possible carrying out the cultivation on chromonikelin and copper electrodes. No problems with proliferation and viability of cells were observed on the test plates. The obtained results make it possible to assess the possibilities of using chromonikelin and copper in various biotechnological applications.

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S14.P1

ASYMMETRIC PROFILE OF SPONTANEOUS SEQUENTIAL CHANGES OF BLOOD PRESSURE COUPLED WITH MONOTONIC CHANGES OF SUCCESSIVE HEARTBEATS IN UNRESTRAINED NORMOTENSIVE RATS

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An intriguing physiological phenomenon is occurrence of short periods of monotonic beat-to-beat changes of systolic blood pressure (SBP, increasing or decreasing runs) accompanied by unidirectional runs of RR intervals (RRi deceleration or acceleration). The study was performed to assess the occurrence of spontaneous sequential changes in BP coupled with monotonic changes of intervals of successive heartbeats (RR intervals; RRi) in rats in resting conditions. The experiments were performed on unrestrained male Wistar rats (N=11, 300–350 g). ECG and systolic blood pressure (SBP) were recorded continuously at sampling rate 1.5 kHz. Sequences of 3 to 6 unidirectional changes of SBP and RRi were identified. Proportion of the SBP sequences coupled to the monotonic changes of RRi time-series was taken as an index of baroreflex sensitivity (BRS). Sequences of SBP increase or decrease were analyzed separately. Two types of SBP sequences were discriminated: the concordant, in which SBP and RRi changed in the same direction (considered the baroreflex effect), and the opposite, where changes of SBP coincided with inverse changes in RRi (regarded as a feed-forward cardiovascular setting). Proportion of the baroreflex-related (concordant) SBP sequences to all SBP sequences were taken as baroreflex efficacy (BEI). SBP was 134 ± 5 mmHg and HR 181 ± 6 bpm. The sequences of an increase of SBP involved 10.1% of all cardiac cycles and were more frequent than its declining (7.4%). RRi prolongation sequences (10.5%) were less frequent than those of RRi shortening. Proportion of RRi sequences coupled with SBP-increase sequences was about 69% higher in the feed-forward sequences (^SBP and ¡RRi than in the concordant ones (^SBP and ^RRi). In contrary, the feed-forward sequences of SBP decrease (¡SBP and ^RRi) occurred less frequent than the opposite ones (¡SBP and ¡RRi). Spontaneous variability of SBP and RRi have a well-determined irregularity. More frequent attempts to adjust high blood pressure are coordinated with an increased reflex control against its reduction. Analysis of the beat-to-beat fluctuations of SBP and RRi revealed non-random pattern of spontaneous hemodynamic oscillations. It is recommended, in light of non-uniform profile of sequential beat-to-beat changes of RRi and SBP, that the sequences of either an increase or a decrease of SBP should be analyzes separately.

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S14.P2

IMPAIRED BLOOD PRESSURE REGULATION IN SHR RATS ASSESSED BY DETAILED ANALYSIS OF MONOTONIC RUNS OF BLOOD PRESSURE AND HEART RATE

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Spontaneously hypertensive rats (SHR) represent experimental model corresponding to human hypertension of mostly neurogenic background. Observation of spontaneous fluctuations and coherence between major hemodynamic variables such as systolic blood pressure (SBP) and heart rate (HR) offers an advanced insight to the regulatory aspects of hypertension. The study was performed to compare the occurrence of spontaneous sequential changes in SBP coupled with monotonic changes of intervals of successive heart cycles (RR intervals; RRi). ECG and systolic blood pressure (SBP) were recorded at sampling rate 1.5 kHz in previously instrumented (insertion of arterial line, ECG electrodes) conscious male spontaneously hypertensive rats (SHR; n=7; 306–344 g), and their respective control (WKY; N=7; 302–355 g). Sequences (Seq) of 3 to 6 unidirectional changes of SBP and HR were identified. Proportion of the SBP sequences coupled to the HR (cSeq) ones was taken as an index of baroreflex sensitivity (BRS). Two types of cSeq were discriminated: the concordant, in which SBP and HR changed in the same direction (interpreted as a feed-forward baroreflex setting), and the opposite (considered the baroreflex effect), where changes of SBP coincided with inverse changes in HR. Proportion of the baroreflex related SBP sequences to all cSeq sequences were taken as baroreflex efficiency (BEI). SHR exhibited higher SBP and lower HR than WKY (191 vs. 135 mm Hg; 307 vs. 319 beats/min). Compared to the WKY control, in SHR rats: 1) frequency of runs of an increase of SBP was higher, while occurrence of sequential SBP decrease was lower; 2) higher frequency of HR acceleration with lower deceleration runs was observed; 3) higher BEI of an increase of SBP, and lower BEI for a SBP decrease was found. In SHR the latency between the beginning of an increase of SBP and the onset of the following monotonic HR runs was prolonged. BRS was reduced in either cSeq of an increase and a decrease of SBP. Our data indicate profound regulatory dysfunction in SHR rats. The observed regulatory profile reflects reduced chance for the reflex correction of an increase in blood pressure, with impaired counter-regulatory defense against its decrease. Moreover, an increased phase shift between the HR and SBP reflex responses may promote sudden critical cardiovascular incidents.

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S14.P3

HOW DATA SCIENCE MAY SUPPORT PHYSIOLOGICAL EXPERIMENTS? A REVIEW OF EXAMPLES AND POSSIBILITIES

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Nowadays, scientific research in the field of life sciences, including human physiology, is carried out with the use of numerous devices (such as monitors of blood pressure, ECG, muscle tension analysers, pulsoximeters, breathing gas analysers etc.), which are able to collect data in digital form. As a result of an enormous sensitivity and accuracy of the measurements performed during each physiological examination, single test or experiment can serve as a source of huge amounts of data. At the same time, the classic approach to experiments and analysis based on statistics (comparison of values before and after the intervention, correlation analysis) excludes taking full advantage of the amount of collected digital information. During a cooperation with specialists in the field of data science, we decided to transfer some solutions based on modern methodology of large data-sets analyses to physiological experiments in the field of autonomic regulations of cardiovascular and respiratory systems at rest as well as during an exercise, which are carried out within the Department of Physiology and Pathophysiology of WMU. The attempts which were made to date show that data science (including methods such as collective clustering, neural networks, association rules, machine learning, deep learning and related) can be widely used in analyzing physiological data, which may include: forming predictions (eg. predicting a missing signal from another signal or predicting changes of signals based on their initial values and changes registered during first seconds of the examination) proposing more precise methods of signal filtering and many other applications.

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S14.P4

CARDIAC AND NON-CARDIAC SOURCES OF T WAVE MORPHOLOGY

K. RAMS, M. OZIMEK, M. ANDRZEJEWSKA, T. BUCHNER

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When the morphology of the ECG is analyzed, there is often a tendency to interpret the observed symptoms as a sole result of electric activity of cardiac muscle, and to treat all the factors that modify the ECG as environmental noise, even if it is a symptom itself, as for pericarditis or P pulmonale. In order to circumvent these opinions we have performed a thorough analysis of patients in THEW database - Holter ECG, 200 Hz sampling, 24 h signals. Study group consists of 235 patients: 125 healthy, 86 w/LQTS1, 21 w/LQTS2, 2 w/LQTS3. Gender ratio was close to 0.5 with 129 females, and 106 males. We started from a detailed analysis of QT/RR relationship and we found that the idea of restitution: i.e the dominant role of the APD/DI relation on the whole QT and RR dynamics does not hold, as each of signals may exhibit a certain extent of its own dynamics. Of special importance are the QT increases at increasing HR, which correspond to the negative QT(RR) regression slope (Baranowski, Buchner, *European Heart J* 2003). They may appear as isolated islands in QT-RR plot. It is an open question whether this discrepancy may be interpreted as a symptom of ischemia (J.M. Starobin, Y.B. Chernyak, US patent 6,361,503). We also show, that the amplitude of the T wave does not directly follow the amplitude of the QRS, so these two variables are to some extent statistically independent. This means, that the T wave possesses a different source of information, not necessarily related to both the interval and the amplitude of the QRS. This well corresponds to the clinical value of T-wave axis, both in CAD patients (Scherer *et al*., *Scand Cardiovasc J* 2009) and in population with high prevalence of Chagas disease (Moraes *et al*., *Am J Cardiol* 2018). Postural changes of ST-T may even mimic myocardial ischemia (Lachman *et al*., *Circulation* 1965). The question of the origin of the observed changes, their relation to the position of the body and their potential clinical correlates is a matter of an ongoing study.

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S14.P5

HEART RATE DYNAMICS IRREVERSIBILITY AND INFORMATION FLOW IN TYPE 1 LQTS PATIENTS UNDER BETA BLOCKER TREATMENT

M. ANDRZEJEWSKA, M. OZIMEK, J.J. ZEBROWSKI, K. RAMS, T. BUCHNER

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There is a big question of statistical independence in physiological timeseries: which physiological variables can be treated as independent sources of clinical data and which just mimic each other. Another question concerns time-irreversibility: is the studied signal a sum of responses to some unknown stimuli? In such a case the time symmetry of the signal is broken due to signal causality constraint. We decided to answer this question on a big database of Holter recordings. Two databases from the THEW Project were used to provide the RR, QT and the DI intervals: E-HOL-03-0202-003 (202 ECG of healthy individuals) and E-HOL-03-0480-013 (480 ECGs of the Long QT Syndrome patients forming 4 subgroups by genotype). In this paper, we analyze only the LQTS1 patients - this is the most frequent type of the long QT syndrome. We limited the study group to age subgroup 18–50 years obtaining 84 (42 women) ECGs for the healthy and 65 (45 women) cases for the LQTS1 case (Ozimek *et al*., 2021). The results show, that with $p < 0.01$ both irreversibility and information flow shows no response to beta blocker treatment. This result indirectly shows, that the key factor, which determines such quantities of the signal as its irreversibility and information flow is the parasympathetic nervous system, at least in LQTS 1 patients. Typically, the role of sympathetic nervous system in baroreflex is emphasized, note, however, that for Anrep *et al*. regulation of right atrium pressure was the method to set the vagal tone in dog experiments (Anrep 1936). Hence, we support the opinion on a dominant role of parasympathetic over sympathetic mechanisms, expressed by Karemaker and Wesseling (Cardiovasc Eng, 2008).

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SESSION XV

MISCELLANEA

Thursday (September 16, 2021; 10:15 – 11:20)
Friday (September 17; 2021; 12:00 – 13:05)

Chair:

Prof. Pawel Winklewski
Department of Human Physiology, Medical University of Gdansk, Gdansk, Poland

Assoc. Prof. Tomasz Wierzba
Department of Physiology, Medical University of Gdansk, Gdansk, Poland

DETAILED SESSION XV SCHEDULE

Opening lecture (Thursday, September 16, 2021; 10:15 – 10:45; *virtual stream A*):

S15.L1 WHAT THE P-VALUE IS, AND WHAT IT IS NOT. **J. Piskorski** (Institute of Physics, University of Zielona Gora, Zielona Gora, Poland).

Oral presentations (Thursday, September 16, 2021; 10:45 – 11:20; *virtual stream A*):

S15.L2 THE ASSESMENT OF THE BIDIRECTIONAL INFORMATION TRANSFER BETWEEN BLOOD PRESSURE AND HEART RATE. **G. Graff[1], B. Graff[2], K. Tessmer, K. Narkiewicz[2]** ([1]Gdansk University of Technology, Faculty of Applied Physics and Mathematics, Gdansk, Poland, [2]Medical University of Gdansk, Department of Hypertension and Diabetology, Gdansk, Poland).

S15.L3 REAL TIME ANALYSIS OF PHYSICAL ACTIVITY AND QUALITY OF SLEEP (PAS STUDY) IN EARLY AND LATE NIGHT EATER HYPERTENSIVE PATIENTS WITH TYPE 2 DIABETES, USING WEARABLE FITNESS TECHNOLOGY. **S. Rastogi, N. Verma** (King George's Medical University, Lucknow, India).

Questions and answers

Poster session (Friday, September 17; 2021; 12:00 – 13:05; *virtual stream C*):

S15.P1 THE USE OF GASEOUS HYDROGEN IN THE TREATMENT OF SARS-COV-2 VIRUS INFECTION. **K. Michalak** (Adam Mickiewicz University in Poznan, Laboratory of Vision Science and Optometry, Poznan, Poland).

S15.P2 THE ROLE OF NEUROTENSIN AND ENDOMORPHIN PATHWAYS IN THE ANTI-INFLAMMATORY ACTION OF PK20 HYBRID IN MOUSE MODEL OF NON-ATOPIC ASTHMA. **E. Russjan[1], D. Zajac[1], D. Sulejczak[2], P. Kleczkowska[3,4], K. Kaczynska[1]** ([1]Department of Respiration Physiology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [2]Department of Experimental Pharmacology, Mossakowski Medical Research Institute, Polish Academy of Sciences, Warsaw, Poland, [3]Department of Pharmacodynamics, Centre for Preclinical Research (CBP), Medical University of Warsaw, Warsaw, Poland, [4]Military Institute of Hygiene and Epidemiology, Warsaw, Poland).

S15.P3 ANALYSIS OF ANTIOXIDANT ENZYMES IN PATIENTS WITH NEUROENDOCRINE NEOPLASMS OF THE LUNG, GASTROINTESTINAL TRACT AND PANCREAS. **M. Budek, J. Nuszkiewicz, K. Szewczyk-Golec** (Department of Medical Biology and Biochemistry, University Nicolaus Copernicus in Torun, Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland).

S15.P4 THE INFLUENCE OF ANTIMICROBIAL NEUTROPHIL EXTRACT AND PENTOXIFYLLINE ON OVINE NEUTROPHILS ISOLATED DURING THE INSERTION TITANIUM IMPLANT IN A SHEEP MODEL. **J. Zdziennicka[1], J. Wessely-Szponder[1], T. Szponder[2], M. Latalski[3]** ([1]Sub-Department of Pathophysiology, Department of Preclinical Veterinary Sciences, Faculty of Veterinary Medicine, University of Life Sciences, Lublin, Poland, [2]Department and Clinic of Animal Surgery, Faculty of Veterinary Medicine, University of Life Sciences, Lublin, Poland, [3]Department of Pediatric Orthopedics, Medical University, Lublin, Poland).

S15.P5 miR 511-5p EXPRESSION AS A PREDICTOR OF NUTRITIONAL STATUS DISORDERS IN PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPHY DUE TO HEAD NECK CANCER. **M. Mazurek[1], R. Mlak[1], I. Homa-Mlak[1], T. Powrozek[1], A. Brzozowska[2], T. Malecka-Massalska[1]** ([1]Department of Human Physiology, Medical University of Lublin, Poland, [2]II Department of Radiotherapy, Center of Oncology of the Lublin Region St. John of Dukla, Poland).

S15.P6 SILICON - A NOT-ESSENTIAL ELEMENT? **M. Blaszczyk** (University of Applied Sciences in Nysa (PWS-Nysa), Nysa, Poland).

S15.P7 SPATIAL ORIENTATION IN ADOLESCENTS. **K. Pagava[1], H. Phagava[2]** ([1]Department of Child and Adolescent Medicine, Tbilisi State Medical University, Tbilisi, Georgia, [2]Department of Epidemiology and Biostatistics, Tbilisi State Medical University, Tbilisi, Georgia).

S15.P8 HOW VISION AFFECTS OUR TASTE SENSITIVITY? **P. Redmer, E. Leszkowicz** (Department of Animal and Human Physiology, University of Gdansk, Gdansk, Poland).

S15.L1

WHAT THE P-VALUE IS, AND WHAT IT IS NOT

J. PISKORSKI

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June 10, 2016 the American Statistical Association published the official statement on what the P-value and statistical significance are. This could be considered strange and unnecessary - everyone has been using the P-value and the concept of statistical significance for decades. However, in the view of the ASA, as well as many others, these concepts are not well understood. This has led to the „reproducibility crisis“ which has rendered whole branches and subbranches of the biomedical sciences useless. In this lecture we will tackle the problem of the interpretation of the P-value and statistical significance, their usage, some of the misconceptions related to these concepts as well as the recommendations of the ASA on their correct usage.

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S15.L2

THE ASSESMENT OF THE BIDIRECTIONAL INFORMATION TRANSFER BETWEEN BLOOD PRESSURE AND HEART RATE

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In patients with cardiovascular diseases the cardiovascular regulation is often altered which might negatively impact the prognosis. Previous studies have shown that methods based on the information transfer concept might be useful in the assessment of bidirectional influences of heart rate (HR) and blood pressure (BP). The aim of the study was twofold: first, to test if the methods based on transfer entropy computed for 20-minutes recordings of ECG and blood pressure are able to differentiate groups of normotensive volunteers and hypertensive patients and second, to check what are most important cardiovascular factors which are related to the values of transfer entropies. Bidirectional interaction between heart rate and blood pressure seems to be decreased in patients with hypertension. Information transfer between BP and HR is related to age, blood pressure variability and vascular properties. The prevailing direction of the information flow did not differ in both groups.

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S15.L3

REAL TIME ANALYSIS OF PHYSICAL ACTIVITY AND QUALITY OF SLEEP (PAS STUDY) IN EARLY AND LATE NIGHT EATER HYPERTENSIVE PATIENTS WITH TYPE 2 DIABETES, USING WEARABLE FITNESS TECHNOLOGY

S. RASTOGI, N. VERMA

King George's Medical University, Lucknow, India

In India, the incidence of hypertension and type 2 diabetes is very high. Invariably, patients of both diseases come to the Out Patient Department (OPD) regularly. PAS study aims to study the effect of walking 8000 steps five days a week on various parameters in early and late night eater hypertensive patients with type 2 diabetes, to study the effect of early and late meal intake on the quality of sleep in early and late night eater hypertensive patients with type 2 diabetes and to draw an inference regarding the compliance of early and late night eaters on the above parameters. One hundred patients from OPD-Endocrinology, King George's Medical University in Lucknow, were randomly divided into 2 groups of 50 patients each: first group of early night eaters (TRM group) and the second group of late night eaters. Anthropometric parameters like height, weight, neck size, waist, hip size, waist hip ratio, BMI and biochemical parameters blood sugar fasting, post-prandial, HbA1c, blood pressure, systolic, diastolic and heart rate were measured in the first visit and then after 6 months. Patient was then, made to wear MI Fit, a wearable real time tracker of heart rate, quality of sleep, pedometer, modes of walking, swimming, training on treadmill, exercise mode which the user can change according to whichever physical activity he or she is doing. Data was received on the mobile app of MI Fit on the phone of the owner of the Fit band *via* blue tooth. Subjects wore the band for 10 days, then data was collected and analysed. Standard Convention Treatment of diabetes was followed by both groups of patients. Mean arterial pressure, pulse rate, diastolic blood pressure, waist and neck size were not significantly different. BMI, hip size, systolic blood pressure, HbA1c, blood sugar (fasting and post-prandial) were significantly different ($p < 0.05$). The average heart rate of TRM was 86.89 beats per minute vs. 92.46 beats per minute control group. Quality of sleep in both groups was markedly different with deep sleep approximately 1 hour more in early night eaters, time for which a patient was awake at night was 25 mins in TRM group and 1 hour 29 min in control group. Early night eaters were more compliant in their goal of walking 8000 steps daily when compared to late night eaters. This study shows that time restricted meal intake holds the potential and is a promising method which can be used as an adjunct along with the standard treatment been given to patients of type 2 diabetes. It is one of the first studies which have been undertaken in Indian hypertensive and type 2 diabetes patients, correlating the quality of sleep, sugar and blood pressure control with the time of dinner and physical activity in Indian patients.

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S15.P1

THE USE OF GASEOUS HYDROGEN IN THE TREATMENT OF SARS-COV-2 VIRUS INFECTION

K. MICHALAK

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Sars-Cov-2 virus can provoke an inflammatory storm by excessively activating the immune system, causing severe inflammatory damage to the lungs and extrapulmonary tissue, which is also the main cause of death. It is postulated that the spike protein S of Sars-Cov-2 possesses the activity of neuraminidase being able to cut off the sialic acid molecules on the surface of lymphocytes and causing their activation. On the other side, angiotensin-converting enzyme 2 aminopeptidase (ACE-2), the human receptor for SARS-CoV-2 cell entrance is reduced on the surface of human cells during infection leading to overactivity of angiotensin II. This causes further regulatory metabolic disturbances including bronchial smooth muscle constriction, blood clothing and inflammation storm. Gaseous hydrogen is a novel molecule being potentially useful in the treatment of Sars-Cov-2 virus infection. Its metabolic activity of confines the reduction of inflammatory cytokines: IL-1a, IL-1b, IL-6, IL-8, IL-10, TNF-α, Fas, FasL, INF-γ, NF-κB; activation of antioxidative system: NRF-2, HO-1; reduction of endoplasmatic reticulum stress factors: GRP78, TRAF2; reduction of ROS and RNS levels: OH*, $ONOO^-$; activation of OXPHOS in mitochondria, reduction of apoptosis: increase of BCL-2, Bcl-xL and decrease of BAX, caspase-3, -8 and -12; reduction of pyroptosis, ferroptosis and autophagy. Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (7^{th} edition) issued by China National Health Commission recommended the inhalation of oxygen mixed with hydrogen gas (33.3% O2 and 66.6% H_2), bringing H_2 to the forefront of contemporary therapeutic medical gas research.

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S15.P2

THE ROLE OF NEUROTENSIN AND ENDOMORPHIN PATHWAYS IN THE ANTI-INFLAMMATORY ACTION OF PK20 HYBRID IN MOUSE MODEL OF NON-ATOPIC ASTHMA

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Hybrid compounds represent a new approach in experimental models of different diseases. One of such compounds is PK20 hybrid, which comprises two structural elements - endomorphin-2 and neurotensin pharmacophores. It has been proven that PK20 exhibits anti-inflammatory activity in non-allergic asthmatic mice, however the exact mechanism of its action remain unexplained. The object of the present study was to assess the contribution of opioid and neurotensin pathways in beneficial effects of tested hybrid by using a murine model of non-atopic asthma. Airway hyperresponsiveness (AHR) to methacholine nebulization, infiltration of inflammatory cells (including neutrophils) in bronchoalveolar lavage fluid (BALF), concentration of pro-inflammatory cytokines in BALF and lungs, levels of malondialdehyde and mouse mast cell protease in lung tissue, and activity of secretory phospholipase 2 were determined in five experimental group. The experimental design included negative and positive control mice, a group treated with PK20 hybrid and mice in which PK20 injection was preceded by pretreatment with mu opioid (naloxone hydrochloride) and neurotensin receptor NTS_1 (SR142948) antagonists to show involvement of particular pathways in anti-inflammatory activity of the hybrid. Inhibition of neurotensin NTS_1 or mu opioid receptors did not affect PK20 activity in terms of alleviating AHR. On the other hand, BALF cell studies revealed that advantageous effects of hybrid is related to the activation of NTS_1 receptor. In turn, in cytokine and biochemical analysis, the results differ significantly. In part of the studies, both pathways (endomorphin or neurotensin) contributed to PK20 action, in other only one type of receptors was responsible for the obtained effect or pretreatment with both antagonists did not alter concentrations of tested parameters. To sum up, it appears clear that full anti-inflammatory activity of PK20 peptide requires simultaneous stimulation of both opioid and neurotensin receptors.

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S15.P3

ANALYSIS OF ANTIOXIDANT ENZYMES IN PATIENTS WITH NEUROENDOCRINE NEOPLASMS OF THE LUNG, GASTROINTESTINAL TRACT AND PANCREAS

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Oxidative stress is defined as the imbalance between the production of reactive oxygen species and the antioxidant capacity of biological systems. Excessive production of by-products of oxygen metabolism has a detrimental effect on essential cell components, i.e. proteins, lipids, nucleic acids, which may be responsible for inducing or aggravating various disease entities: cancer, diabetes, and cardiovascular diseases. One of the cell defense mechanisms are antioxidant enzymes: superoxide dismutase, catalase and glutathione peroxidase. The conditions of long-term oxidative stress favor the increase of mutations and DNA damage, as a consequence initiating neoplastic transformations. The aim of the study is to analyze antioxidant enzymes in patients with neuroendocrine tumors of the lung, gastrointestinal tract and pancreas. The study group consists of 75 patients with neuroendocrine neoplasms. These are preliminary studies comparing antioxidant enzymes in neuroendocrine neoplasms in separate locations (lungs, gastrointestinal tract, pancreas). Research is ongoing and numerous analyzes are carried out. In recent years, knowledge about the relationship of reactive oxygen species with cancer has increased. However, little information is available on the antioxidant activity of cell defense mechanisms in the presence of neuroendocrine tumors. Efforts are still being made to obtain the best diagnostic methods and identify effective and sensitive biomarkers that would suggest changes characteristic of neuroendocrine neoplasms.

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S15.P4

THE INFLUENCE OF ANTIMICROBIAL NEUTROPHIL EXTRACT AND PENTOXIFYLLINE ON OVINE NEUTROPHILS ISOLATED DURING THE INSERTION TITANIUM IMPLANT IN A SHEEP MODEL

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Titanium (Ti) is the metal commonly used in orthopedic field. Titanium is highly resistant to corrosion. However, Ti ions might slowly diffuse into surrounding tissue where they would be transported into circulation and may interact with blood cells, causing their excessive activation. Autologous neutrophil extract (AMP) was previously considered as factor to decrease of excessive response of leukocytes. Pentoxifylline (PTX) is a competitive non-selective phosphodiesterase inhibitor, which acts anti-inflammatory, enhances microcirculation, blood flow and tissue oxygenation. It also stimulate bone formation and could be considered in management of osseointegration. The aim of this study was to assess of neutrophil *in vitro* response to implantation of biomaterial into the tibia with or without treatment with AMP or PTX. The study was conducted on 8 sheep, females, BCP local breed, 4 months old, from the Bezek Experimental Farm. The procedure consisted of inserting a Ti implant into the proximal tibial physis. Blood sampling necessary to obtain AMP was done 7 days before implantation. For the determination of neutrophil activity, blood was collected at three time points: 7 days before implantation, 1 h and 24 h after implantation. The secretory activity of neutrophils was estimated on the basis of the degranulation and free radicals generation at above time-points, after *in vitro* stimulation with 20 µg/mL AMP or PTX added to final concentrations of 0, 1, and 100 µg/ml of culture of ovine neutrophils. The obtained results show that the addition of AMP and PTX in concentration of 1 µg/ml to the neutrophil suspension decrease of activity of neutrophils. Our study showed that AMP and PTX added at the stated concentrations to the neutrophil suspension isolated during implantation of a Ti implant into the proximal tibial physis reduces the pro-inflammatory response of neutrophils.

S15.P5

MIR 511-5P EXPRESSION AS A PREDICTOR OF NUTRITIONAL STATUS DISORDERS IN PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPHY DUE TO HEAD NECK CANCER

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Every year approximately 630,000 cases of head and neck cancer (HNC) are diagnosed and 350,000 patients die from this cancer. The 90% of HNC cases is squamous cell carcinoma and the most common localization are pharynx, larynx and oral cavity. Malnutrition and cancer cachexia are often observed in patients with HNC and occur in 44–88% patients during treatment. The main factor contributing to the development of cachexia is the ongoing inflammatory process.Due to the potential regulatory properties (posttranslational alteration of expression of genes whose protein products are involved in inflammation) of miR-511-5p, it may play an important role in the development of nutritional status disorders. Therefore, the aim of this study was investigate the role of miRNA-511-5p in prediction of nutritional status disorders in 60 HNC patients subjected to Intensity-Modulated Radiation Therapy (IMRT). The miR-511-5p expression analysis was performed using commercial molecular probes and real-time PCR method. Study group was dominated by man(85%) and the most common localization of tumor was larynx (55%). The study included patients in advanced stage of HNC: stage III - 26.67%, stage IVA-IVC - 73.33%. Patients with good nutritional status had significantly higher expression of miR-511-5p compared to patients with moderate or severe malnutrition (SGA A vs. B or C) (6.27 vs. 0.93; p=0.0001). Patients with critical weight loss (CWL) had significantly lower miR-511-5p expression compared to those without CWL (1.64 vs. 0.51; p=0.0025). The assessment of miR-511-5p expression was characterized by 84.2% sensitivity and 88.9%specificity in detecting patients with moderate or severe malnutrition (AUC=0.90; p <0.0001). Moreover, the assessment of this biomarker allows for the detection of patients with CWL with 50% sensitivity and 90% specificity (AUC=0.78; p=0.0003). The lower expression of miR-511-5p was significantly related with a 37-fold higher risk of moderate or severe malnutrition (OR=37.33; p=0.0013). In patients with lower expression of miR-511-5p significantly higher risk (7-fold)of CWL was observed (OR=7.36; p=0.0039). Assessment of miR-511-5p expression may be a useful tool in prediction of the nutritional disorders in patients undergoing IMRT due to HNC.

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S15.P6

SILICON - A NOT-ESSENTIAL ELEMENT?

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The importance of silicon for broadly understood health has been suggested for a long time, especially in the context of the condition of skin appendages - hair and nails. This tradition is part of a later, more serious approach based on scientific research that tried to find an objective link between silicon and health. In the second half of the 20th century, attempts were made to characterise the physiological role of silicon. Very few facts have been discovered - namely, that silicon is present in trace amounts in connective tissues, especially in the blood vessels. Few studies have also been carried out to demonstrate the necessity of silicon for the development of the organism - specifically, it was implied that it is necessary for the development of connective tissues (bones). However, a consistent theory regarding the actual physiological mechanisms has never been proposed, usually limited to the claim that collagen is essential for the synthesis of collagen (in fact there is no known silicon involvement in this process). It was also impossible to repeat the research from 40 years ago, the only one on the basis of which the thesis about the necessity of silicon has been repeated so far in thousands of publications. Nevertheless, due to many years of interest in silicon, despite the lack of scientific premises, the WHO determined the amount of the human body's need for this element. The aim of the present study was to summarize the current state of knowledge in this field. The analysis of the available literature showed that despite half a century of proliferation of publications on the importance of silicon: 1) there is no documented physiological mechanism involving silicon; 2) there is no biochemical structure in which silicon is necessary; 3) a state of silicon deficiency in the body is not possible.

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S15.P7

SPATIAL ORIENTATION IN ADOLESCENTS

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The aim was to study was to study spatial orientation in visually impaired adolescents. Performance of early and late blind adolescents was compared (n=16, 8 early blind and 8 late blind adolescents, 4 girls and 12 boys, age range from 10 to 19). Orientation in the locomotor space was studied in a closed room by means of changing location of the poles with toys. Orientation in the manipulatory space was studied using the rotatable table and changing placement of the toys on the table. Participants had to explore, remember location and after the change, try to identify it. Performance as well as the strategy of the participants has been studied. Findings have shown that the late blind adolescents show better spatial orientation in both, locomotor and manipulatory spaces.

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S15.P8

HOW VISION AFFECTS OUR TASTE SENSITIVITY?

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There is little doubt that what we see affects our perception of behavioural responses to food and drink. We hypothesised that those effects are partially associated with changes in taste sensitivity thresholds, which was suggested by a study with congenitally blind people (Gagnon *et al*., *Chem Senses* 2013). To test our hypothesis we studied taste recognition thresholds for five basic tastes in two conditions: in subjects with (1) open eyes and (2) closed eyes. Based on previous studies we expected that taste sensitivity thresholds would differ between those conditions. Twenty four volunteers (18–45 years old) without taste disorders participated in the study. Five basic tastants: sweet (sucrose, 0.94–12.00 g/l), salty (sodium chloride, 0.34–2.00 g/l), sour (citric acid, 0.2–0.6 g/l), bitter (caffeine extract, 0.09–0.27 g/l) and umami (monosodium glutamate, 0.17–1.00 g/l) were dissolved in mineral water, and five sets of six different concentrations (samples) were prepared. Each participant tested the sets at random order. Subjects were presented with 6 samples (15 ml) in a set in successive solutions, and were asked if any taste (taste detection) and what taste (taste recognition) they identified. After each sample, they rinsed their mouth with mineral water. The sensory testing was done in two conditions: first, when participants had their eyes open, and next, when they had their eyes closed. Bitter taste was recognized at lower concentrations in the closed-eyes (13 subjects) than open-eyes (5 subjects) condition (a Wilcoxon signed-rank test indicated that the median open-eyes ranks were significantly higher than the median closed-eyes ranks $T=19$, $Z=2.72$, $p=0.006$). For sweet taste, there was a clear tendency to identify the taste at a lower concentration with eyes closed (14 subjects) than with eyes open (8 subjects), though the difference did not reach a significance level of $p=0.05$ (a Wilcoxon signed-rank test $T=58.8$, $Z=1.74$, $p=0.08$). Differences in recognition thresholds of salty, sour and umami tastes were less pronounced, esp. for sour and umami. The number of subjects with higher taste sensitivity in the closed-eyes than open-eyes condition and vice versa was respectively: 13 and 7 for salty; 9 and 5 for sour; 6 and 9 for umami. Our results suggests that vision may change taste recognitions thresholds for some of the basic five tastes, especially bitter and sweet, which could account for a visual component in taste perception. Yet, contrary to previous studies, taste sensitivity is rather higher then lower when there is no visual contribution to taste perception. Further study is foreseen with a larger group of subjects to obtain more conclusive outcomes.

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PECIAL WORKSHOP SESSIONS

ANIMALAB DEMONSTRATIONS AND VIRTUAL WORKSHOPS

Wednesday (September 15, 2021; 13:20 – 14:05)

Thursday (September 16, 2021; 9:00 – 9:40; 13:30 – 14:15)

DETAILED ANIMALAB LECTURES AND PRESENTATIONS SCHEDULE

(Wednesday 15, 2021; 13:20 – 14:05; *virtual stream B*)

Sp1.S1 PHYSIOLOGY COMPLEXITY AND ITS TECHNOLOGY. EXAMPLES FROM MOTOR FUNCTION TO CIRCADIAN RHYTHMS BY UGO BASILE, ITALY. **Federico Montechiaro,** (UGO Basile, Gemoni, Italy).

(Thursday 16, 2021; 9:00 – 9:40, *virtual stream C*)

Sp1.S2 HEART RATE VARIABILITY, TIME DOMAIN AND FREQUENCY DOMAIN ANALYSIS. **Federico Cardona** (ADInstruments, Oxford, United Kingdom).

(Thursday, 16, 2021; 13:30 – 13:55, *virtual stream B*)

Sp1.S3 THE USE OF SMALL ANIMAL TELEMETRY IN PHYSIOLOGY. **Holger Russig** (TSE Systems, Bad Homburg, Germany).

(Thursday, 16, 2021; 13:55 – 14:15, *virtual stream B*)

Sp1.S4 NEW APPROACHES TO TEACHING PHYSIOLOGY **Tony McKnight, Federico Cardona** (ADInstruments, Oxford, United Kingdom).

PHYSIOLOGY COMPLEXITY AND ITS TECHNOLOGY. EXAMPLES FROM MOTOR FUNCTION TO CIRCADIAN RHYTHMS BY UGO BASILE, ITALY

F. MONTECHIARO

UGO Basile, Gemoni, Italy

Animal physiology is such a large field. Today we will approach it from the behavioural angle as Ugo Basile is a leading provider of behavioral instrumentation for animal research in physiology. We will demonstrate in a live session from Italy the following instruments:

- Muscle function/exercise:
  Whole Animal: horizontal treadmill, rotarod for rats and mice, Grip strength meter.
  Isolated tissues: smooth and striated muscles coupled to chemical or electrical stimulation for measurement of contraction in isometric
  or isotonic mode.
- Central nervous system:
  Memory: fear conditioning, active/passive avoidance, water maze, radial maze, videotracking.
  Pain: central and peripheral nervous system interaction.
- Fatigue: treadmill.
- Heart, cardiovascular and respiratory: volume-controlled ventilators and gas anaesthesia systems.
- Aging: a number of aging index to evaluate physical activity, motor function and aging in general.

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