Turkish Society of Physiological Sciences

47th Turkish Physiology Congress

1-4 November 2022

Antalya, Türkiye

Contents

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Scientific Program

1 November 2022 Tuesday

15.30 - 15.45 Congress Opening Session

15.45 - 16.30 Respect to the Masters Session
(Prof. Dr. Gülderen Şahin, Prof. Dr. Ayşe Doğan and Prof. Dr. Aysel Ağar)
Chair: Erdal Ağar

16.30 – 17.30 **Conference 1**
Oleg Krishtal: "Acid-Sensing Ion Channels in Mammalian Brain: Ubiquitously Present and Multiple in Functions"
Chairs: Erdal Ağar & Bayram Yılmaz

17.30 – 18.30 Poster Oral Presentations
(PC04, PC11, PC13, PC17, PC23, PC24, PC25, PC26, PC31, PC34, PC43, PC44, PC55, PC56, PC57, PC59)
Chairs: Vural Küçükatay & Erkan Kılınç

18.30 – 19.30 Reception

2 November 2022 Wednesday

09.00 - 11.00 Oral Communications – I
Hall A: OC01-OC08
Chairs: Güler Öztürk & Çiğdem Özer
Hall B: OC09-OC16
Chairs: Sibel Dinçer & Ayhan Bozkurt
Hall C: OC17-OC24
Chairs: Kubilay Uzuner & S. Arzu Vardar

11.00 – 11.30 Break

11.30 – 12.30 **Conference 2**
George Hasko: "Purinergic Regulation of Sepsis and Trauma"
Chair: Ertuğrul Kılıç

12.30 – 13.30 Poster Communications – I (PC01-PC30)

13.30 – 14.30 Lunch

14.30 – 16.30 **Sempozyum 1:** "Hypothalamic Regulation of Feeding and Metabolism"
Yasemin Önder: "Understanding Neural/Glial Biology Underlying Metabolic Adaptation"
Yavuz Yavuz: "Opioid Modulation of Hypothalamic Arcuate AgRP Neurons"
Caner Çağlar: "Restriction of Food Intake by Dorsomedial Hypothalamic Nuclei"
Chairs: Haluk Keleştimur & Lütfiye Kanıt

14.30 – 16.30 **Panel 1:** "The Microbiota-Gut-Brain Axis: Neuronal Excitability"

Sezin Kıroğlu Uzun: "Intestinal Microbiota and Host Interactions"

Berna Karakoyun Laçin: "Effects of Intestinal Microbiota on the Enteric Nervous System"

Mustafa Ayyıldız: "Effects of Gut Microbiota on the Central Nervous System"

Mehmet Yıldırım: "Epilepsy in the Microbiota-Gut-Brain Axis"

Chairs: H. Oktay Seymen & Mustafa Ayyıldız

16.30 – 17.00 Break

17.00 – 17.45 European Animal Research Association (EARA) Conference

Kirk Leech: Animal Research: Time to Talk!

Chair: Ahmet Ayar

18.00 – 19.00 AGM Turkish Society of Physiological Sciences

3 November 2022 Thursday

09.00 – 10.30 Oral Communications – II

Hall A: OC25-OC30

Chairs: Hale Sayan Özaçmak & Sinan Canpolat

Hall B: OC31-OC36

Chairs: K. Gonca Akbulut & Berna Karakoyun

Hall C: OC37-OC42

Chairs: Süleyman Sandal & Bilge Pehlivanoğlu

10.30 – 11.00 Break

11.00 – 12.00 **Conference 3**

David Paterson: "Cardiac Neurobiology of Arrhythmia in Human Cell Models: Novel Therapeutic Targets"

Chair: Bayram Yılmaz

12.00 – 13.00 Poster Communications – II (PC31-PC59)

13.00 – 14.00 Lunch

14.00 – 16.00 **Symposium 2:** "Genetic Basis of Rare and Complex Diseases in Humans"

Onur Emre Onat: "Discovery of Novel Causative Genes for Obesity Using a Familial Rare Variant Association Approach"

Serkan Belkaya: "Genetic Investigation of Severe Viral Diseases in Children"

Chairs: Berrak Yeğen & Caner Çağlar

14.00 – 16.00 **Symposium 3:** "Development of Multifunctional Nanomaterials and Their Potential Use in Nanomedicine"

İsmail Öçsoy: Nanotechnology and its Applications

Güven Akçay: Nanotechnology in Neurology

Çağla Çelik: Nano-Biosensors

Chairs: Nevzat Kahveci & M. Alper Erdoğan

16.00 – 16.30 Break

16.30 – 17.30 **Conference 4**

Demet Araç: “Mechanism and Functions of Adhesion-type G-protein Coupled Receptors (GPCRs)”

Chair: Melek Bor Küçükatay

19.30 – 23.00 Gala Dinner

4 November 2022 Friday

09.00 – 10.30 Oral Communications – III

Hall A: OC43-OC48

Chairs: Şeref Erdoğan & Selda Kabadere

Hall B: OC49-OC54

Chairs: Selim Kutlu & Mehmet Yıldırım

Hall C: OC55-OC60

Chairs: Neyhan Ergene & Yasemin Aydın

10.30 – 11.00 Break

11.00 – 12.00 **Conference 5**

Maeve Caldwell: “The Role of Astrocytes in Neuroinflammation and Neuronal Cell Death”

Chair: Numan Ermutlu

12.00 – 13.00 Lunch

13.00 – 14.30 **Symposium 4:** “Cerebral Autoregulation Impairments and Intensive Care of Traumatic Brain Injuries - Concept of Optimal Cerebral Perfusion Pressure”

Arminas Ragauskas: "Transient Function of Cerebral Autoregulation Monitoring During Cardiac Bypass Surgery"

Yasin Hamarat: “Ultrasonic Non-Invasive Cerebrovascular Autoregulation Real-Time Monitoring”

Özgür Kasımay: “Exercise Physiology and Clinical Practice Areas”

Chairs: Fatma Töre & Özgür Kasımay

14.30 – 14.45 Break

14.45 – 15.15 Awards and Closing Ceremony

Conferences

Conference 1: Acid-Sensing Ion Channels in Mammalian Brain: Ubiquitously Present and Multiple in Functions

Oleg Krishtal

National Academy of Sciences of Ukraine, Bogomoletz Institute of Physiology, Kyiv, Ukraine

Every mechanism of ion permeability expressed in mammalian brain occupies its niche in respect to the function(s) played and represents corresponding pharmacological target. Acid-sensing ion channels (ASICs) have been discovered later than the prevalent majority of ion channels (1980). Their role(s) in the brain function are still far from being clear. ASICs are Na^+-permeable ion channels, predominantly expressed in the nervous system and activated by protons. ASICs act as pH sensors leading to neuronal excitation. At least eight different ASIC subunits (including ASIC1a, ASIC1b, ASIC2a, ASIC2b, ASIC3, ASIC4, ASIC5) are encoded by five genes (ASIC1–ASIC5). Functional ASICs assembled in the plasma membrane are homo- or heteromeric trimers. ASIC1a-containing trimers are of particular interest because, besides sodium ions, they also conduct calcium ions and thus can trigger/regulate multiple cellular processes. ASICs are widely, but differentially expressed in the central and peripheral nervous systems. In the mammalian brain a prevalent majority of neurons express at least one ASIC subunit.

Several recent reviews have summarized findings about the role of ASICs in the peripheral nervous system, in particular in nociception and proprioception, as well as the structure-function relationship of ASICs. However, there is little coverage on recent findings regarding the role of ASICs in the brain.

Presently the roles of ASICs in mammalian brain can be summarized as follows: (i) postsynaptic receptors activated by protons coreleased with glutamate at glutamatergic synapses; (ii) modulators of synaptic transmission at glutamatergic synapses and GABAergic synapses; (iii) in synaptic plasticity, memory and learning; (iv) in some pathologies such as epilepsy, mood disorders and Alzheimer's disease.

Key words: Synaptic transmission; Calcium ions; Learning; Glutamatergic; GABAergic; Epilepsy; Alzheimer's disease, Depression.

Conference 2:
Purinergic Regulation of Sepsis and Trauma

George Hasko

Columbia University, Medical School, Department of Anesthesiology, New York, NY, USA

Abstract: The purinergic signaling complex comprising extracellular nucleotides and nucleosides, and their receptors, the P2 and P1 purinergic receptors, respectively, as well as catabolic enzymes and nucleoside transporters is a major regulatory system in the body. The purinergic signaling complex can regulate the development and course of immunity in trauma and sepsis. Here I provide an overview on the role of purinergic signaling in controlling immunity, inflammation and organ function following trauma and sepsis.

Conference 3: Cardiac Neurobiology of Arrhythmia in Human Cell Models: Novel Therapeutic Targets

David J Paterson

University of Oxford, Department of Physiology, Anatomy & Genetics, Burson Sanderson Cardiac Science Centre, Oxford, UK

Heightened sympathetic drive (dysautonomia) is a hallmark of several cardiovascular diseases including SARS-CoV-2. It is also a powerful prognostic predictor for arrhythmia and sudden cardiac death, especially in patients with channelopathies (long QT syndrome-LQTS, and catecholaminergic polymorphic ventricular tachycardia-CPVT). However, little is known about the molecular targets underlying this dysautonomia. We have identified a novel pathway using a combination of single cell and bulk RNAseq, neurochemistry, FRET imaging and single cell electrophysiology. This pathway involves impairment of cyclic nucleotide coupled phosphodiesterases (PDE) linked to enhanced intracellular calcium transients and exocytosis from rat sympathetic neurons. In particular, the adaptor protein Nos1-ap, Pde2A, and Ace2 are associated with sympathetic hyperexcitability. These proteins are also conserved in human stellates from patients with LQTS and CPVT, although their role in neuronal-myocyte cellular function is unknown. We have developed a unique human iPSC sympathetic-cardiac co-culture model for target discovery in LQTS and CPVT. The lecture will highlight the use of gene manipulation of these proteins to determine their role in driving abnormal transmission and arrhythmia.

Reference:

Herring N, Kalla M, Paterson DJ. (2019). The Autonomic Nervous System and Cardiac Arrhythmias: Current Concepts and Emerging Therapies. *Nat Rev Cardiol,* 16: 707–726.

Conference 4:
Structural and Functional Basis of Adhesion G Protein-Coupled Receptors

Demet Araç

Department of Biochemistry and Molecular Biology, and Institute for Neuroscience, The University of Chicago, Chicago, IL, 60637, USA.

Adhesion family of G Protein-Coupled Receptors are cell surface receptors that mediate cellular communication and play critical roles in numerous physiological functions that range from embryonic and neural development. However, their mechanisms of action remain poorly understood. In the past several years, three-dimensional structures of several adhesion GPCRs have been reported at atomic resolutions and revealed distinct protein folds and unique structural features. In this presentation, we will discuss these structures which, together with structure-guided biochemical and functional analyses, provide hints for the mechanisms of trans-cellular communication at the synapse and other cell-cell contact sites.

Conference 5:
The Role of Astrocytes in Neurounflammation and Neuronal Cell Death

Maeve Caldwell

Trinity College Dublin, School of Medicine, Discipline of Physiology, Trinity College Institute for Neuroscience, Dublin, Ireland

For many years neuropathology has been dominated by neuron centric views where all conceptualisation of brain pathology was focused on neurons; on their survival or death. However, recent findings are challenging this view, implicating non-cell autonomous mechanisms of neurodegeneration with astrocytes as central players in both acute and chronic diseases.

Astrocytes are one of the most abundant cell types in the vertebrate nervous system, their projections encapsulate neuronal synapses and promote synaptogenesis and have also been shown to promote neuronal differentiation. They were once thought to be solely ancillary cells but it is now known that they can become reactive and can produce proinflammatory factors such as interleukin-6 and tumour necrosis factor-a and contribute to neuronal death.

This presentation will describe how astrocytes can be protective to neurons but under conditions of stress can cause damage. These astrocytes can be differentiated from human induced pluripotent stem cell lines and how they can respond to an inflammatory insult in terms of changes in gene expression and cytokine release will be described. This supports the involvement of astrocytes in neuroinflammation and so has implications for their role in neurodegenerative disease.

European Animal Research Association (EARA) Conference: Animal Research: Time to Talk!

How National Transparency Agreements and Openness Are Transforming the Conversation with the Public on the use of Animals in Research

Kirk Leech

The European Animal Research Association (EARA), 3.04 LABS Atrium, London NW1 8AH, UK

In a growing number of countries, public and private research institutions have made the bold decision to adopt new persuasive practices and policies to engage with the public on the benefits and achievements of using animals in scientific and biomedical research.

In Europe there are now eight National Transparency Agreements on animal research in Spain, Portugal, Belgium, France, Germany, Netherlands, Switzerland and the UK involving close to 500 institutions where research institutions have collectively agreed to commitments on pursuing greater openness with the public. A similar agreement exists in New Zealand with work progressing in Australia and the United States.

These commitments are that institutions; will be proactive in seeking opportunities to explain when, how and why they use animals in research; will provide information to the media and the general public about the conditions under which research using animals is carried out and will explain the benefits obtained from using them compared to other methods of research; will develop initiatives that generate greater public knowledge and understanding about the use of animals in scientific research; will place an animal welfare statement on their institution's website.

The belief is that being more open and transparent about their use of animals in research will help improve public understanding and acceptance of the use of animals for scientific purposes. The need for a collective commitment is also important.

There is simultaneously growing political pressure in the USA and Europe to transition towards 'animal free science'. The research community needs to make a stronger and clearer public case for the use of animals in research. This presentation will evaluate the experience in these countries of greater openness on the use of animals in research, and explain why we need to talk more openly about animal research in Turkey.

Symposia

Symposium 1: Hypothalamic Regulation of Feeding and Metabolism

Symposium 1.1. Analysis of Adaptive Mechanisms in Inhibitory Neurocircuitry Underlying Metabolic Control

Yasemin Önder

Kadir Has University, Faculty of Engineering and Natural Sciences, Department of Molecular Biology and Genetics, İstanbul, Türkiye

Obesity is a global epidemic with many co-morbidities such as heart disease, stroke and type 2 diabetes. The hypothalamus critically regulates energy balance to maintain body weight via balancing food intake and energy expenditure. This coordination is achieved by complex neuronal networks that respond dynamically to nutrient status and other hormonal signals from the periphery. The ventromedial hypothalamus (VMH) has been shown to be essential for energy and glucose homeostasis [1, 2]. Brain derived neurotrophic factor (BDNF) and its receptor tyrosine kinase TrkB which play critical roles in synaptic plasticity in other brain regions, are expressed in the VMH and their expression in this region is dynamic based on nutrient status and critical for energy balance regulation[3-5]. Moreover, *Bdnf*Val66Met mutation which impedes BDNF signaling has been linked to neuropsychiatric disease in humans including eating disorders [6]. It is now recognized that feeding circuits are not hardwired but highly plastic and remodel in response to caloric signals to meet the energy demands of the animal [7, 8]. γ-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the central nervous system. The VMH is mainly comprised of excitatory glutamatergic neurons that suppress appetite; although it is surrounded by inhibitory (GABAergic) neurons in the dorsomedial hypothalamus (DMH) that project to the VMH. Additionally, $GABA_A$ receptors ($GABA_ARs$) are abundant in this region. How different $GABA_AR$ subunit expression and localization would affect VMH neural circuits functionally and how this is shaped by different metabolic states is not known. The role of GABA transporters in the VMH regulating metabolic function and specifically the role of astrocytic GABA reuptake in this regulation has been largely overlooked. Here we performed immunofluorescence studies showing increased inhibitory synapse number in the fed state as well as altered inhibitory neurotransmission based on feeding status. Additionally, we show that: 1) Gabra5 expression is increased in the fasted state 2) Tonic inhibition is present in the VMH and it is tightly controlled by GABA reuptake 3) Gene expression of GABA transporters (GAT1 and GAT3) is increased in the fasted state. Based on these findings, this project will test the hypothesis that astrocytic GAT3 (gene name: Slc6a11) is critical for energy balance regulation in the VMH and it will characterize the feeding status and BDNF/TrkB signaling-dependent molecular and structural changes in inhibitory neurotransmission in the VMH. Ultimately, these studies can help us unravel root causes of metabolic and neuropsychiatric diseases.

References:

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2. Storlien LH et al. Localization of CNS glucoregulatory insulin receptors within the ventromedial hypothalamus. Brain Res, 1975. 96: 156-60.
3. Unger T.J., et al., Selective deletion of Bdnf in the ventromedial and dorsomedial hypothalamus of adult mice results in hyperphagic behavior and obesity. J Neurosci, 2007. 27: 14265-74.
4. Xu B et al., Brain-derived neurotrophic factor regulates energy balance downstream of melanocortin-4 receptor. Nat Neurosci, 2003. 6: 736-42.
5.Tran PV et al. Diminished hypothalamic BDNF expression and impaired VMH function are associated with reduced SF-1 gene dosage. J Comp Neurol, 2006. 498: 637-48.
6. Shimizu E et al. Ethnic difference of BDNF 196G/A (val66met) polymorphism frequencies: the possibility to explain ethnic mental traits. Am J Med Genet B Neuropsychiatr Genet, 2004. 126: 122-3.
7. Pinto S et al. Rapid rewiring of arcuate nucleus feeding circuits by leptin. Science, 2004. 304: 110-5.
8. Zeltser LM et al. Synaptic plasticity in neuronal circuits regulating energy balance. Nat Neurosci, 2012. 15: 1336-42.

Symposium 1.2. Opioid Modulation of Hypothalamic Arcuate AgRP Neurons

Yavuz Yavuz

Yeditepe University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

Agouti-related peptide (AgRP) neurons, localized in the arcuate nucleus (ARC) of the hypothalamus, have a central role in the regulation of appetite, metabolism, and energy homeostasis. We aimed to characterize possible functional changes of the μ-opioid receptor agonist on AgRP neurons by electrophysiological and Ca^{+2} activity imaging methods. Male and female AgRP-Cre mice were used. *Ex vivo* effects of DAMGO (a μ-opioid receptor agonist) on AgRP neurons were examined by optogenetic and electrophysiological (cell attach and whole cell) methods, *in vivo* effects of μ-opioid receptor activation were investigated by feeding behavior, locomotor activity and fiber photometry Ca^{+2} imaging methods. DAMGO significantly reduced the firing frequency of AgRP neurons and hyperpolarized the resting membrane potential (P<0,0001). In addition, it was observed that this μ-opioid agonist significantly reduced the frequency of excitatory post-synaptic currents to the AgRP neurons, without changing the frequency of inhibitory post-synaptic currents. In $ARC^{AgRP \rightarrow PVH}$ synaptic connection experiments using the optogenetic technique, the synaptic peak amplitude decreased significantly after drug administration (P<0,05). Five days after intraperitoneal administration of DAMGO, amount of food consumption tended to increase. DAMGO treatment significantly decreased the distance traveled by the animals while their speed did not change. We used fiber photometry technique to monitor the in vivo Ca^{+2} activity of AgRP neurons. When DAMGO was administered to mice that were fasted for 16 hours, Ca^{+2} activity in AgRP neurons was significantly reduced (P<0.05). In our study, μ-opioid receptor modulation of AgRP neuronal activity is demonstrated for the first time. When the available data was considered, it can be suggested that μ-opioid agonism is effective in regulating the activity of AgRP neurons, which have an important role in appetite regulation.

Key words: Opioids, AgRP mice, Optogenetic, Electrophysiology, Fiber Photometry, Feeding Behavior.

Symposium 1.3. Restriction of Food Intake by Dorsomedial Hypothalamus

Caner Çağlar

Bezmialem Vakıf University, Life Sciences and Biotechnology Institute, Department of Molecular Biology, Istanbul, Türkiye

Leptin deficient ob/ob mice eat excessively and their food intake is considerably suppressed by leptin injection. Leptin exerts its effects in part by modulating the activity of AGRP and POMC neurons in the arcuate nucleus as well as other brain regions. In order to identify novel sites of leptin action, we used the phosphotrap method to molecularly profile leptin responsive neurons in the hypothalamus and brain stem. In addition to identifying several known and novel neural populations that are responsible for mediating leptin`s effect on food intake, we also found that neurons in the Dorsomedial Hypothalamus (DMH) expressing Ppp1r17 are activated in ob/ob mice but do not express leptin receptor that are indirectly suppressed by leptin treatment. While these data initially suggested that these neurons would activate food intake, we in fact observed the opposite. Chemogenetic excitation of Ppp1r17 neurons decreased food intake and body weight in ob/ob mice while chemogenetic inhibition of Ppp1r17 neurons increased food intake and body weight. Similarly, in a scheduled feeding protocol that elicits Food Anticipatory Activity (FAA), mice ate more when Ppp1r17 neurons were inhibited and less when they were activated without altering food anticipatory activity, body temperature and oxygen consumption. These data suggest that Ppp1r17 neurons in DMH play a key role in restricting excessive food intake and leptin suppresses their activity indirectly by reducing food intake. These results reveal that pathways that increase food intake can activate neural populations that can restrain food intake as a compensatory mechanism. This finding has potential implications for an understanding of binge eating and other nutritional disorders.

Symposium 2: Genetic Basis of Rare and Complex Diseases in Humans

Sempozyum 2.1: Discovery of Novel Causative Genes for Obesity Using a Familial Rare Variant Association Approach

Onur Emre Onat

Departments of Translational Medicine and Genomic Studies, Institute of Health Sciences, Acıbadem Mehmet Ali Aydınlar University, İstanbul, Türkiye

Obesity is a complex multifactorial disease and it has been assumed that more than one billion people worldwide are obese (BMI>30 kg/m2, percentile>95%). As in many complex diseases, it has been shown that genetic heterogeneity is much higher than expected in obesity, and it has been determined in the literature that genes associated with genetic obesity explain a small part of the pathogenesis of the disease. Here, we aimed to solve the missing heritability in obesity and their role in the pathogenesis of the hunger pathways. From our DNA database, 1.087 samples from 799 families (obese proband and obese/thin family members) were sequenced by exome sequencing and 36 candidate genes associated with obesity were identified using rare and deleterious variant association bioinformatics/statistics approaches. Fifteen of these were associated with the obesity-defining phenotype group by PheWAS analysis in the Mount Sinai BioMe database. Segregation analyzes were performed in extended families by sampling one or two families carrying mutations in these 15 genes. As a result of genetic evidence-based analysis, the STEAP1B, KCNQ5 and UCP1 genes were most strongly associated with obesity. For the allelic variants of our three candidate genes, segregation studies are continued by sampling other families and polygenic risk analyzes are continued to understand the phenocopy in the family and additive effects of other genes on the phenotype. In order to understand the causality of variants, we will perform genetic mapping to eliminate other candidates in a family with many affected individuals in 3-4 generations, in silico protein modeling and simulations to understand the deleterious effect of variants on protein, in vitro cell studies to detect expression profiles in human and mouse brain, glycerol and fatty acid secretion by lipolysis assay in mutant and wild-type human adipose cells, functional determination of the role of candidates in AGRP and POMC neurons in the hypothalamus that control appetite in humans, animal models and metabolic investigations in human neuron cell lines of the variants. Here, we analyzed next generation sequencing data with family-based rare variant association approach and combined it with phenonome-wide approach, reverse phenotyping approach and molecular cytogenetics techniques such as linkage analysis, homozygosity mapping and SNP genotyping. In order to solve the missing heritability in complex phenotypes, we describe a disease gene discovery strategy, using the obesity example, and how causality can be established.

Symposium 2.2: Genetic Investigation of Severe Viral Diseases in Children

Serkan Belkaya

Bilkent University, Department of Molecular Biology and Genetics, Ankara, Türkiye

Why do some children develop life-threatening viral diseases, while the majority have only mild infection or remain asymptomatic when exposed to same viruses? Over the past 30 years, several studies have demonstrated that single-gene inborn errors of immunity can explain susceptibility to severe infectious diseases of childhood. Some of these diseases display tissue-specific phenotypes, such as viral encephalitis or hepatitis due to genetic defects in brain- or liver-intrinsic innate immunity. Candidate disease-causing mutations in patients with such diseases were discovered by whole exome sequencing and functionally investigated with in vitro disease models including infections and co-culture systems. These findings have far-reaching basic and clinical implications, providing novel insights into disease mechanisms, the basis of genetic diagnosis and counseling in affected families, and support for the development on novel therapeutic strategies.

Symposium 3: Development of Multifunctional Nanomaterials and Their Potential Use in Nanomedicine

Sempozyum 3.1: Nanotechnology and its Applications

İsmail Öçsoy

Erciyes University, Faculty of Pharmacy, Department of Analytical Chemistry, Kayseri, Türkiye

Nanotechnology is the provision of size control of matter at the atomic and molecular level. Accordingly, it deals with the synthesis of colloidal nanomaterials such as metallic nanoparticles (NP) or polymeric nanoparticles. It is seen that nanomaterials are widely used in a wide range of biomedical applications due to their specific electronic, optical and magnetic properties depending on their shape and size. Developed Ag, Au or Cu plasmonic nanoparticles are used in many fields for purposes such as imaging, therapy, drug delivery, proteomics, and biosensing in medicine. In addition, polymeric, carbon-based and metallic nanomaterials are also used to develop new generation antimicrobials against pathogenic bacteria. With the recent developments in nanobiotechnology, multifunctional hybrid nanoparticles have attracted great attention as they offer multi-purpose use possibilities compared to their use alone. Various hybrid structures including metal-metal oxide, metal-graphene oxide, organic-inorganic NPs have been synthesized for enhanced physicochemical and biological properties. The high surface area of organic-inorganic hybrid nanomaterials has made it possible to simultaneously carry multiple functional groups such as nucleic acids, aptamers, peptides, and small chemical molecules. Although selective drug carriers have been developed with their easy functionalization properties, they can be used as imaging agents by binding fluorescent dyes. As a new immobilization technique, the synthesis of hybrid nanocomposites has been carried out recently. By using organic molecules and metal ions as inorganic fractions, nanocomposites were synthesized and their antioxidant, antimicrobial, anticancer and catalytic activities were investigated. Nanobiotechnology, which has made progress with the active use of nanomaterials in health technologies, has a high potential to solve existing problems in the treatment, diagnosis and disease prevention stages.

Symposium 3.2: Nanotechnology in Neurology

Güven Akçay

Hitit University, Faculty of Medicine, Department of Biophysics, Çorum, Türkiye

Current treatment options for central nervous system diseases only relieve symptoms. However, these treatments cannot significantly reduce or stop the progression of the underlying pathology of the disease. Therefore, there is an urgent need to develop more effective treatments. However, it is predicted that this need can be achieved with an in-depth understanding of the mechanisms and agents that play a role in the development of each disease. In these cases, the method of treatment with therapeutic compounds in diseases of the nervous system comes to the fore. However, the blood-brain barrier plays an important role in this treatment method. Since ischemic stroke is recognized as one of the most serious public health problems, there is an urgent need to design and develop smart drug carriers with physicochemical and biological properties that will provide enhanced drug delivery with specific targeting capability to the ischemic region. Recently, targeted nanoparticles (NPs) have been developed that can easily pass the BBB, thanks to nanobiotechnological developments. Among them, Selenium (Se) nanoparticles show promise in the treatment of CNS diseases. Se nanoparticles show high antioxidant activity and, accordingly, selenoproteins strengthen the endogenous antioxidant system. Iron oxide nanoparticles (Fe3O4 NP) are widely used in biomedical fields due to their excellent magnetic properties, biocompatibility and biodegradability. The surface of Fe3O4 NPs can be easily functionalized with small molecules, polymers and other inorganic materials. Given this flexibility, Fe3O4 has the potential to be used in many biomedicine applications, including MR imaging, photothermal therapy, chemotherapy and magnetothermal therapy. As a result, the fact that the cargo molecule carrying the active substance in nanoparticle-based drug delivery systems has antioxidant activity, is biocompatible and has a dual function to provide both treatment and imaging are promising studies that can increase the quality of diagnosis and treatment in neurological diseases.

Symposium 3.3: Nano-Biosensors

Çağla Çelik

Hitit University, Vocational School of Health Sciences, Çorum

Multi-drug-resistant microorganisms are significant threat to public health. The World Health Organization published a global action plan in 2015 to combat antibiotic resistantance. Many diagnostic tests are used in hospitals for the diagnosis and detection of these microorganisms. There is a need to develop biosensors that provide rapid and sensitive bacterial diagnosis in order to detect infection and antibiotic resistance. Accordingly, diagnostic tests in which gold nanoparticles (AuNPs) are integrated are used for rapid and sensitive bio-detection or bio-diagnosis due to their unique surface plasmon resonance properties. If Au NPs aggregate for any reason in solution, the red wine color shifts to purple/blue and the absorbance point at 525 nm will shift to wavelengths of 575 nm and higher. Thus, this localized surface plasmon resonance feature of Au NPs has been used as a colorimetric sensor for the determination of many molecules. In addition, Au NPs synthesized from anthocyanin molecules isolated from plants as a natural pH indicator enable sensitive measurement in the diagnosis of bacteria as a colorimetric biosensor. By using anthocyanins directly as the basic biomolecule, tests have been developed to detect the diagnosis of H. pylori, which is the causative pathogen in gastric ulcer, based on its urease activity. In addition, natural indicator-based nanosensors were rationally designed for the detection and identification of antibiotic resistant bacteria. Apart from the fact that the color changes of colorimetric biosensors are visible to the naked eye, semi-quantitative results can be obtained by analyzing them with color image processing. In order to minimize the equipment device need compared to existing methods, the analysis is carried out with a mobile application integrated into the mobile phone. In the light of developments in nanobiotechnology, clinically usable nano-biosensors are designed and diagnostic tests are developed that can contribute significantly to the treatment of infection.

Symposium 4: Cerebral Autoregulation Impairments and Intensive Care of Traumatic Brain Injuries - Concept of Optimal Cerebral Perfusion Pressure

Symposium 4.1: Transient Function of Cerebral Autoregulation Monitoring During Cardiac Bypass Surgery

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Postoperative cognitive dysfunction and delirium are the common complications after cardiac surgery with cardiopulmonary bypass (CPB). Such complications are associated with dose and duration of ischemic or hyperemic brain insults during surgery. Real-time identification of a start time points of brain insults is a challenge for brain physiological monitoring technology. Neurons are dying in seconds. Ideally, sub-minute temporal resolution is needed for periodic identification of cerebral autoregulation (CA) status in order to manage cerebral perfusion pressure (CPP) value and to restore CPP value close to optimal CPP for individual patient in seconds. Our hypothesis is that periodic rectangular modulation of blood flow during cardiac surgery with CPB and with sub-minute modulation period opens possibility to monitor CA transient functions and to identify start times of ischemic or hyperemic insults. Fast feedback from a non-invasive CA transient function monitor to surgical theater is a way to make ischemic and hyperemic episodes a short as possible and, as a result, to decrease a rate of postoperative cognitive dysfunction and delirium. We proposed a novel operating mode of heart and lung machine – blood flow with rectangular modulation.

Prospective observational clinical study is being conducted in Kaunas Clinics, the hospital of Lithuanian university of health sciences. The study is registered in ClinicalTrials.gov Identifier: NCT04943458. The ongoing study at the moment includes 41 patients. We are able to record CA transient functions as the reactions of rising and falling fronts of rectangular blood flow with pulse period T=30s. Rectangular blood flow is a cause of rectangular arterial blood pressure (ABP(t)) modulation. We are able to monitor transient functions of CA using robotic two channel transcranial Doppler technology or ultrasonic volumetric time-of-flight technology. Shape of transient CA functions reliably identifies CA impairments and a start time points of ischemic or hyperemic events.

Symposium 4.2: Ultrasonic Non-Invasive Cerebrovascular Autoregulation Real-Time Monitoring

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Cerebrovascular autoregulation (CA) is a process which is maintaining an appropriate blood flow to the brain. The brain has a high metabolic demand, that's why adequate brain perfusion is required for proper brain function and viability. By means of CA the sufficient blood containing oxygen and nutrients were delivered and CO2 and other waste products were removed from brain tissues. The aim of this project is to develop and validate the method for monitoring of CA status on Ophthalmic artery (OA) by using a two-depth transcranial Doppler (TCD) on transorbital acoustic window. Two 2-MHz probes were mounted on an individually fitted headframe. The blood flow velocity (BFV) was recorded by using a two-depth TCD. A single measurement consisted of an hour's blood flow velocity recording, simultaneously with invasive ABP recording. The sampling frequency of raw ABP and ICP data was 300 Hz, and the sampling frequency of raw BFV was 1 Hz. The Bandpass-Chebyshev type I filter (specific order 10) was used to extract the slow ABP(t), ICP (t) and BFV(t) waves in the frequency range from 0.0083 to 0.02 Hz (50 sec to 2.0 minutes). The invasive CA index PRx was calculated as moving correlation coefficient between the slow waves of ICP(t) and ABP(t). The non-invasive CA index by using OA is defined as a non-invasive pressure reactivity index VORx (t) which is calculated as a moving correlation coefficient between the slow waves of BFV(t) and ABP(t). Preliminary results of 7 TBI patients showed that the correlation coefficient between PRx (t) and VORx(t) slow waves is 0.76. It is possible to use BFVP slow waves as ICP surrogate for calculating the VORx cerebral autoregulation index. This research project is funded by the European Social Fund according to the 2014–2020 Operational Programme for the European Union Funds' Investments, under measure's No. 09.3.3-LMT-K-712 activity "Promotion of postdoctoral fellowships studies".

Symposium 4.3. Exercise Physiology and Clinical Practice Areas

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Exercise Physiology is a principal division of Clinical Physiology. In Clinical Exercise Physiology Laboratories, performance tests and/or individualized exercise prescription are applied to athletes and variant patient types. The outcomes regarding aerobic and anaerobic performances are obtained via performance tests. Individual physiological responses to exercise is able to be analyzed via cardiopulmonary exercise test (CPET), that shows aerobic performance. Individually performance level is provided by metabolic measurements, such as maximum oxygen consumption (VO2max), carbon dioxide production, ventilation, respiratory equivalents, in CPET. Postoperative survival rates are estimated by measuring VO2max and respiratory reserve levels via preoperative CPET in patients with lung carcinoma and patients that will go on pulmonary endarterectomy or lung transplantation surgery. The CPET performed in cardiac transplantation patients provides data

related with necessity of transplantation. Peak power of leg muscles are determined by Wingate test that shows anaerobic performance in athletes. The athletes who experience dyspnea during exercise are evaluated regarding exercise induced bronchospasm by pulmonary function tests performed pre and post maximal exercise test. Following risk analysis, individualized exercise prescription is organized more frequently for the patients with obesity and diabetes and for all other patient groups and for healthy children or adults who want to exercise. The anthropometric properties as weight, height, fat percentage, fat mass and fat free mass of patients are measured. Bio-impedance analysis and skinfold measurements are done to determine anthropometric properties. According to the need of individuals, the issues related with nutritive physiology are informed, and daily total energy consumption is evaluated by basal metabolic rate measurement and daily physical activity assessments if necessary. In athletes, the anthropometrical properties are measured, the issues regarding sports nutrition are recommended, risk analysis are done. If necessary, ECG, aerobic and anaerobic exercise tests and pulmonary function tests are performed. Exercise Physiology, that works with Pediatric and Adult Obesity and Diabetes Centers, Pulmonary Medicine, Thoracic Surgery, General Surgery, Internal Medicine, Cardiology, Oncology, Child Psychiatry and Family Medicine, is a substitute of Clinical Physiology.

Keywords: Exercise Physiology, Cardiopulmonary Exercise Test (CPET), Exercise Prescription.

Panel 1: The Microbiota-Gut-Brain Axis: Neuronal Excitability

Panel 1.1. Intestinal Microbiota and Host Interactions

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The intestinal microbiota (IM) is a complex, dynamic and heterogeneous ecosystem with many microorganisms (1). Microbiota-host interactions have become one of the prominent research topics recently. As it is the largest micro-ecosystem in the human body, its effects on homeostasis are reported increasingly. The microbiota-host relationship is bidirectional and is affected by factors that change throughout the person's life such as diet, age or antibiotic usage. While this situation causes the development of individual differences (2); intestinal microbiota also affects host's health with its dynamic changes during life span. It has been shown that the high diversity in the microbiota usually affects health parameters positively. However, in dysbiosis, this interaction is reversed. The fact that the changes in the Firmicutes / Bacteriodes ratio, which is an indicator of dysbiosis, correalate to several diseases, highlights the importance of the distributions in this micro-ecosystem (3). The effects of IM on organ systems indicate that it is not only a commensal colonization form. While contributing to the maintenance of epithelial-barrier function in the gastrointestinal tract; it is also in contact with the enteral and the peripheral nervous system. Additionally, the density of immune cells in the gastrointestinal tract makes the interaction between microbiota and the immune system inevitable(4). Besides its local effects, IM may affect distant organ systems through its metabolic products. At the top of the list comes the cardiovascular system due to associations between dysbiosis and hypertension/ atherosclerosis. In the literature, there are opinions that the elimination of dysbiosis can contribute to the healing process in asthma and COPD, in which inflammatory events increase dramatically (5). Another major area of study is endocrine and metabolic diseases. Its relationship with obesity, its role in insulin resistance and hepatosteatosis, and the increased risk of developing diabetes in regarding dysbiosis are examples of metabolic effects (6). There are also opinions in favor of many nervous system diseases (mainly neurodegenerative) and the IM may be related. Therefore, with a holistic approach, IM seems to have remarkable importance in host health status.

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Panel 1.2: Effects of Intestinal Microbiota on the Enteric Nervous System

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The gastrointestinal (GI) tract is densely innervated by a mesh-like network of 200-600 million neurons which comprise the enteric nervous system (ENS) as a “second brain”. Although the ENS can autonomously influence the GI functions, it also communicates in a bidirectional manner (gut-brain axis) with the central nervous system by both vagal parasympathetic and sympathetic pathways (1). The ENS is regarded as the bridge between the intestinal microbiota and the nervous system, the so-called “microbiota-gut-brain axis” (2). The intestinal microbiota consists of a community of trillions of bacteria, virus, archaea, and fungi, which is primarily established at birth (3). More than 90% of the intestinal microbiota composition is represented by bacteria from the phyla Proteobacteria, Firmicutes, Actinobacteria and Bacteroidetes, but its composition and activity can vary throughout life by the multiple factors such as host-related factors (age, sex, genetic background and the immune system) and external factors (diet and the use of antibiotics or other pharmacological agents) (4). As the second-largest genome in the human body, the intestinal microbiota can effect ENS’ development and function either directly or indirectly. Evidence suggests that the microbiota can influence the ENS through generation of microbe- or host-derived components, or neuroactive metabolites which affect enteric nervous excitability and GI functions (1). The ENS is vulnerable to neurological or systemic diseases, thereby, understanding the underlying mechanisms of intestinal microbiota-ENS interactions and how intestinal microbiota act on the ENS have been significant research topics over the past decade (5). Possible contributions of intestinal microbiota to the ENS could provide new insights into furthering our understanding of neurological (e.g. Parkinson’s disease, Alzheimer’s disease), behavioral (e.g. anxiety and/or depression) and metabolic (e.g. type 2 diabetes, obesity) disorders.

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Panel 1.3: Effects of Gut Microbiota on the Central Nervous System

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The gut microbiota, which consists of bacteria, viruses, fungi, yeasts, and bacteriophages, begins to develop in humans after birth and continues for two to three years until a stable composition. The microbiota composition, which continues to be affected by different environmental and lifestyle factors, differs significantly even among healthy individuals (1). Metabolites such as short-chain fatty acids and neurotransmitter precursors produced by the gut microbiota can stimulate the enteric nervous system to produce neuropeptides or neurotransmitters. Furthermore, microbiota-derived components can activate both nerve vagus and circulating immune cells. Thus, the neural-immune-endocrine pathways activated by the direct effects of the bacteria that constitute the microbiota or the metabolites they produce create a dynamic communication network in the microbiota-gut-brain axis (2).

The imbalance in the microbiota's ecosystem is called dysbiosis and seems to be associated with the development of various diseases. The complex structure of the gut microbiota, unique to each organism, is associated with the individual's well-being and the health problems caused by the development of pathogenic microorganisms known as pathobionts (3). The interaction of the gut microbiota with the central nervous system has a significant impact on the disclosure and progression of neurodegenerative disorders in some cases. Neurological diseases such as Alzheimer's, Parkinson's and multiple sclerosis are thought to be associated with gut microbiota changes, which are more related to genetic or environmental factors (4). It has been reported that environmental factors such as feeding behavior, lifestyle habits, and antibiotic use affect the gut microbiota and pave the way for certain neurological and psychiatric diseases (5). In recent clinical and preclinical studies, a direct link has been established between the change in the amount of spesific bacterial species in the gut microbiota and neurological and psychiatric diseases. It has been stated that these bacteria, which can vary in amount, can be used as biomarkers (4). Recent progresses in the literature has displayed that the microbiota-gut-brain axis is a highly dynamic bidirectional process beyond what is supposed. Current studies have shown that gut microbiota has an essential role in the pathophysiology of many neurological diseases. There is a need to clarify further this connection between the microbiota-gut-brain axis and neurological diseases with future studies.

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Panel 1.4: Epilepsy in the Microbiota-Gut-Brain Axis

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Epilepsy is a disease that has neurological, cognitive, psychological and social consequences and affects more than 50 million people worldwide. Approximately 30% of epilepsy patients have seizures resistant to existing antiepileptic drugs. In order to control these drug-resistant seizures, there is a need for new treatment methods that can support or be an alternative to the classical pharmacological approach. On the other hand, epileptogenesis, which expresses the process related to the development of epileptic seizures, needs to be adequately clarified. Regarding this process, an adequate understanding of the events that cause the reorganization of neuronal networks, neurogenesis, neuro-inflammation, abnormal neurotransmitter release and axonal sprouting seems important for the treatment of epilepsy (1). The gut microbiota includes 100 billion-100 trillion bacteria and other microorganisms (viruses, protozoa, archaea and fungi) in 1000 different species (2). The composition of the gut microbiota is dynamic and is affected by sleep-wake, feeding-fasting cycles, diet, drugs, infections and antibiotic treatments. The microbiota affects their human host and is also affected by the host. One of the organs where this interaction takes place intensively is the brain. There is increasing evidence that the microbiota-gut-brain axis is not unidirectional, but that the brain and gut produce signals that interact to coordinate functions in health and disease (3). In the microbiota-gut-brain axis, one of the most open neurological diseases to interact with the microbiota is epilepsy. It is known that gastrointestinal symptoms are frequently seen in epilepsy patients, and people with inflammatory bowel disease are more susceptible to epilepsy (4). The first hypothesis for the interaction between epilepsy and gut microbiota dates back to the beginning of the 20th century with the concept of "Bacillus epilepticus" (5). With this theory, it was assumed that a possible gut microorganism might play a role in the onset and maintenance of epilepsy. Although this theory has not been proven, nearly 100 years later, it has come to the fore again and strongly that the gut microbiota can affect epilepsy via neuronal, endocrine and immune pathways (2).

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Oral Communications

OC-01

Effects of Melatonin Supplementation and Different Exercise Models on Cognitive Function in Long-Term Exposure to Constant Light in Rats

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AIM: Circadian arrhythmia affects cognition adversely, benefits of exercise are known. Effects of different exercise models on circadian arrhythmia and cognition are objects of interest. Effects of continuous moderate-intensity and high-intensity intermittent exercise and melatonin supplementation on cognition were investigated in rats with circadian arrhythmia caused by long-term exposure to constant light.

METHODS: After ethical approval (72.2021mar); Rats, including control group, were divided into seven groups (n=8/group); sedentary (SED), moderate-intensity continuous training (CMT), high-intensity intermittent training (HIIT) and melatonin (MEL) added groups. Control group was housed in light/dark, other animals were housed in light/light cycle. Exercise were performed on treadmill for 6 weeks (5 days/week), along last 3 weeks constant light was applied, respective rats received daily intraperitoneal melatonin injection (10 mg/kg). Cognition via object recognition test, spatial memory via Y-Maze, anxiety level via hole-board and elevated plus-maze tests were evaluated. Biochemical and histological evaluations were done in brain.

RESULTS: Cognition was suppressed in SED with light, improved with melatonin and/or exercise ($p<0.05$-0.01). Melatonin and/or exercise recovered spatial memory impaired by light ($p<0.05$-0.001). Exercise decreased anxiety level ($p<0.05$-0.001). Melatonin increased glutathione levels ($p<0.05$-0.001). Myeloperoxidase activity increased with circadian arrhythmia, was suppressed in melatonin groups ($p<0.05$-0.001). Catalase activity decreased with MEL, improved with both exercises ($p<0.05$-0.01). Irisin levels increased in HIIT and MEL groups ($p<0.05$). Brain-derived neurotrophic factor level decreased with exercise and/or melatonin ($p<0.05$-0.01). SED had pycnotic nuclei and degenerative changes; those were reduced with MEL or exercises in cortex and hippocampal CA3 region. Application of MEL and exercise together and HIIT provided more beneficial effects and increased neurogenesis.

CONCLUSION: Melatonin reduced degeneration of neurons. HIIT, CMT increased neurogenesis; HIIT increased angiogenesis. Our results show that melatonin and exercise improve suppressed working and spatial memory with circadian arrhythmia and recover neurodegeneration. Melatonin and exercise may be effective through different antioxidants.

Keywords: Exercise, HIIT, Melatonin, Rat, Circadian Rhythm.

OC-02

The BDNF-TrkB Signaling Pathway is Partially Involved in the Neuroprotective Effects of Hydrogen Sulfide in Parkinson's Disease

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AIM: This study aimed to examine the effects of hydrogen sulfide (H2S) on neural damage in Parkinson's disease (PD) and to reveal the role of the brain-derived neurotrophic factor (BDNF) - tropomyosin-related kinase B (TrkB) pathway in its possible effect.

METHODS: PD model was created with 1-methyl-phenyl-1,2,3,6-tetrahydropyridine (MPTP) in male C57BL/6 mice. Animals were randomly divided into six groups as Control, K252a, MPTP, MPTP+K252a, MPTP+NaHS, and MPTP+NaHS+K252a (n=12). Sodium hydrosulfide (NaHS) as a H2S donor and TrkB receptor antagonist K252a were administered intraperitoneally. Motor control and balance tests were performed before the subjects were sacrificed. Apoptotic cell death was histologically evaluated in the substantia nigra. Tissue cystathionine beta-synthase (CBS), 3-mercaptopyruvate sulfurtransferase (3-MST) levels and BDNF levels were determined by ELISA and TrkB expression was examined using RT-PCR. Statistical analysis was performed by one-way ANOVA and Tukey as a post hoc test.

RESULTS: While MPTP group show an increased time in motor behavior tests, NaHS treatment shortened the time spent in the balance beam and pole tests. The BDNF pathway played a role in the shortening of this period. Apoptotic index was 9.87±1.41% in the MPTP group, significantly reduced in MPTP+NaHS group (2.43±0.24, $p<0.0001$). This value increased to 4.56±0.32% in MPTP+NaHS+K252 group (difference from MPTP+NaHS, $p<0.01$). Striatal BDNF levels were significantly increased in the MPTP group ($p<0.05$, difference from control). While 3-MST levels remained unchanged, CBS levels were found to be decreased ($p<0.05$) in the MPTP+K252 group, compared to the MPTP group. TrkB-mRNA levels also remained unchanged in all groups.

CONCLUSION: The findings of the present study display that the BDNF-TrkB pathway partially plays a role in the protective effect of H2S in the experimental mouse model of PD. It is likely that changes in TrkB-activated intracellular signaling pathways rather than TrkB receptor itself play a role in this protective effect.

Keywords: Parkinson's disease, Hydrogen sulfide, BDNF, TrkB receptor, Apoptosis, K252a.

OC-03

Effect of Circadian Cycle Changes on Learning and Memory

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AIM: Circadian rhythms are physical, mental, and behavioral changes that follow a 24-hour cycle. The aim of this study; to investigate changes in hippocampal learning and memory in young-adult male offspring of mothers with different circadian cycle conditions.

METHODS: This study was performed in 48 male rats born from 18 pregnant rats (2-3 rats from each mother). Six pregnant rats were housed on a 12-hour dark and 12-hour light cycle, and their offspring continued in this cycle after birth (artificial photoperiod group, APG, n=16). The remaining 12 pregnant rats were housed on a 16-hour dark and 8-hour light cycle, and 16 randomly selected male pups were maintained on the same cycle after birth (extended photoperiod group, EPG, n=16), while the remaining 16 rats were exposed to a 12-hour dark and 12-hour light cycle from birth. (restored APG, rAPG). The offspring rats were kept under appropriate conditions until they were 60 days old. At day 60, rats were subjected to learning trials in the Morris Water Maze (MWM) using the 5-day hidden platform discovery protocol. Repeated measure Anova and One-way Anova tests were used for statistical analysis. $p<0.05$ was considered statistically significant.

RESULTS: According to MWM results, distance movement, escape latency and swimming speed did not differ statistically between the groups. Mean distance to platform values, Group*Day*Trial interaction were found significant (p=0.016). The post-hoc Tukey test showed that the rAPG group rats swam closer to the platform than the APG and EPG groups.Measurements of time spent in the target quadrant on the 5th day showed a significant difference between the groups (p=0.019). The rAPG group rats spent more time in the target quadrant than the APG and EPG group rats

CONCLUSION: Restoring the dark-light cycle after birth in rats whose dark-light cycles were changed during the intrauterine period had a positive effect on memory.

Keywords: Circadian Rhythm, Learning and Memory, Light-Dark, Morris Water Maze.

OC-04

The Effect of Resveratrol on Hyperalgesia Induced by REM Sleep Deprivation

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AIM: Resveratrol is a naturally occurring polyphenol found in a variety of food products. Studies have demonstrated the existence of anti-inflammatory, neuroprotective and antinociceptive effects of Resveratrol. In this study, the antinociceptive effect of Resveratrol was investigated in a 72-hour REM sleep deprivation-induced hyperalgesia model.

METHODS: After ethical approval, 40 male Wistar Albino rats, 8-12 weeks old, were divided into four groups of ten animals (PLS, placebo; RES2, Resveratrol 2mg/kg; RES5 Resveratrol 5mg/kg; RES10, Resveratrol 10mg/kg). All groups were subjected to 72-hour REM sleep deprivation protocol using modified multiple pot technique and pain assessment was performed with hot-plate and tail-flick tests at the beginning, end and after drug administration of the sleep-deprivation period. Mean values for pain assessment were produced from triple measurements and expressed in seconds. Following post-sleep-deprivation measurements, drugs and placebo were administered as a single dose by intraperitoneal injection. In order to compare the hot-plate and tail-flick measurements between groups before and after sleep-deprivation, the change from the first test to the post test was calculated for each condition. Kolmogorov-Smirnov was used to determine the normal distribution of the groups, and one-way ANOVA and Post-hoc Tukey were used to determine the difference between groups in pain measurements.

RESULTS: Sleep deprivation caused hyperalgesia in all groups (Hot-plate time decreased at the stated rates: PLS=51.1%; RES2=63.4%; RES5=60,4%; RES10=60.6% ($p<0,05$); decreases in tail-flick test PLS=53.2%, RES2=56.5%, RES5=70.9%, RES10=66.3% ($p<0,05$). Resveratrol showed an analgesic effect at a dose of 10mg/kg (Hot-plate pain measurement change PLS = 13.8% decreased while RES10=37.5% increase ($p<0,05$); tail-flick PLS =19.6% decreased, RES10=21.9% increase) ($p<0,05$).

CONCLUSION: Resveratrol showed analgesic effect in sleep deprivation-related pain model. This finding suggests that it has the potential to be used in the treatment of painful syndromes associated with sleep disturbance in the clinic.

Keywords: REM Sleep Deprivation, Hyperalgesia, Resveratrol.

OC-05

The Effects of Physical Activity on Cognitive Functions and Serum BDNF, GDNF, VEGF, Phoenixin-20 and IL-12 Levels of Elderly Individuals

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AIM: It is known that regular exercise protects and improves not only the physical and motor functions of individuals but also their cognitive functions in the coming years. In this study, it was aimed to examine the relationship between serum levels of related neuroprotective molecules and cognitive and memory functions.

METHODS: Our study was carried out with the experimental group (n:20) aged 50-69 who did exercise regularly in the last year and the control group aged (n:20) 50-69 who did not exercise regularly. Mini Mental Test, Visual Response Time Tests (Simple Visual Response Time, Complex Visual Response Time, Simple Recognition Visual Response Time, Complex Recognition Visual Response Time, Öktem - Verbal Memory Processes Test) were performed. BDNF, GDNF, VEGF, Phoenixin-20 and IL-12 levels were analyzed by ELISA method with the serum obtained from venous blood samples taken 24 hours after the last training. In statistical analysis, descriptive statistics were used for the demographic information of the participants. Motor and cognitive test results of groups and serum BDNF, GDNF, VEGF, Phoenixin-20 and IL-12 levels were compared with independent t-test.

RESULTS: Serum IL-12 levels were significantly increased for the experimental group compared to the control group ($p<0.05$). There was no significant difference in serum BDNF, GDNF, VEGF, Phoenixin-20 levels between the groups. The Highest Learning Score was found to be significantly higher in marathon runners ($p<0.05$). Among the groups; there was no significant difference in instant memory score, total learning score and inconsistency scores. Simple visual response time and complex visual response time were significantly reduced for the experimental group compared to the control group ($p<0.05$). There was no significant difference between the groups in terms of simple cognitive-visual reaction time and complex visual reaction time.

CONCLUSION: Our results show that long-distance running has a positive effect on cognitive functions in older ages.

Keywords: BDNF, Cognition, Chronic exercise, GDNF, Phoenixin, VEGF.

OC-06

Therapeutical Effects of Neuropeptide-S on Paraquat-Induced Experimental Model of Parkinson's Disease

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AIM: The aim of the present study was (i) in-vitro investigation of the neuroprotective action of neuropeptide-S (NPS) in a cellular level and (ii) to elucidate the effect of intranasal NPS on motor dysfunction in experimental Parkinson's Disease (PD).

METHODS: For neuronal differentiation, SH-SY5Y cells were cultured with retinoic acid (RA; 10 µM/mL) containing media for 6 days. Paraquat (1 mM) was applied for the PD model. Effects of 0.5-2 µM NPS on cell viability were evaluated. NPS receptor (NPSR) antagonist ML-154 was applied to the cells pretreated with paraquat and NPS. Additionally, Bax gene expression was measured by RT-PCR. Tyrosine hydroxylase (TH) and PGP9.5-positive cells were visualized by immunofluorescence. For in-vivo experiments; following basal motor performance tests, adult male Sprague-Dawley rats received paraquat (10 mg•ml•kg-1) via oral gavage for 7 consecutive days with or without intranasal NPS (40 nmol/20 µL). ML-154 was applied intracerebroventricularly (icv) throughout the NPS regimen. TH and NPSR-positive neurons in substantia nigra pars compacta (SNpc) were visualized by immunohistochemistry. The data were analyzed by Mann Whitney-U test. Experimental procedures were approved by Animal Ethical Committee of Akdeniz University (B.30.2.AKD.0.05.07.00/147).

RESULTS: 0.5 µM NPS exibited neuroprotective effects ($p<0.05$) and 1 µM ML-154 significantly decreased cell viability compared to paraquat+NPS group ($p<0.05$). Lower Bax mRNA levels were observed in NPC-treated groups. NPSR expression was not affected by paraquat. NPSR was detected in TH- and PGP 9.5-positive cells. Motor tests demonstrated that intranasal NPS significantly ($p<0.05$) ameliorated the paraquat-induced parkinsonian symptoms which was reversed by ML-154. Similarly, NPS prevented the paraquat-induced neuronal loss in SNpc, while neuroprotective action of NPS was remarkably impaired by ML-154.

CONCLUSION: Intranasally administration of NPS exerts neuroprotective effect that seems to be involved with a NPSR-dependent anti-apoptotic action. Therefore, brain NPSR could be considered as a target for non-invasive treatment strategies for PD.

Keywords: Neuropeptide-S, NPSR, Parkinson's Disease, SH-SY5Y, Motor dysfunction.

OC-07

Protective Effect of Boldine Against Rotenone-Induced In Vitro Parkinson's Disease Model in SH-SY5Y Cells

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AIM: Rotenone is an organic pesticide often used in animal/cell studies to establish an experimental Parkinson's disease model. Although the strong antioxidant and anti-inflammatory effects of boldin are known, there are not many studies on its protective efficacy against neurodegenerative diseases such as Parkinson's disease. In this study, it was aimed to investigate the protective effects of boldin in an in vitro Parkinson's disease model induced by rotenone in SH-SY5Y cells.

METHODS: In this study, rotenone was administered to SH-SY5Y cells for 24 hours, and the LD50 dose was 200 nM. To investigate Boldin's protective efficacy, cells were pretreated with it for 2 hours. Then, cells were treated with 200 nM rotenone for 24 hours. Cell viability was assessed by the MTS test and colony-forming abilities by the clonogenic assay. Caspase-3 ELISA and Hoechst staining assess cell death. One-way ANOVA was used for statistical analysis.

RESULTS: Our results showed that 200 nM rotenone killed approximately half of the cell population ($p<0.0001$). It was observed that cell survival and colony formation ability increased significantly when 0.1 µM boldin treatment was applied for 2 hours before rotenone (200 nM) application ($p<0.0001$). In addition, 0.1 µM boldin pretreatment reduced rotenone-induced increased chromatin condensation and active caspase 3 levels ($p<0.0001$).

CONCLUSION: The results of our study revealed that rotenone decreased cell viability by increasing apoptotic cell death in SH-SY5Y cells. While Boldin showed an antiapoptotic effect by increasing cell survival and colony formation ability at low doses against rotenone-induced neurotoxicity, it was observed that this protective activity decreased as the dose increased. With this study, the protective efficacy of boldin in an in vitro Parkinson's disease model created with rotenone was demonstrated for the first time. This study was supported by Ege University BAP Coordinatorship (TYL-2021-22429).

Keywords: Boldine, Neurotoxicity, Parkinson, Rotenone.

OC-08

Activation of TRESK Channels Ameliorates Pain and Neurogenic Inflammation in a Nitroglycerin-Induced Migraine Model in Rats

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AIM: Neurogenic inflammation characterized by calcitonin gene-related peptide(CGRP) release, vasodilation, and mast cell degranulation in the meninges is held responsible for migraine pathophysiology. TRESK background-potassium channels, which are widely distributed in trigeminovascular system, play important role in regulation of neuronal excitability. We aimed to investigate effects of different doses of specific TRESK channel activator cloxyquin on pain-behavior and mechanisms responsible for migraine pain in a nitroglycerin-induced migraine model in rats.

METHODS: Wistar male-rats were randomly separated 10 groups (n=7) followed by intraperitoneal administrations: VEH1+VEH1: nitroglycerin solvent(control), NTG+VEH1: 10 mg/kg nitroglycerin and its solvent, NTG+VEH2: nitroglycerin, and cloxyquin solvent, NTG+Cloxy-1, 2 and 3: nitroglycerin, and cloxyquin doses 1, 10 and 50 mg/kg respectively, NTG+A2764+Cloxy: nitroglycerin, 10 mg/kg A2764(TRESK-inhibitor) and effective dose of cloxyquin, NTG+Sum: nitroglycerin and 1 mg/kg sumatriptan used in migraine treatment, NTG+Sum+Cloxy: nitroglycerin, sumatriptan and effective dose of cloxyquin, VEH1+Cloxy: nitroglycerin solvent and effective dose of cloxyquin. Pain-behavior was tested using von-Frey filaments. Plasma and trigeminal ganglion CGRP levels, and brainstem CGRP and C-fos levels were determined by ELISA, and number and degranulation of meningeal mast cells were determined by toluidine-blue staining. Data were compared by one-way ANOVA. Ethical approval:2021/10(BAIBU-HAYEK).

RESULTS: The 10 and 50 mg/kg doses of cloxyquin significantly reduced nitroglycerin-induced pain, and plasma and trigeminal ganglion CGRP levels, and brainstem CGRP and C-fos levels, also number and degranulation of mast cells($p<0.05$), while 1 mg/kg dose was ineffective. A2764 reversed therapeutic effects of cloxyquin($p<0.01$), confirming that the effect was mediated through TRESK channels. Cloxyquin had no effect on baseline values, no superiority over sumatriptan or synergistic effect.

CONCLUSION: Cloxyquin dose-dependently suppresses pain-behavior, increased CGRP, C-fos, and mast cell number and activation by making neuronal excitability difficult in trigeminovascular system. These effects of cloxyquin suggest that it may be effective in migraine treatment by inhibiting components of neurogenic inflammation.
Grant-number:2021.08.02.1513(BAIBU-BAP).

Keywords: Cloxyquin, Mast cell, Migraine, Neurogenic inflammation, TRESK Background Potassium Channels.

OC-09

Effects of Chronic Stress and Caffeine Consumption on Visceral Pain and Emotional Status: The Role of Adenosine and Estrogen Receptors

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AIM: Caffeine, a non-selective adenosine receptor antagonist, is consumed extensively during stressful conditions. Effects of chronic caffeine consumption varies between sexes. It was aimed to investigate contribution of adenosine and estrogen receptors in effects of caffeine intake during chronic stress (CS) on visceral pain, emotional status and oxidative colonic damage in rats.

METHODS: To induce CS, Sprague-Dawley female rats (n=56) were exposed to early-life stress between post-natal 2nd-12th days by separating from mothers for 3-h/day, and starting by 10th week, they were exposed to reversed-light cycle and cat-litter 2 days/week for 4 weeks. No stress was applied to control group (n=8). Stressed-rats drank plain or caffeinated-water (5, 10, 25 mg/kg/day), or in addition to caffeinated-water they were injected subcutaneously with adenosine A1-receptor antagonist (DCPPX; 1mg/kg/day), G-protein coupled estrogen receptor antagonist (ERA) (300µg/kg/day) or non-selective ERA (1mg/kg/day) for 4 weeks. On last 5 days, spontaneous locomotor activity, tail-suspension test, and visceromotor reflex (VMR) were determined. Glutathione and malondialdehyde levels were measured in colonic tissues. One-way ANOVA was used for statistical evaluation.

RESULTS: In non-caffeine-treated CS-group, intrarectal volume evoking VMR was reduced ($p<0.05$), indicating visceral hyperalgesia; while visceral hyperalgesia was absent in 25 mg/kg caffeine- and DPCPX-treated CS-groups. Compared to control group, locomotor activity was increased in CS-groups ($p<0.001$), and DPCPX prevented enhanced activity ($p<0.001$). Caffeine did not affect streOC-induced increased motor activity, but non-selective ERA+caffeine decreased locomotor activity ($p<0.001$). In non-caffeine-treated CS-group, increased immobility on tail-suspension test ($p<0.01$), indicated depression. All doses of caffeine and DPCPX prevented depression ($p<0.001$), while non-selective ERA+caffeine diminished anti-depressive effect of caffeine ($p<0.001$). Colonic malondialdehyde levels were similar in all groups, and decreased glutathione levels in CS-group ($p<0.05$-0.01) was not changed with treatments.

CONCLUSION: Caffeine suppresses chronic streOC-induced visceral hypersensitivity and depression by blocking adenosine, especially A1 receptors, via the contribution of estrogen receptors.

Keywords: Adenosine Receptor, Caffeine, Depression, Estrogen receptor, Stress.

OC-10

Interaction of Choline and Kynurenic Acid in an Inflammation Model of Established in RAW 264.7 Rat Macrophage Cell Cultures

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AIM: The inflammatory response is controlled by the cholinergic anti-inflammatory pathway in which endogenous acetylcholine (ACh) produced in immune system cells and calcium (Ca^{2+})-permeable alpha 7 nicotinic ACh receptors (α7nAChRs) activated by cholinomimetic agents. It is known that ACh precursor choline and tryptophan metabolite kynurenic acid (KA) can induce immunomodulatory effects and interact with α7nAChRs. The purpose of this study is to investigate the possible interaction of choline and KA on the cyclooxygenase (COX)-2 pathway in a lipopolysaccharide (LPS)-induced in vitro model of inflammation in RAW 264.7 macrophages.

METHODS: The effects of choline and KA (1-3-10-30-100 µM) on COX-2 enzyme expression and COX-2 product prostaglandin E2 (PGE2) and TNFα levels were investigated by RT-PCR and ELISA. The changes in α7nAChR-elevated intracellular Ca^{2+} levels induced by choline and/or KA in the presence of selective α7nAChR antagonist methylylcaconite citrate and nAChR antagonist mecamylamine were examined by a spectrofluorometric method.

RESULTS: Choline and KA, COX-2 increase in the presence of LPS decreased PGE2 and TNFα levels ($p<0.001$), while choline increased intracellular Ca^{2+} levels through α7nAChR activation ($p<0.05$). Co-administration of KA and choline increased the efficacy of choline on inflammatory parameters ($p<0.01$). Increased intracellular Ca^{2+} upon activation of α7nAChR by choline was only partially inhibited in the presence of high concentrations of KA ($p<0.05$).

CONCLUSION: Our findings suggest a possible cumulative interaction between tryptophan metabolite KA and choline in the inflammatory response due to inhibition of COX-2 expression, PGE2, TNFα levels.

Keywords: Choline, Kynurenic acid, Inflammation.

OC-11

A2A Adenosine Receptors Regulate Multiple Organ Failure After Hemorrhagic Shock in Mice

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AIM: Trauma hemorrhagic shock (T/HS) is a clinical condition which causes multiple organ failure (MOF) that needs rapid intervention. Restricted oxygen at the cellular level causes inflammation and subsequent cell death. Adenosine triphosphate is the universal intracellular energy currency and an important extracellular inflammatory signaling molecule. Adenosine, an endogenous nucleotide formed as a result of the breakdown of adenosine triphosphate, is also released during T/HS. Adenosine binds to four G-protein-coupled receptors (A1, A2A, A2B, A3) called adenosine receptors (ARs) or P1 receptors. In the present study, we evaluated the effect of activation, inactivation and genetic absence of A2AAR (A2AAR-/- mice) on T/HS-induced multiple organ failure.

METHODS: Wild-type mice were pretreated (30 minutes before shock induction) with an agonist or antagonist and then subjected to T/HS by withdrawing arterial blood and maintaining the blood pressure between 28 and 32 mmHg. A2AAR-/- mice were subjected to T/HS in the absence of pharmacologic treatment. Neutrophil sequestration was assessed by detecting myeloperoxidase and Evans blue dye (EBD) method was used to analyze lung permeability. Blood and lung inflammatory cytokine levels were determined by sandwich ELISA. The liver enzymes aspartate transferase (AST) and alanine transaminase (ALT) were determined spectrophotometrically from plasma. Activation of the apoptotic cascade was evaluated using a mouse apoptosis array.

RESULTS: Our results demonstrate that the selective A2AAR agonist CGS21680 decreases lung neutrophil sequestration, lung pro-inflammatory cytokines IL-6 and TNF-, and bronchoalveolar lavage EBD. Pretreatment with the selective antagonist ZM241385 and genetic blockade in A2AAR-/- mice increased neutrophil sequestration, pro-inflammatory cytokine levels, and bronchoalveolar lavage fluid EBD. The myeloperoxidase level in the lung was also increased in A2AAR-/- mice. We observed that anti-apoptotic markers decreased significantly with the absence of A2AAR in the lung and spleen after T/HS.

CONCLUSION: Our data demonstrate that activation of A2AAR protects organs against T/HS-induced injury.

Keywords: A2A Adenosine Receptors, CGS21680, Hemorrhagic shock, Lung injury, Purinergic signaling, ZM241385.

OC-12

Antioxidant and Anti-Inflammatory Effect of Apelin-13 in Cyclophosphamide-Induced Lung Injury

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AIM: Apelin-13 is an endogenous adipocytokine with potent antioxidant and anti-inflammatory properties. The aim of the study is to investigate whether Apelin-13 has antioxidant and anti-inflammatory effects in cyclophosphamide (CP)-induced lung injury.

METHODS: Using a total of 24 3-month-old male Wistar albino rats, 4 groups were formed: 1) saline (ip) for 5 days in the control group, 2) saline (ip) for 4 days and a single dose of CP (200 mg/kg, ip) on the 5th day to the CP group, 3) Apelin-13 (10 µg/kg/day, ip) for 5 days to the Apelin-13 group, 4) Apelin-13 for 5 days and a single dose of CP was applied on the 5th day to the CP+Apelin-13 group. mRNA expression of Sirt1, NF-kB, p-53, and apelin receptor (APJ) genes in lung tissues by qRT-PCR, TNF-a, IL-1b, total oxidant (TOS), and antioxidant levels (TAS) were studied by ELISA method. The oxidative stress index (OSI) was obtained by the ratio of TOS to TAS. In addition, lung epithelial-derived surfactant protein-D (SP-D) and Krebs von den Lungen-6 glycoprotein (KL-6) levels, which are accepted as lung tissue damage markers, were studied in plasma samples by the ELISA method. One-way ANOVA was used for intergroup comparisons.

RESULTS: CP administration decreased Sirt1 mRNA expression compared to the control group, while increased NF-kB, p-53, and APJ mRNA expression, TNF-a, IL-1b, and OSI. Plasma SP-D and KL-6 levels were also higher in the CP group ($p<0.05$). Co-administration of CP and Apelin-13 significantly reversed the changes induced by CP treatment alone ($p<0.05$). Sirt1 and APJ mRNA expressions were higher in the group that Apelin-13 applied alone compared to the control group ($p<0.05$).

CONCLUSION: Our findings indicate that Apelin-13 has antioxidant and anti-inflammatory effects in cyclophosphamide-induced lung injury.

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Keywords: Apelin-13, Cyclophosphamide, Lung, NF-kB, p-53, Sirt1.

OC-13

Effect of Apelin-13 Administration on Sirt1, NF-kB Genes and Oxidative Stress in Kidney Tissue of Old and Young Rats

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AIM: Aging is a multifactorial process characterized by oxidative stress and inflammation. Apelin-13 is an endogenous adipocytokine known to have a protective effect on many organs with its antioxidant, and anti-inflammatory properties. In this study, the possible effects of Apelin-13 application on Sirt1 and NF-kB gene expressions and proinflammatory cytokines such as TNFα, and IL1b, as well as total oxidant and antioxidant responses in kidney tissue of old and young rats were investigated.

METHODS: In the study, using 24 male Wistar albino rats, 4 groups were formed: young control (3 months), young apelin (3 months), old control (24 months), and old apelin (24 months). Only saline injection (ip) was applied to the control groups, and apelin-13 (15 µg/kg, ip) was administered to the apelin groups for 10 days. Oxidative stress index (OSI) was calculated by measuring the total oxidant level (TOS) and total antioxidant level (TAS). ELISA method was used for the measurement of TNFα and IL1b proteins. Furthermore, Sirt1 and NF-kB gene expressions in kidney tissue were determined by qRT-PCR. For statistical analysis, Kruskal Wallis, Mann Whitney U test was performed and Spearman r was calculated.

RESULTS: Sirt1 mRNA expression and TAS were decreased in aged rats compared to young controls, while NF-kB mRNA expression, TOS, and OSI were increased ($p<0.05$). It was observed that apelin application in aged rats was effective in reversing these age-related changes ($p<0.05$). There was no significant difference between the groups in TNFα and IL1b protein measurements ($p>0.05$). In addition, a negative correlation was determined between Sirt 1 and TOS and OSI values ($p<0.05$).

CONCLUSION: Apelin may be effective in reducing oxidative stress in aging by affecting the expression of Sirt1 and NF-kB genes in kidney tissue.
This study was supported by Afyonkarahisar Health Sciences University Scientific Research Projects Commission under grant number 21.KARİYER.003.

Keywords: Aging, Apelin-13, NF-kB, Oxidative stress, Sirt1.

OC-14

Effect of SIRT2 Inhibition on Developing Fibrosis in D-Galactose-Induced Aging Model

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AIM: Aging is a risk factor for fibrosis and liver injury. SIRT2 inhibition has been shown to have a protective effect on the mechanism of renal interstitial fibrosis. In our study, it was aimed to determine the effect of SIRT2 inhibition by AGK-2 on liver functions and its role in the fibrosis process in the aging model caused by D-galactose (D-GAL).

METHODS: A total of 32 3-month-old Sprague Dawley rats were used in the study. Rats were divided into 4 groups as Control, D-GAL, Solvent+D-GAL, D-GAL+AGK2+Solvent. D-galactose (150 mg/kg/day), AGK-2 (10µM/bw) as a specific SIRT2 inhibitor, 4%DMSO+PBS as a solvent were applied to the experimental groups and physiological saline was applied to the control group for 10 weeks. Biochemical parameters (ALT, AST, platelet count, LDH, HDL, VLDL, total cholesterol, triglyceride) were measured in plasma.

AST-ALT Ratio, AST-Platelet Ratio Index (APRI), liver index (liver weight/body weight) were calculated. SIRT2 levels in liver tissues were determined by western blot (WB) and immunohistochemical (IHC) analysis. The expression level of TGF β, β catenin, PDGFBB genes was determined by real-time-polymerase chain reaction. Histopathological scoring was performed to detect tissue damage. For statistical analysis, the data obtained from the study were presented as "mean±standard deviation". One-way ANOVA (post-hoc LSD) test was used to determine the intergroup differences, and Pearson correlation test was used to determine the relationshipsbetween the variables($p<0.05$).

RESULTS: D-Galactose administration increased AST, AST-ALT ratio, APRI, SIRT2 protein expression, TGF β, β catenin mRNA levels in liver tissue. AGK-2 application decreased all these parameters. SIRT2 expression (WB) is positively correlated with AST, APRI index, TGF β1, β-catenin mRNA expression. SIRT2 (IHC) is positively correlated with AST/ALT and APRI index.

CONCLUSION: It is thought that SIRT2 inhibition may be effective in improving aging-related fibrotic changes in the liver and preventing aging-related loss of function.

Keywords: D-Galactose, Fibrosis, SIRT2 inhibition, TGFβ, β catenin, Liver.

OC-15

The Level of Humanin, a Mitochondrial Peptide is Higher in Breast Cancer Patients

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AIM: Breast cancer is the most common type of cancer in women and the leading cause of cancer death worldwide. Breast cancer, a multifactorial disease, is known to be affected by mitochondrial dysfunction. However, it is unknown whether humanin, a peptide derived from mitochondria, is altered in breast cancer patients. The present study aims to investigate the relationship between humanin levels and the risk of developing breast cancer.

METHODS: The target population included in the study were patients diagnosed with primary invasive ductal breast cancer. Patients with metabolic diseases, liver disease, diabetes mellitus, severe psychiatric conditions and gynaecological disease were excluded. While the breast cancer sample consisted of 45 female patients from the Oncology Clinic who met these criteria, 45 healthy women participated in the study as voluntary controls. There is no difference in the demographic characteristics (age, height, weight, and body mass index) of the control group and the breast cancer patients. Humanin level was measured in the serum of the subjects included in the study by the ELISA method.

RESULTS: The serum humanin levels of breast cancer patients increased when compared to healthy individuals (309.51±71.59 vs 223.74±38,63 pg/ml $p < 0.001$). The increase in serum humanin level of breast cancer patients was statistically significant ($p<.001$).

CONCLUSION: As a result, our study provides preliminary evidence that serum humanin levels may be a new marker for early detection of breast cancer.

Keywords: Humanin, Mitochondrial Dysfunction, Breast Cancer.

OC-16

Apoptotic and Metastatic Effect of Taurine in Triple Negative Breast Cancer Treated with Doxorubicin

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AIM: Breast cancer is the most common type of cancer among women. It is characterized by strong invasion, easy metastasis, and poor prognosis. Triple negative breast cancer (TNBC) is characterized by a deficiency of estrogen, progesterone receptor and human epidermal growth factor receptor-2. Doxorubicin (Dox) is used in breast cancer treatment. Taurine (Tau) is the major intracellular free β amino acid found in mammalian tissues. It has been shown to induce apoptosis in cancer cells, reduce the levels of proteins that are effective in metastatic pathway, inhibit cell proliferation and tumor growth in vivo. We aimed to investigate the effect of taurine on the anti-cancer role of doxorubicin through apoptotic and metastatic pathways in TNBC.

METHODS: BALB/c female mice aged 6-8 weeks were used. Solid tumors were formed by injecting TNBC cells (4T1) subcutaneously into the left breast. Tau (100 mg/kg i.p) was administered daily, and Dox (4 mg/kg i.p) every 5 days for 21 days. At the end of the experiment, lung and tumor tissues were weighed. Apoptotic and metastatic protein levels were determined by ELISA. The difference between groups was assessed at $P<0.05$ with Kruskal-Wallis/Wilcoxon post-hoc test (Project no: THD-2021-19181, Ethics committee: 2020/10-10; This study is part of a project. Histopathological studies are ongoing).

RESULTS: There was a decrease in animal weights ($P<0.05$) in Dox and Dox+Tau groups, and a decrease in tumor volumes in Dox group ($P<0.05$). Although lung weights and Bax/Bcl-2 ratio decreased in Dox and Dox+Tau groups, the difference was not significant. Bcl-2, Caspase-3 and MMP-2 levels were higher in Dox+Tau group ($P<0.05$). There was no difference between groups in Bax, MMP-9 and VEGF.

CONCLUSION: When Dox and Tau were given together, it could not completely prevent metastasis in mouse TNBC model and caused a decrease in tumor volume with its partial effect in apoptotic pathway.

Keywords: Doxorubicin, Taurine, Triple Negative Breast Cancer, Apoptosis, Metastasis.

OC-17

Aortic Injury via Ischemia Reperfusion and the Preventive Role of Fluoxetine

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AIM: The thoracic or infrarenal abdominal aortic croOC-clamping is frequently performed in the aneurysm and peripheral vascular surgery and leads to ischemia-reperfusion (IR). The aim of the present study was to investigate the potential antioxidant, anti-inflammatory, and antiapoptotic effects of fluoxetine (FLX), which is a selective serotonin reuptake inhibitor and widely used as a preoperative anxiolytic, on aortic tissue injury induced by IR of the infrarenal abdominal aorta in rats.

METHODS: Wistar rats were randomized into three groups as (1) control (sham laparotomy); (2) IR without Flx (60-min ischemia and 120-min reperfusion); (3) IR with Flx (Flx + IR) (Flx; 20 mg/kg/d i.p. dosage), intraperitoneally for 3 d before surgery. Aortic tissue samples were homogenized and oxidative, inflammatory, and apoptotic biochemical analyzes were performed. Lipid hydroperoxide (LOOH), malondialdehyde (MDA), reactive oxygen species (ROS), total oxidant status (TOS), superoxide dismutase (SOD), glutathione (GSH), total antioxidant status (TAS), myeloperoxidase (MPO), tumor necrosis factor-alpha (TNFα), interleukin-1 beta (IL-1 β), interleukin-6 (IL-6), interleukin-10 (IL-10), nuclear factor-kappa B (NF-kB), nitric oxide (NO), metalloprotease (MMP), caspase-9, 8-hydroxy-2'-deoxyguanosine (8-OHdG), synthase and hyaluronan (HA) were evaluated. Histologic evaluation of the tissues was also performed.

RESULTS: LOOH, MDA, ROS, TOS, MPO, TNFα, IL-1β, IL-6, NF-kB, MMP, caspase-9, 8-OHdG, NO, and HA levels in the IR group were significantly higher ($p<0.05$) whereas the activity of SOD, GSH, TAS, and IL-10 levels were lower than the control($p<0.05$). FLX significantly decreased LOOH, MDA, ROS, TOS, MPO, TNFα, IL-1β, IL-6, NF-kB, MMP, caspase-9, 8-OHdG, NO, and HA levels($P<0.05$) while increasing IL-10, SOD, GSH, and TAS compared to IR($P<0.05$). Flx attenuated the morphological changes associated with aortic tissue injury ($p<0.001$).

CONCLUSION: Our study is the first study to evaluate the aortic tissue damage caused by ischemia reperfusion of the infrarenal abdominal aorta that can be suppressed by the antioxidant, anti-inflammatory and antiapoptotic effects of Flx.

Keywords: Ischemia reperfusion, Aortic injury, Fluoxetine.

OC-18

Effects of Topiramate, a Carbonic Anhydrase Inhibitor, on Erythrocyte Osmotic Fragility and Whole Blood Viscosity

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AIM: Peripheral paraesthesia is common side effect of carbonic anhydrase (CA) inhibiting, antiepileptic drugs such as TPM, acetazolamide and zonisamide. CAII, which is abundant in erythrocytes, has physical connections with HCO3- transporter Band-3 protein. Band-3 is an important part of erythrocyte cytoskeleton and one of the determinants of deformability. Therefore, we investigated dose-dependent effects of topiramate on hemorheological parameters, which may result in deformability and microcirculation problems by affecting the Band-3 with CA inhibition.

METHODS: Wistar albino rats (270±50g) were divided into 3 groups (6/group) and received TPM (50-100 mg/kg/day, po) or distilled water for 3 weeks. Animals were euthanized by cardiac exsanguination, hematocrit, erythrocyte osmotic fragility (spectrophotometrically), whole blood (high shear rate, original hematocrit) and plasma viscosity were determined. CA activity was measured using Wilbur-Anderson method. Data are represented as mean±std deviation. Kruskal-Wallis and Mann-Whitney-U test utilized when appropriate and significance was accepted when $P<0.05$. GU.ET-21.056

RESULTS: 50 mg/kg TPM increased osmotic fragility ($P=0.018$). Although increased fragility seemed to cause a decrease in hematocrit levels, the difference wasn't significant. 100 mg/kg TPM decreased whole blood viscosity, but did not significantly affect plasma viscosity when compared with the control group (cPoise, control: 5.04±0.66; 100TPM: 4.16±0.33, $P=0.028$). Although 100 mg/kg TPM decreased CA activity, the difference was not significant.

CONCLUSION: Since 50 and 100 mg TPM changed hemorheological parameters in the opposite direction, we concluded that TPM probably exerts these effects through different mechanisms. While the increase in fragility seen at 50 mg/kg dose precipitates paraesthesia, which is more common in the early stages of treatment, the decrease in viscosity caused by 100 mg/kg TPM may balance this effect and explain the frequent disappearance of paraesthesia in the later periods. These mechanisms need to be explored and clarified in order to improve treatment outcomes and reduce side effects in the future.

Keywords: Topiramate, Erythrocyte Osmotic Fragility, Whole Blood Viscosity.

OC-19

Investigation of the Effects of TGF- β and TGF- β Inhibitors on Cell Proliferation and Senescence in Human Corneal Endothelial Cells

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AIM: The in-vivo proliferation capacity of human corneal endothelial cells (HCECs) is limited. Under pathological conditions, endothelial cell loss causes permanent vision loss due to corneal edema. Currently, the only treatment for corneal endothelial insufficiency is corneal transplantation. However, serious problems in supplying corneal donors worldwide lead researchers developing cell-based approaches based on in-vitro propagation of HCECs. In this study, it was aimed to investigate the effects of TGF-β, ITD-1 (TGF-β inhibitor) and SB431542 (TGF-β receptor inhibitor) on proliferation, function and senescence properties of HCECs.

METHODS: In this study, control, TGF-β1, ITD-1, SB431542, TGF-β1+ITD-1 and TGF-β1+SB431542 groups were formed using HCEC line. Proliferation abilities were evaluated by BrdU analysis, corneal endothelial cell markers, ZO-1 and COL8A2, by RT-PCR, cell senescence by SA-β-Gal staining and TGF-β1 levels by Elisa method. Cell groups were treated with TGF-β1 (2 ng/ml), ITD-1 (10 µM), SB431542 (10 µM), TGF-β1 (2 ng/ml)+ITD-1 (10 µM), and TGF-β1 (2 ng) /ml)+SB431542 (10 µM) for 24 and 48 hours. For ELISA and RT-PCR experiments, 2 ng/ml TGF-β1, 10 µM ITD-1 and 10 µM SB431542 were selected as effective dose and 48 hours as effective time. For cell senescence, cell groups were fixed at the end of the 1st and 7th days and stained with SA-β-Gal.

RESULTS: In this study, TGF-β1 reduced HCEC proliferation; ITD-1 and SB431542 increased cell proliferation ($p<0.05$). ZO-1 and COL8A2 expressions were increased in the SB431542 group ($p<0.05$). TGF-β and TGF-β inhibitors did not affect senescence at 7th day, while TGF-β receptor inhibitor improved senescence findings in the early period, which disappeared over time. Based on these findings, TGF-β suppresses proliferation, accelerates senescence and decreases expression of endothelial cell markers in HCECs.

CONCLUSION: Therefore, ITD-1 and especially SB431542 can prevent/reduce negative effects of TGF-β on HCECs. These results may contribute to development of cell-based therapies in corneal endothelial insufficiency.

Keywords: Cornea, Endothelium, Proliferation, TGF-β, Cellular Senescence.

OC-20

Effect of Erythrocytes on ATP Mediated Vascular Relaxation Responses in Preeclampsia

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AIM: Preeclampsia (PE) that occurs after the 20th week of pregnancy is characterized by protein excretion in the urine and increased blood pressure. The major change observed in PE is generalized peripheral vasoconstriction. The endothelial dysfunction is the most important component of PE pathogenesis. The aim of our study is to investigate whether erythrocytes obtained from PE patients affect the vasodilation response to Adenosine triphosphate (ATP).

METHODS: Thoracic aortic rings obtained from 2-month-old male Wistar rats were used in our study, which was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee and Animal Experiments Local Ethics Committee (2020.02.005). Vascular relaxation responses were recorded by applying ATP (10-4-10-8 M) on precontracted vessels segments in the presence of erythrocytes obtained from preeclamptic pregnants. Vascular responses were also recorded in the presence of the eNOS substrate L-arginine and the purinergic 2X receptor (P2X) antagonist pyridoxalphosphate-6-azophenyl-2',4'-disulfonic acid (PPADS). In addition, the responses of P2X receptor agonist α,β-methylene ATP (10-5 M) on precontracted vessel segments were also investigated. ANOVA test was used to evaluate the results. Statistical significance was $p<0.05$.

RESULTS: ATP-mediated relaxation responses recorded in the presence of erythrocytes from PE patients were found significantly reduced at 10-5M and 10-4M ATP concentrations compared to the control group ($p<0.05$, $p<0.001$). No significant difference was observed in the relaxation responses to α,β-methylene ATP. A significant increase was observed in the ATP-mediated relaxation responses recorded after L-arginine incubation ($p<0.01$) in the PE group. PPADS incubation did not cause difference in the ATP-mediated relaxation responses in all of the groups.

CONCLUSION: Erythrocytes obtained from PE patients induced reduction of ATP-mediated vascular relaxation of rat thoracic aortas. Reduced erythrocyte-derived NO production and altered P2Y receptors signalization might contribute to PE pathogenesis.
This study was supported by Akdeniz University Scientific Research Projects Coordination Unit.

Keywords: ATP, eNOS, Erythrocyte, Preeclampsia, Vasodilation.

OC-21

Effect of Fospropofol, a Water Soluble Propofol Precursor, on Contraction Response of Vascular Smooth Muscle

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AIM: Propofol is a hypnotic agent commonly used for general anesthesia including coronary artery bypass graft (CABG) surgery and for and sedation during intensive care period. Besides its preferable properties like short half-life, high clearance rate and fast action, its use is limited due to side effects like systemic vasodilation and hypotension. Fospropofol is a water-soluble prodrug, metabolized to propofol by endothelial alkaline phosphatases, seems more favorable than propofol as its systemic side effects are considerably lower. Since its effects on human vascular smooth muscle has not been studied previously, we aimed to compare the effects of fospropofol and propofol on in vitro contraction response of left internal mammary artery (LIMA) and to examine the contribution of ion channels to its mechanism of action.

METHODS: The arterial rings (3mm) of the LIMA pieces excised for CABG surgery were studied in fospropofol (n=34) and propofol (n=23) groups and mounted in baths filled with Krebs' solution, gassed with 5%CO2 and 95%O2 at 37°C. After equilibration for 60 min, maximum contraction response to KCl (120mM) for 10 minutes was recorded followed by cumulative dose-response curves with 10-7-10-5M fospropofol and propofol. The above protocol was repeated in Ca+2 channel blocker nifedipine (10-5M) and K+ channel blocker iberiotoxin (10-5M) treated rings in fospropofol group.

RESULTS: KCl-induced contraction of artery was lower in fospropofol and propofol groups. The attenuated vascular tonus was significantly lower for fospropofol group at all doses ($p<0.005$). The results obtained with nifedipine and iberiotoxin pointed out that the share of K+ channels are more prominent in fospropofol effect ($p<0.05$).

CONCLUSION: Fospropofol, approved and preferred for brief diagnostic and treatment procedures and outpatient interventions, acts through the same mechanism as propofol, can be considered as effective and safe for anesthesia induction and sedation, with its lower systemic side effects such as hypotension.

Keywords: Vascular tonus, K+ channel blocker, Ca+2 channel blocker, Fospropofol, Propofol.

OC-22

Effects of MOTS-c Peptide on the Heart and Aorta in a Model of Cardiac Hypertrophy Induced by Abdominal Aorta Constriction

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AIM: Physiologically or pathologically, the development of cardiac hypertrophy may cause progressive disruption of cardiac functions. Although the role of humanin, one of the mitochondrial peptides, in the prevention of cardiovascular diseases is known, the effect of another mitochondrial peptide, MOTS-c, on cardiovascular diseases is unknown. Our aim in this study is to reveal the possible therapeutic effects of MOTS-c on cardiac damage serum parameters and histopathological changes in cardiac hypertrophy induced by abdominal aortic constriction (AAK).

METHODS: Male Wistar albino rats grouped as (2 months) sham+saline (SF;1 ml/kg, n=6), sham+MOTS-c (5 mg/kg, n:6), AAC+saline (1 ml/kg, n=8) and AAK+MOTS-c (5 mg/kg, n:8). The abdominal aorta was surgically ligated using 4.0 silk sutures. The 14 days fter surgical recovery treatments were administered intraperitoneally for 21 days. Following the treatments, the rats were sacrificed and serum and tissue samples were taken. Troponin, ALT, AST, creatinine, LDH, urea levels were measured in serum samples. Immunohistological staining with hematoxylin-eosin, Masson trichrome and Toluidin blue were performed on thoracic and abdominal aorta and heart tissue. Data were given as mean ± standard error, statistical analyzes were compared with t-tests in independent groups.

RESULTS: While serum troponin, ALT and AST levels increased significantly in the AAK+saline group ($p<0.05$), this increase were limited in the AAK+MOTS-c group ($p<0.05$). Histopathological examinations showed no significant changes in the thoracic aorta and cardiac tissues. But abdominal aorta tissues in the AAK+saline group, there were deteriorations in the vessel wall structure, and the parallel and concentric arrangement of the elastic lamellas in the tunica media was impaired. However, AAK+MOTS-c group vessel wall structure was preserved.

CONCLUSION: We revealed the role of MOTS-c in the cardiac hypertrophy model for the first time in the literature. Further studies are needed in which we will apply various configurations on duration and dose.

Keywords: MOTS-c, Cardiac hypertrophy, Aorta.

OC-23

Exploring the Impact of AGK-2 Treatment on Sirtuin-2, Oxidative Stress and Apoptosis in Aged Pancreatic Tissue

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AIM: Aging is an important risk factor underlying many diseases such as metabolic, cardiovascular, neurodegenerative diseases and cancer. Sirtuin-2 (SIRT2), one of the longevity proteins, plays a role in many metabolic processes. Our aim in this study was to investigate the relationship between AGK-2, a specific SIRT2 inhibitor, and programmed cell death and oxidative stress markers, which are popular theories for explaining the aging process in pancreatic tissue.

METHODS: In our study, 24 Wistar albino male were used. Young (n=12, 3 months old) /elderly (n=12, 22 months old) rats were randomly divided into experimental(n=6) and control (n=6) subgroups. AGK-2 (10µM/bw) was applied to the experimental group and the same volume (4% DMSO + PBS) was applied to the control group for 30 days. Total oxidant status (TOS) and total antioxidant status (TAS) were measured in pancreatic tissue. Oxidative stress index (OSI) was calculated as the ratio at TOS to TAS levels. SIRT2 was measured by both sandwich ELISA and Western Blot methods. Caspase-3(Casp-3) was evaluated by sandwich ELISA method. ANOVA and Pearson-r were used for statistical evaluation. For statistical significance $p < 0.05$ was accepted.

RESULTS: Our findings showed that aging increased TOS level, Casp-3 and SIRT2 expressions in pancreatic tissue. It was observed that AGK-2 application was more effective in elderly rats and decreased TOS, Casp-3 and SIRT2 levels, which are increased with aging and increased TAS level compared to elderly control ($p<0.05$).

CONCLUSION: In the light of these, the treatment of AGK-2 reversed the increased oxidant stress and apoptosis in aging pancreatic tissue. Increasing antioxidant defense level may show protective activity in aging pancreas.

*Gazi University Scientific Research Project Foundation (project no. 01/2019-09) provided the financial support for this study.

Keywords: Aging, Sirtuin-2, Oxidative Stress, Apoptosis, AGK-2.

OC-24

Effect of Melatonin 2 Receptor Antagonist 4-PPDOT on Isolated Rat Myometrial Contractions

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AIM: Melatonin is known to inhibit rat myometrial contractions, but it's unclear which receptor(s) play a role in this effect. It was aimed to investigate the effect of 4-PPDOT, a specific melatonin 2 membrane receptor (MT2) antagonist, on rat myometrial contractions in this study.

METHODS: Myometrium strips from female rats were placed in an isolated organ bath and the isometric contractions were constituted under 1.5g tension. Oxytocin-induced contractions were partially inhibited at 1.5mM melatonin concentration and then effect of 4-PPDOT was determined. Increasing concentrations of 4-PPDOT were cumulatively applied on spontaneous and oxytocin-induced contractions in next step. After first 10 minutes of contractions were recorded as control, 4-PPDOT administrations were carried out. The amplitude and frequencies of contractions in each period were recorded as mean±SEM and statistically evaluated with ANOVA.

RESULTS: At 1.5mM melatonin concentration, amplitude and frequency of oxytocin-induced contractions were significantly decreased ($p<0.01$ and $p<0.001$, respectively). Application of 4-PPDOT at dose of 0.02mg/ml caused complete inhibition. In second stage, 0.002mg/ml 4-PPDOT dose did not affect spontaneous contractions, while it decreased amplitude parameter significantly at 0.01mg/ml concentration ($p<0.001$) and did not change the frequency. Contractions were greatly inhibited at 0.02mg/ml 4-PPDOT concentration ($p<0.001$). While the first dose of 4-PPDOT had no effect on oxytocin-induced contractions, partial inhibition was observed at 0.01mg/ml concentration ($p<0.001$) and significant inhibition at 0.02mg/ml dose ($p<0.000$).

CONCLUSION: Data from this study indicate that MT2 do not mediate the inhibitory effect of melatonin on uterine contractions in rats. Because, the contractions partially inhibited by melatonin did not return with 4-PPDOT. Similar to melatonin, 4-PPDOT inhibits both spontaneous and oxytocin-induced contractions in a dose-dependent manner. This suggests that 4-PPDOT may have physiological properties other than its melatonin receptor antagonist effect.

This study was financially supported by TUBITAK (Project No: 1919B012001033).

Keywords: Rat Myometriyum, 4PPDOT, Isometric Contraction, Melatonin.

OC-25

The Effects of Hypothalamic Paraventricular Oxytocin Neurons on the Hypofrontality in Transgenic Male Mice

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AIM: Oxytocin is a neuropeptide synthesized in the neurons of hypothalamic paraventricular and supraoptic nuclei and has a modulatory effect on various social behaviors. Several studies have shown that hypothalamic oxytocin neurons project to the prefrontal cortex. Dopamine has an important role in regulating the cognitive function of the prefrontal cortex and it is thought that oxytocin and dopamine systems work together and have similarities in the areas of organization and projection. In this study, it was aimed to investigate the effects of oxytocin on hypofrontality-induced behavioral disturbances and the interaction of oxytocin and dopamine neurons in the prefrontal cortex.

METHODS: Adult male oxytocin-cre mice carrying cre-recombinase enzyme in oxytocin neurons were used in this study. Recombinant adeno-associated virus with stimulatory hM3D subunit or inhibitory hM4D subunit were injected into paraventricular area in order to activate and inhibit oxytocin neurons. Then, the effects of manipulation of oxytocin neurons on several behaviours were evaluated. Anxiety, locomotor activity, social interaction and short-term memory were examined by using an elevated plus maze, open field test, social interaction test and T-maze test, respectively. Fiber photometry Ca2+ imaging was used to investigate the interaction of oxytocin and dopamine neurons in the prefrontal cortex. This study was approved by Yeditepe University Animal Research Ethics Committee.

RESULTS: Inhibition of paraventricular oxytocin neurons significantly decreased the social novelty preference of oxytocin-cre mice and could cause short-term memory impairment according to T-maze test. Further, Ca2+ recordings from prefrontal dopamine neurons were taken before and during acute activation of paraventricular oxytocin neurons, but no significant effect of paraventricular oxytocin neurons on the activity of prefrontal dopamine neurons was found.

CONCLUSION: In this study, the effects of manipulation of oxytocin neurons on various behaviors was revealed. Thus, modulation of prefrontal dopaminergic neuronal activity by chemical activation of oxytocin neurons was examined for the first time.

Keywords: Oxytocin, Dopamine, Prefrontal Cortex.

OC-26

Asprosin Increases Sexual Motivation in Female Rats

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AIM: Asprosin is a novel adipokine discovered by Romere in 2016. Asprosin, synthesized from white adipose tissue, released into the circulation during fasting, and can cross the blood-brain barrier, act via the OLFR734 receptor. Pheromones can play an essential role in sexual behaviour. Asprosin is a hormone that strengthens the sense of smell, and its role in sexual behaviour is not fully known. We aim to investigate the effects of asprosin on sexual behaviour in female rats.

METHODS: In this study, 24 Sprague-Dawley rats 21 days old (weight 35 ± 2 g) were randomly divided into two groups, control and asprosin (n=12). From the postnatal 21st day, the animals in the control group were given saline (1 ml/kg), and the animals in the asprosin group were given asprosin (500 ng/kg) every day for an average eight weeks. The 10-minute sexual behaviour test was applied to all animals in the experimental group. Afterwards, the effects of asprosin on sexual motivation (anogenital exploration) and sexual performance (lordosis quotient and lordosis degree) were analyzed. The degree of lordosis was rated on a 4-point scale (0-3). The independent samples t-test (student t-test) was used for statistical analysis.

RESULTS: When the asprosin group was compared with the control group, it was found that the rate and quality of lordosis did not change ($p>0.05$). However, anogenital explorations reflecting sexual motivation in animals was found to be significantly increased in the asprosin administered group compared to the control group ($p<0.05$).

CONCLUSION: Findings show that chronic asprosin administration increases sexual motivation. Chronic administration of asprosin, known to increase the sense of smell, suggests that it may have increased sexual motivation in female rats through similar pathways. In conclusion, long-term asprosin therapy may be a treatment for lack of sexual motivation.

Acknowledgement: This work was supported by TUBITAK (Proje# 220S744).

Keywords: Asprosin, Adipokine, Sexual behaviour, Sexual Motivation.

OC-27

Neuroprotective Effects of Darbepoetin Alpha on The Hippocampus in Experimental Ethanol Administration

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AIM: Ethanol has harmful effects on the brain and many organs. The most important of the main targets of ethanol toxicity in the brain is the hippocampus. Darbepoetin alpha (DA) is an analogue of recombinant human erythropoietin. DA has neuroprotective effects. In our study, we aimed to investigate the neuroprotective effects of DA against neuronal damage caused by ethanol in the hippocampus in rats.

METHODS: 40 Wistar-Albino male rats were divided into four groups of control (C) (3.15 ml/kg saline, ig), ethanol (E) (3 g/kg 20% ethanol solution, ig), DA (0.25 µg/kg, ip) and E+DA. Over a 30-day period, ethanol solution was given for 2 consecutive days, at 2-d intervals, and DA was given once every 3 days. S100-β, NSE, CAT, GR levels and GPx enzyme activity in brain tissue and serum samples were analyzed by ELISA method. MDA levels and SOD enzyme activity in brain tissue were analyzed by spectrophotometric method. Brain tissue were evaluated by histopathological methods. Statistical significances between the groups were determined by the Student-t test.

RESULTS: S100-β (brain $p<0.01$; serum $p<0.05$), NSE (brain $p<0.05$; serum $p<0.01$) and MDA ($p<0.001$) levels were significantly higher, and SOD ($p<0.05$), GPx ($p<0.001$ brain, $p<0.05$ serum), CAT ($p<0.05$ brain, $p<0.001$ serum), GR ($p<0.01$ brain, $p<0.001$ serum) were significantly lower in group E compared with group C. S100-β (both brain and serum $p<0.05$), NSE (serum $p<0.05$) levels and MDA ($p<0.001$) levels were significantly lower, and CAT (serum $p<0,05$), GPx (brain $p<0.05$) were significantly higher in group E+DA compared with group E. Histopathologically, there was moderate neurodegeneration in group E and mild neurodegeneration in group E+DA in the dentate gyrus of the hippocampus.

CONCLUSION: Our findings suggest that DA has antioxidant effects and neuroprotective effects on long-term intermittent ethanol intoxication.

Keywords: Ethanol, Darbepoetin alpha, Hippocampus, Neurodegeneration, Neuroprotection.

OC-28

Investigation of the Electrical and Behavioral Effects of Chronic High-Fat Diet on Leptin Receptor Neurons in the Tuberomammillary Nucleus in Transgenic Mice

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AIM: Neuronal histamine is produced by histamine neurons in the tuberomammillary nucleus (TMN) in the posterior hypothalamus. Hypothalamic neurons have excitatory wake-promoting effect and some studies show that gamma-aminobutyric acid (GABA) suppresses and glutamate increases wakefulness by activating TMN. However, the underlying mechanism(s) is not fully understood. Thought that this mechanism may be related to nutrition. Currently, there is no study examining a relationship between histaminergic neurons and leptin receptor (LepR) neurons in TMN about food intake. Therefore, we have investigated electrical and behavioral effects of high-fat diet (HFD) on LepR neurons in the TMN area in LepR-Cre transgenic mice.

METHODS: Fourty female and male (3-4 months aged) transgenic LepR-Cre mice were used, some were fed a standard diet for six weeks, others on chronic HFD. Adeno-associated-viruses containing hM3D receptor (for activation), hM4D receptor (for inhibition) and GFP (control group) were intracranially injected into TMN. Behavioral effects were evaluated by open field test. Chronic activation/inhibition were performed by intraperitoneal administration of N-Oxide Clozapine. Electrical activity of LepR neurons labeled GFP virus were recorded by electrophysiology technique. Student's t test and One-Way ANOVA were utilized for statistical analysis. This study has ethical approval dated 28.01.2022 and decision number 2022/01-3.

RESULTS: Firing frequency of LepR neurons was significantly reduced in mice fed HFD. Besides mice fed HFD had a significant increase in weight ($p<0.05$). In behavioral tests, inhibition of these neurons caused a significant increase in the spent time in the center zone ($p<0.05$), activation/inhibition of these neurons did not significantly affect the distance and speed of the animals.

CONCLUSION: Electrical and behavioral effects of LepR neurons in TMN in mice fed a chronic HFD were investigated for the first time in this study. Our findings have shown that HFD alters neuronal activity, weight gain and behavioral characteristics in LepR-Cre transgenic mice.

Keywords: Leptin, Histamine, Chronic High-Fat Diet, Electrophysiology, Behavioral tests.

OC-29

Investigation of Time-dependent Alterations in Adipokine Levels in Patients with Laparoscopic Sleeve Gastrectomy

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AIM: Laparoscopic sleeve gastrectomy (LSG) is a treatment option for obese patients who can't lose weight despite diet, exercise, medical treatment. The effects of adipokines on food intake, energy balance, lipid, glucose metabolism are known. The time-dependent alterations of wingleOC-type inducible signaling protein 1 (WISP1), neuregulin 4 (Nrg4), asprosin and spexin (SPX) levels after LSG in obese individuals are unknown. We aimed to investigate the time-dependent alterations in adipose tissue and serum WISP1, Nrg4, asprosin, SPX levels in response to LSG in obese individuals.

METHODS: Blood samples were obtained preoperatively and postoperatively (1st, 3rd, 6th months) from 18-64 years-old morbidly obese patients who underwent LSG (n=19) and compared with age-matched subjects who underwent cholecystectomy and/or abdominal hernia surgery (control group, n=19). Omentum and subcutaneous adipose tissue were obtained during surgery. Adipokine levels were measured by commercial kits. Mann Whitney-U, t, Friedman tests, variance analysis were used for statistical analyzes. $p<0.05$ was considered statistically significant. The study was approved by the Non-Interventional Clinical Research Ethics Committee (24.07.2020/14).

RESULTS: Preoperative body mass index of obese individuals was 45.3 and decreased to 31.35 6 months later ($p<0.05$). Body weigth of the subjects decreased significantly in 3 months ($p<0.05$). There was no significant difference in glucose, triglyceride, total cholesterol and LDL levels between the groups. Glucose, insulin, and triglyceride levels of obese patients were significantly reduced at 6-month follow-up ($p<0.05$). Omental adipose tissue WISP1 and subcutaneous adipose tissue WISP1, SPX levels of obese patients were higher than control ($p<0.05$). Obese individuals had higher serum asprosin, WISP1 and lower Nrg4 levels ($p<0.05$). At 6 months postoperatively, the difference between serum WISP1, Nrg4 levels and control disappeared.

CONCLUSION: Our data show that postoperative weight changes cannot be fully explained by measured adipokine levels, and follow-ups longer than 6 months are needed to obtain more detailed information.

Keywords: Asprosin, Laparoscopic sleeve gastrectomy, Neuregulin 4, Obesity, Spexin, WingleOC-type Inducible Signaling Protein 1.

OC-30

Evaluation of Cardiopulmonary Fitness and Cognitive Functions in Children with Obesity

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AIM: Obesity is a disease caused by an imbalance between energy intake and energy expenditure, and its prevalence begins to increase in childhood. Obesity-related physical changes are known to cause psychological issues like anxiety and depression and to impair cognitive function, which lowers academic performance. In our study, we aimed to investigate the differences in cardiopulmonary fitness and cognitive functions in children with obesity compared to healthy controls in the same age group.

METHODS: After ethical approval (09.2021.1043), experiments were performed in 9-16 years old patients diagnosed with obesity and in healthy controls at Marmara University Sports Physiology Department (n=39). Blood samples were taken from the patients, anthropometric measurements were made, and cardiopulmonary exercise test (CPET) was performed. Psychiatric rating scales were filled, and the MOXO attention test was used to evaluate cognitive functions. Data were analyzed by student's t and Mann-Whitney U tests; $p<0.05$ was considered as significant.

RESULTS: Weight-SDS, BMI (body mass index)-SDS, BMI percentile and fat% were observed to be higher in children with obesity compared to healthy controls ($p<0.001$). According to the SNAP-IV Parent Rating Scale (for Attention Deficit Hyperactivity Disorder), children with obesity had higher scores ($p<0.05$), while MOXO test attention performance scores tended to be higher than healthy controls. Oxygen consumption was measured lower at both peak exercise ($p<0.01$) and anaerobic threshold ($p<0.05$) in children with obesity problems. Similarly, VE (ventilation)/VO2 and VE/VCO2 values of these children were recorded lower at peak exercise ($p<0.01$-0.001). Physiological dead space (VD) increased significantly in both groups, with peak exercise compared to rest, more prominently in the obesity group ($p<0.01$-0.001).

CONCLUSION: The data of the study indicate that obese children have decreased cardiopulmonary fitness, and also a profile that tends to exhibit difficulty in responding correctly and maintaining focus. This study was supported by Marmara University Scientific Research Committee (Number: TDK-2022-10430).

Keywords: Cognitive Function, CPET, Obesity.

OC-31

The Role of Apelin in 2,4,6-Trinitrobenzene Sulfonic Acid-Induced Colitis in Rats

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AIM: The apelinergic system has role in the regulation of inflammation and oxidative stress. But little is known about the effects of this system in inflammatory bowel disease (IBD). The aim of this study was to evaluate the role of apelin in 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced IBD model.

METHODS: Adult male Wistar rats (200-250 g) were randomly divided into four groups (n=18 in each group): 1) Control; 2) TNBS; 3) TNBS+F13A, and 4) F13A. Colitis was induced through intrarectal administration of 500 µl of TNBS solution (30 mg/kg in saline) mixed with absolute ethanol in 1:1 ratio. In the TNBS+F13A and F13A groups, apelin receptor antagonist, F13A (30 µg/kg/day for 3 days, i.v.), was administered immediately after the TNBS or distile water application, respectively. All animals were evaluated for weight change and development of diarrhea. At the end of the experiment, colon samples were collected for analysis. Myeloperoxidase activity (MPO), apelin and proinflammatory cytokine levels and macroscopic damage were determined in the colon using biochemical and immunohistochemical methods. Data are expressed as means ± standard error of the mean (S.E.M.). Comparisons between multiple groups were performed using one-way analysis of variance (ANOVA) followed by Tukey's post-hoc test. Additionally, when the variances were not homogeneous, Mann–Whitney U test was used.

RESULTS: In animals with TNBS-induced colitis, while body weight decreased ($p<0.001$), the occurrence of diarrhea significantly increased ($p<0.001$). Also, TNBS application increased macroscopic damage ($p<0.001$), amount of apelin ($p<0.001$), levels of TNF-α ($p<0.001$), IL-1β ($p<0.001$) and IL-6 ($p<0.001$) and MPO enzyme activity ($p<0.05$) in colon tissue compared with control group. F13A administration after TNBS significantly reduced TNBS-mediated changes.

CONCLUSION: These findings suggest that apelin has a role in TNBS-induced colitis in rats.

This work was supported by Akdeniz University Scientific Research Projects Coordination Unit (Project code: TYL-2021-5554).

Keywords: TNBS, Colitis, Apelin, F13A.

OC-32

Role of Oxytocin in Small Intestinal Fasted Myoelectric Activity of Rats

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AIM: Oxytocin (OT) is a peptide neurohormone produced mainly by magnocellular neurons in hypothalamic paraventricular and supraoptic nuclei. The only known receptor of OT is oxytocin receptor (OTR), which is Gq protein-coupled. It has been shown that OT and OTRs are present in the gastrointestinal (GI) system, and also has been reported that OT has important effects on gastric emptying, peristalsis and defecation by activating OTRs. However, the effect of OT on the migrating myoelectrical komplex activity, which is the source of small intestinal fasting motility, is still unknown. The aim of our study was (a) to investigate the effects of peripherally administered OT on the fasting myoelectrical activity of the small intestine (b) to investigate the role of OTRs in the effect of oxytocin on MMC pattern.

METHODS: Bipolar electrodes were placed in 3 different regions of the jejunum of adult male Sprague-Dawley rats for MMC recording. Following the recovery period, experiments were performed after an 18-hour fasting period. Following one-hour recording of baseline myoelectric activity, oxytocin (4-32 µg/kg) was administered intraperitoneally (i.p.). In the combination group, which is carried out to investigate the role of OTRs in the effect of oxytocin on MMC, animals received OTR antagonist atosiban (i.p., 2 mg/kg) 10 minutes before OT (i.p., 16 µg/kg) administration. One-way analysis of variance (ANOVA) test was performed for statistical analysis and Tukey-Kramer post-hoc test was used for multiple comparisons between groups.

RESULTS: Oxytocin (4, 8, 16, 32 µg/kg) administered intraperitoneally inhibited MMC pattern by causing a dose-dependent decrease in spike activity and the number of MMC cycles ($p<0.05$-0.001). In the combination group, inhibitory effect of OT (16 µg/kg) was completely abolished by pre-administration of atosiban (2 mg/kg) ($p<0.01$).

CONCLUSION: Our findings suggest that exogenous-administed oxytocin inhibits the fasting myoelectric pattern through OTRs in fasted male rats.

Keywords: Migrating myoelectric complex (MMC), Small intestine Motility, Oxytocin (OT), Oxytocin Receptor (OTR), Rat.

OC-33

The Inhibitory Effect of Central Neuropeptide-W on Gastric Motor Functions

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AIM: Accumulating evidence suggests the modulatory role of central neuropeptide-W (NPW) in autonomic functions including vagal afferent signaling, however, the action of central exogenous NPW on gastric motor functions has not been tested. This study aimed to investigate (i) changes in gastric motility following microinjection of NPW-23 into dorsal motor nucleus of vagal nerve (DMV), (ii) alterations in gastric emptying (GE) after intracerebroventicular (icv) application of NPW-23 and (iii) to clarify whether NPW receptor NPBWR1 is expressed in gastro-projecting vagal cells.

METHODS: Adult male Sprague-Dawley rats (n=7) were anesthetized with sodium thiobutabarbital (125 mg/kg, i.p.) and gastric antral motility was recorded through a strain gage transducer. NPW-23 was administered into DMV (1 nmol/60 nL) by microinjection. Electrocardiography was recorded through monopolar limb electrodes to analyze heart rate variability (HRV) for assessment of sympathovagal balance. Another group of rats (n=5) underwent stereotaxic icv catheterization. Following 5-day recovery, GE was measured in rats received NPW-23 (10 nmol/5 µl, icv) or vehicle. To determine whether NPBWR1 is expressed in vagal gastro-projecting cells, a retrograde tracer was serosally applied to stomach (n=2). Double immunofluorescence was performed in brainstem sections obtained 14 days after tracer application. Data were analyzed with Mann-Whitney-U test. Experimental protocols were approved by Animal Ethical Committee of Akdeniz University (B.30.2.AKD.0.05.07.00/63).

RESULTS: Intra-DMV application of NPW-23 significantly inhibited antral tone and motility. Compared to controls (62.4% ± 6.4), NPW-23 significantly delayed GE (51.3% ± 5.8, $p<0.05$). Microinjection of NPW-23 caused a remarkable reduction (27.1% ± 6.5) in high frequency component of HRV, while creating approximately 3-fold increase in sympathovagal balance. The findings of double immunofluorescence revealed that NPBWR1 is expressed in gastro-projecting cells in DMV expressing choline acetyltransferase.

CONCLUSION: The present findings indicate the modulatory action of central NPW on gastric motility which appears to be involved with inhibition of vagal outflow.

Keywords: Neuropeptide-W, NPBWR1, Gastric Emptying, Gastric Motility, Sympathovagal balance, Retrograde Neuronal Tracing.

OC-34

The Effects of L-Carnitine on Gastrointestinal Contractility and Histological Changes in Rat Intestinal Ischemia-Reperfusion Injury

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AIM: Ischemia-reperfusion (IR) of the small intestine causes serious abdominal pathologies including tissue dysfunction and organ failure. We aimed to investigate the effects of IR injury on intestinal contractility and morphologic damage of rat ileum and duodenum and if there is any protective effects of L-Carnitine(L-C) application on IR damage.

METHODS: Wistar rats were divided into four groups. Control group, IR group; superior mesenteric artery was ligated and 45 minutes of ischemia and 45 minutes of reperfusion were performed, IR+L-C group, L-C (200mg/kg iv) was administered 5 minutes before reperfusion, L-C group; only L-C administered. Segments were hung in the isolated organ bath and response to contraction with acetylcholine, relaxation with phenylephrine were recorded. Segments were stained with hematoxylin-eosin, IR injuries were scored under the light microscope. Villus lengths were recorded using the Fiji/Imagej program. Results were evaluated with the graphpad prism 8.3.1. One-Way ANOVA was used to compare differences between groups, Tukey's test was used for multiple comparisons. $P\leq0.05$ were considered statistically significant.

RESULTS: Contraction responses; there was a significant difference in the ileum in the IR and IR+L-C groups when compared in control group ($p<0.05$). It was highest in the L-C group. In the duodenum, it was significantly higher in the IR+L-C and L-C groups compared to the IR group ($p<0.05$, $p<0.005$). Relaxation responses; ileum it was low in the all experimental groups ($p<0.005$, $p<0.05$). It was lower in the duodenum in IR group ($p<0.05$). Responses in IR+L-C and L-C were higher in the I/R groups. Intestinal morphology of the IR group was damaged. Statistically, the largest changes in morphology were significantly lower in villus height in the IR group ($p<0.001$, $p<0.001$). Villus height were significantly higher in the IR+L-C group compared to the control group ($p<0.033$, $p<0.033$) and the IR group ($p<0.002$, $p<0.002$).

CONCLUSION: It showed that IR injury reduces intestinal contractility, L-C removes negative effects. Histological results showed that I/R caused tissue damage, L-C reduced mucosal damage. The findings of this study will be a starting point for further research.

Keywords: Cadmium, Ischemia-reperfusion, L-carnitine.

OC-35

Investigation of the Possible Protective Effect of Phoenixin-14 on Small Intestine and Lung Damage Due to Mesenteric Ischemia in Rats

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AIM: Characterized by insufficient intestinal blood flow, mesenteric ischemia is a surgical emergency with high mortality/morbidity, and its major complication is lung injury. Phoenixin (PNX), expressed in brain, gastrointestinal system, heart and lung, was protective in myocardial ischemia-reperfusion (I/R) injury. It was aimed to investigate possible protective effects of PNX against small intestinal I/R-injury.

METHODS: Under anesthesia, intestinal I/R was produced in Sprague-Dawley male rats (n=40) by clamping superior mesenteric artery (SMA) for 60-min followed by 90-min reperfusion. In control group (n=8), SMA was exposed without clamping. Just before reperfusion, randomly saline or PNX-14 (1,5,25,50 µg/kg) was injected intravenously. After serosal blood flow in jejunum was measured by laser-doppler, intestines and lungs were removed to evaluate microscopic damage and to measure malondialdehyde level (lipid peroxidation), and reactive oxygen metabolites using luminol- and lucigenin-chemiluminescence. One-way ANOVA was used for statistical analysis.

RESULTS: Decreased serosal blood flow in jejunums of saline-treated I/R-group ($p<0.01$) was increased in 25 and 50 µg/kg PNX-14-treated I/R-groups ($p<0.05$-0.001). In saline-treated I/R-group, intestinal luminol- and lucigenin-chemiluminescences were increased ($p<0.001$), but luminol values were decreased by PNX-14 at 1, 5 and 25 µg/kg doses ($p<0.01$), while lucigenin was decreased at all PNX doses ($p<0.001$). Compared to saline-treated I/R-group, malondialdehyde level in intestines was reduced in 25 and 50 µg/kg PNX-14-treated groups ($p<0.05$). High histological damage score in small intestine of saline-treated I/R-group was reduced by 25 and 50 µg/kg doses of PNX-14 ($p<0.001$). Microscopic damage score of distant organ lung was decreased in 25 and 50 µg/kg PNX-14-treated I/R-groups ($p<0.001$), and pulmonary luminol levels were reduced in PNX-14-treated groups at 1 and 50 µg/kg doses, while lucigenin was reduced by all PNX-14 doses ($p<0.01$).

CONCLUSION: Novel peptide PNX-14, by increasing intestinal blood flow and delimiting oxygen radical generation, reduces ischemia-reperfusion-induced oxidative injury of the intestine and distant organ lung.

Keywords: Ischemia/Reperfusion, Mesenteric ischemia, Phoenixin-14.

OC-36

Asprosin Takes a Protective Role in Mice Established Experimental Acute Kidney

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AIM: Acute kidney injury (AKI) due to ischemia-reperfusion (IR);It has a pathophysiology characterized by inflammation, oxidative stress and apoptosis. Asprosin (Asp) is a recently discovered adipokine secreted from white adipose tissue (WAT).It has been reported that Asp hormone is secreted from kidney tissue as well as WAT and its receptors are also localized in kidney tissue. It has been demonstrated Asp reduces oxidative streOC-related parameters and apoptosis markers in different tissues. In the light of this information, this study was conducted to investigate the effects of Asp on AKI.

METHODS: 32 male Balb-c mice were divided into 4 groups as control, IR, 1µg/kg Asp(ASP1) and 10µg/kg Asp(ASP10) administered group(n=8). Control group was not treated,22 minutes of ischemia and 24 hours of reperfusion were performed in both kidneys in the other groups. Two different doses of Asp(1-10µg/kg) were administered intravenously animals in ASP1 and ASP10 groups before ischemia. End of experiment, animals were sacrificed and their blood and kidney tissues were taken.BUN, creatinine, IL-1β and TNF-α levels in collected serum were determined by ELISA method. In kidney tissue, MDA,SOD,CAT and GSH levels were determined. In addition, histopathological examination of kidney tissue was performed and caspase-3 reactivity was determined by immunohistochemical method. Comparisons between groups were made using the Mann Whitney-U test with Bonferroni correction in IBM-SPSS 24 package program.

RESULTS: Asp administration dose-dependently decreased serum BUN, creatinine, IL-1β and TNF-α levels and MDA levels in kidney tissue of mice($p<0.05$). On the other hand, Asp administration caused an increase in GSH, SOD and CAT enzyme activity in the kidney tissue of mice and this increase was dose dependent except for SOD($p<0.05$). In the histopathological evaluation,it was determined that Asp application decreased caspase-3 reactivity in kidney tissue compared to the IR group ($p<0.05$).

CONCLUSION: Consequently, it was revealed that Asp administered intravenously may have a protective effect against AKI caused by IR. This study supported by the Scientific Research Projects Unit of İnönü University (BAP; Project # TCD-2022-2841).

Keywords: Asprosin, Apoptosis, IR, Inflammation, ROS, AKI.

OC-37

Effects of High Protein Ketogenic Diet and Exercise on Acute Seizures Experimentally Established with PTZ

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AIM: Epilepsy is very common neurological disease in the world. Keeping the ketogenic diet high in fat and low in carbohydrates causes the brain to use fats instead of glucose. Ketone bodies appear as fats are burned. With the use of ketone molecule in the brain, abnormal excessive discharges in neuron cells are reduced. Thus, acute seizures are controlled. It is anticipated that exercise may have acute antiepileptic effects. In our study, it was aimed to examine the effects of ketogenic diet and exercise on acute seizure behaviors, serum ion and oxidative stress parameters on an experimental epilepsy model created with PTZ in rats.

METHODS: Ethical permission was obtained for this study from the BAİBU DEHAM Research Ethics Committee with the decision number2021/3. In the study, 42 male wistar albino rats, 2-4months old, weighing between 200-250g (n=7/group). Group: Epilepsy+Standard feed, Group: Epilepsy+Ketogenic feed, Group: Epilepsy+Exercise+Standard feed, Group: Epilepsy + Exercise + Ketogenic feed was divided into 6 groups as Group: Epilepsy + Diazem + Standard feed, Group: Epilepsy + Diazem + Ketogenic feed. 21 rats in ketogenic diet groups were fed ketogenic diet for 6 weeks. 14 rats in the exercise groups were given 15-minute treadmill exercise for 6 weeks. At the end of the 6 weeks, 50mg/kg PTZ was administered intraperitoneally to the animals and epiletic seizure behavior scoring was performed for 20 minutes. Immediately afterwards, blood samples were taken from the animals, and oxidative stress parameters and serum ion changes were analyzed. The datas were evaluated in the IBMSPSS statistical package program. The normal distribution of the data belonging to the numerical variables was evaluated with the Shapiro Wilktest of normality and Q-Qgraphs. Comparisons between groups were made with one-way analysis of variance for normally distributed variables, and Kruskal-Wallisanalysis for non-normally distributed variables. Tukey-HSD was used for normally distributed variables and Dunn-Bonferronnitest was used for non-normally distributed variables as multiple comparison test. $P<0.05$ was considered statistically significant.

RESULTS: It was determined that ketogenic diet and exercise application decreased the seizure behavior score in the experimental epilepsy acute model. However, no statistically significant difference was observed between the groups in serum ion values of Totalthiol, Nativethiol, Disulfite, Mg+2, Ca+2, Na+, Cl.

CONCLUSION: It has been observed that ketogenic diet and exercise can have positive effects in order to lower seizure thresholds in acute epilepsy.

Keywords: Behavior Scoring, Epilepsy, Ketogenic Diet, Treadmill Exercise.

OC-38

The Effect of Rivastigmine on Spike-Wave Discharges and Interaction with T-Type Calcium Channels in WAG/Rij Rats

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AIM: The role of T-type calcium channels in the absence epilepsy is known. Rivastigmine (RIVA) has been suggested to inhibit T-type calcium channels with in vitro studies. This study aims to investigate the effect of RIVA in the absence epilepsy and its interaction with T-type calcium channels.

METHODS: After Ethics Committee approval (OMU-HADYEK 2022/08), 6-9 months old WAG/Rij rats (n=66) were divided into 11 groups totally and then tripolar electrodes and intracerebroventricular (i.c.v.) cannulas were implanted into the skulls of all animals. ECoG recordings were obtained from all animals for a total of 4 hours: 1 hour before the injection and 3 hours after the injection. In the first stage, after the control group; 0.125; 0.25; 0.5; 1; 2; and 4 mg/kg RIVA (i.p.) groups were studied, the ineffective and effective doses of RIVA were determined. And then, after the effective and ineffective dose of T-type calcium blocker NNC 55-0396 was studied, 5µg NNC55-0396 (no effective dose, i.c.v.) + 0.125mg/kg RIVA and 20µg NNC55-0396 (effective dose, i.c.v.) + 2mg/kg RIVA groups were combined. Post-hoc Bonferroni test was applied to the data after the statistical one-way ANOVA with GraphPad Instat (v3.06) software.

RESULTS: 0.25; 0.5; 1; 2 and 4 mg/kg doses of RIVA completely prevented SWDs from about the first half an hour after the injection to the end of the recording (3 hours) depending on the dose ($p<0.001$). 0.125mg/kg RIVA was ineffective compared to the control group ($p>0.05$). The combination of effective NNC55-0396 (20µg) and the most effective dose RIVA (2mg/kg) prevented SWDs same as in the effective RIVA groups. The combination of ineffective NNC55-0396 (5µg) + ineffective RIVA (0.125mg/kg) significantly decreased the number of SWDs ($p<0.05$).

CONCLUSION: Our results suggest that the acetylcholine esterase enzyme inhibitor RIVA dose-dependently inhibits absence seizures and interacts with the T-type calcium channel.

Keywords: Absence epilepsy, Electrocorticogram, NNC 55-0396, Rivastigmine, Spike-Wave Discharge.

OC-39

The Interactions of Ketamine and Propofol in The Experimental Status Epilepticus Induced by Lithium-Pilocarpine

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AIM: The mechanism responsible for resistance in refractory status epilepticus(RSE) is seen as the internalization of active GABAA receptors over time and increased expression of NMDA receptors. In this study, it was aimed to electrophysiologically investigate the efficacy and interactions of different ketamine and propofol doses in RSE induced by lithium-pilocarpine in Sprague-Dawley rats.

METHODS: In the study, a total of 72 Sprague Dawley rats were used in 9 groups (SBU-HADYEK-2020-06/11). RSE model was created by injecting subcutaneous lithium-Cl (5 mEq/kg) and intraperitoneal pilocarpine-HCl (320 mg/kg) into rats placed with tripolar EEG electrode (MS333/2A). Animals with RSE were intraperitoneally administered ketamine (30, 60 and 90mg/kg), propofol (20, 40 and 80mg/kg) doses and combinations of both drugs (15+20 and 30+40 mg/kg). Video-EEG recordings were taken during status epilepticus and on 2nd and 7th days after status. Kruskal-Wallis and Mann-Whitney U test was used in the statistical analysis of data on seizures.

RESULTS: Compared with RSE control group, it was determined that 30 and 60 mg/kg ketamine doses provided effective seizure control and prevented mortality($p<0.001$), but 90 mg/kg dose ketamine had a toxic effect and caused mortality in all animals administered. It was determined that propofol provided seizure control at a dose of 80 mg/kg and reduced mortality rate to 16.7% ($p<0.002$), however, mortality rate was 100% at a dose of 20 mg/kg. It was determined that low-dose ketamine+propofol (15+20 mg/kg) combination provides early-onset (from 10.min), long-term seizure and epileptiform activity control, as effective as 80 mg/kg high-dose propofol($p<0.05$).

CONCLUSION: It was concluded that with the combination of low dose ketamine and propofol, RSE control can be achieved without the need for high doses in monotherapy for seizure control and the undesirable effects due to dose increase can be avoided.

(This work was supported by SBU-BAP. Project no:2021/027).

Keywords: EEG, Ketamine, Lithium-pilocarpine, Propofol, Status Epilepticus.

OC-40

Effects of Short-Term Uridine Treatment on Blood-Brain Barrier Integrity and Brain Edema in Li-Pilocarpine-Induced Status Epilepticus

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AIM: Blood-brain barrier (BBB) disruption following status epilepticus (SE) plays a vital role in epileptogenesis. While neuroprotective, antiepileptic and antiepileptogenic effects of uridine has been shown in experimental epilepsy models, its mechanism of action is not clearly understood. In this study, we investigated the effects of uridine on BBB damage and brain edema in Li-pilocarpine-induced SE model.

METHODS: The study was approved by the Local Ethics Committee on Experimental Animal Research of Bursa Uludag University (2019-13/07). In the study, 200-250 g, 6-8 weeks old, male 112 Sprague-Dawley rats were used. Status epilepticus was induced by lithium and pilocarpine. Following SE, rats were received 500mg/kg uridine or 0.9% NaCl twice a day for 48 hours and then sacrified under isoflurane anesthesia. Endothelial tight junction proteins (ZO-1 and occludin), aquaporin-4 (AQP4) and its anchoring protein α1-syntrophin expression in hippocampus were analyzed with Western-blotting. Brain edema was assessed by wet-dry weight method. We also evaluated serum S100B levels with ELISA as indicator of BBB permeability. Normally distributed data were assessed by one-way ANOVA followed by the Holm-Sidak test. The statistical significance level was determined as $\alpha=0.05$.

RESULTS: Status epilepticus significantly decreased hippocampal ZO-1 and α1-syntrophin expression ($p<0.001$) and increased serum S100B levels and brain edema ($p<0.001$). Uridine treatment significantly prevented the reduction in ZO-1 and α1-syntrophin proteins ($p<0.001$ and $p=0.023$, respectively) and decreased serum S100B levels ($p<0.001$). Contrary to expectations, brain edema is further enhanced in uridine-treated group ($p<0.001$). No significant difference was reached for hippocampal occludin and AQP4 expression between intervention groups.

CONCLUSION: In this study, we showed that uridine might provide neuroprotection by the maintaining BBB integrity and enhancing AQP4 polarization in Li-pilocarpine-induced SE. Long-term effects of uridine on epileptogenesis will be further investigated.

The project was supported by the funds from Bursa Uludag University Scientific Research Projects Council (ID: KUAP(T)-2020/3)

Keywords: Aquaporin-4, Brain edema, Blood-brain barrier, Epileptogenesis, Status epilepticus, Uridine.

OC-41

Interaction of Midazolam with Antiepileptic Drugs Used in Second Line Treatment in Experimental Status Epilepticus

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AIM: In status epilepticus treatment guidelines, a treatment course based on three-stage monotherapy is specified. In the present study, it was aimed to investigate the interactions of midazolam (MDZ), one of the most commonly used benzodiazepines in the first-line treatment of status epilepticus, with second-line antiepileptics levetiracetam (LEV), lacosamide (LCM), valproic acid (VPA) and fosphenytoin (fPHT). In this way, it was aimed to determine the most effective combination of first and second-line antiepileptic drugs in current use as a polytherapy option in order to provide a faster and more effective status epilepticus control.

METHODS: In the experiments, 48 adult male Sprague-Dawley rats divided into 6 groups were used (SBU-HADYEK 2020-03/15). An experimental refractory status epilepticus model was created by administering subcutaneous lithium chloride (5 mEq/kg) and intraperitoneal pilocarpine hydrochloride (320 mg/kg) to rats 7 days after EEG electrode (MS333/2A) implantation. Experimental groups were given MDZ (9 mg/kg) with antiepileptic drugs (200 mg/kg LEV, 50 mg/kg LCM, 300 mg/kg VPA, 100 mg/kg fPHT) combinations was intraperitoneally injected. Video-EEG was recorded on the 2nd and 7th days after status epilepticus process and status. In the statistical analysis of the seizure data (spike frequency and amplitude), the Mann-Whitney U test was used after Kruskal Wallis analysis of variance.

RESULTS: Mortality rate, spike frequency and spike amplitude significantly decreased and seizures were suppressed in the MDZ and other four combination groups compared to the status epilepticus group ($p<0.01$). When compared with MDZ monotherapy, spike frequency and amplitude with mortality rate decreased significantly ($p<0.01$) in the MDZ+LCM group, while mortality and spike frequency increased ($p<0.01$) in the MDZ+LEV group.

CONCLUSION: In the lithium-pilocarpine-induced status epilepticus model, the combination of MDZ+LCM was found to be the most effective polytherapy option in preventing seizures and mortality.
This study was supported by SBU-BAP. Project no: 2020/092.
Keywords: Antiepileptic Drugs, Midazolam, Status Epilepticus.

OC-42

The Effect of GLP-1 Agonist Liraglutide on Emotional-Cognitive Behaviors with CREB, BDNF, Trk-B Expressions in Experimental Schizophrenia-Like Behavior Model Induced by MK-801

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AIM: Neuroprotective effects of the GLP-1agonist Liraglutide have been demonstrated in previous studies. However, there is no study in the literature for the effects of Liraglutid on MK-801-mediated NMDA receptor antagonism. In our study, the effects of Liraglutide on CREB, BDNF, Trk-B expressions and emotional-cognitive behaviors were investigated in an experimental schizophrenia-like behavior model induced by MK-801.

MATERIALS-METHODS: In our study, 8-10weeks-old-male-Balb/c mice (n=78) were injected with MK-801 (0.25 mg/kg, 0.1mL/kg body weight) and/or Liraglutide (300 mcg/kg body weight) intraperitoneally once-a-day for 7 weeks. The same volume of saline was administered to the-control-group. Mice were randomly divided into-5-groups: Saline + Saline, MK-801 + Saline, Liraglutide + Saline, MK-801 + Liraglutide-cotreatment and Liraglutide+MK-801 co-treatment. The time interval between each drug administration in all situations was 30 minutes. Following the injection emotional and cognitive behaviors were evaluated with-the-open-field-test, the-elevated-plus-maze and the Morris-water-maze-test. The hippocampus-and-prefrontal-cortex of the mice were isolated and BDNF, Trk-B, CREB-and-p-CREB expressions were evaluated by-Western-blotting. For normally distributed and parametric data, the analyses were performed by one-way ANOVA followed by Tukey's test. For not-normally-distributed-and-parametric-data,the analyzes were performed by Kruskal-Wallis followed by Mann-Whitney-U test. Since Morris-water-maze test didn't fit the normal distribution, Friedman's-ANOVA was used followed by Wilcoxon test for comparison of group within themselves and Mann-Whitney-U test for comparison between-groups. Ethics committee approval was obtained from Çukurova University-Animal-Experiments-Local-Ethics-Committee.

RESULTS: MK-801 administration in mice caused impairment in emotional-cognitive functions. MK-801 increased the p-CREB/CREB ratio in the prefrontal cortex($p<0.001$). In the MK-801+Liraglutide groups, Liraglutide could not reverse the negative effect of MK-801 on cognitive behaviors. Liraglutide administration decreased the p-CREB/CREB ratio in the prefrontal cortex and increased the BDNF/Trk-B ratio in the hippocampus ($p<0.001$)that increased by MK-801 administration ($p<0.001$). In the Liraglutide + MK-801 groups, the positive effects of Liraglutide on spatial learning and memory activity were not affected by-MK-801-administration. Liraglutide administration returned the BDNF/TrkB and p-CREB/CREB ratio in the hippocampus, the p-CREB/CREB ratio in the prefrontal cortex to the control group level.

CONCLUSION: It can be assumed that Liraglutide does not change the emotional and cognitive behaviors caused by NMDA receptor blockade, but it has a protective effect against the impairment on cognitive behaviors. In addition, it can be suggested that in the hippocampus and prefrontal cortex, GLP-1 receptors play a role in the modulation of NMDA receptor activity through CREB activation/deactivation.

Keywords: Anxiety-like behavior, BDNF, Liraglutide, MK-801, Schizophrenia, Trk-B.

OC-43

The Role of Ferroptosis in High Fructose Diet-Induced Renal Dysfunction

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AIM: The increase in the frequency of kidney diseases in parallel with the increase in fructose consumption in the last century suggests a causal relationship between the two conditions. Ferroptosis is a non-apoptotic cell death mechanism that comes to the forefront with iron accumulation and lipid peroxidation. Impairment in lipid and iron metabolism seen in chronic kidney disease (CKD) suggests a possible role of ferroptosis in CKD.In our study, we aimed to investigate the time-dependent change in kidney functions and the role of ferroptosis in this change in rats fed fructose-rich diet.

METHODS: A total of 35 Wistar rats in 4 groups were used in our study. All rats were fed with standard chow. While the control group was given normal drinking water, the other groups (F4, F8, F12) were given drinking water containing 20% fructose for 4, 8 and 12 weeks, respectively. 24-hour urine of the rats was collected. Blood and kidney tissue samples were taken. Urea, creatinine, uric acid, iron, calcium and potassium levels in serum samples, creatinine clearance and FeNa in urine samples, GSH and MDA for oxidation state, ACSL4, GPX4, TFR1, iron levels which are indicators of ferroptosis were examined. One-Way Analysis of Variance and Tukey test were used for statistical analysis. $P<0.05$ was accepted as the statistical significance limit.

RESULTS: Serum creatinine level was higher in the F12 group compared to the other groups ($P= 0.0001$). The serum urea level was lower in all fructose groups compared to the control group ($P<0.0001$). Serum calcium was lower in the F8 group compared to the control group($p=0.078$), FeNa It was found to be lower in fructose groups depending on time ($P<0.001$). The creatinine clearance/body weight ratio was lower in the F12 group compared to the control and F8 groups ($P=0.001$). The level of GPX4, the main regulator of ferroptosis, was lower in the F4 and F12 groups compared to the control. ($P= 0.0161$). ACSL4, TFR1, iron levels were similar between the groups.GSH levels were lower in the F8 and F12 groups compared to the control ($p=0.005$), and MDA levels were higher in the F12 group compared to the control($p=0.027$).

CONCLUSION: It was observed that kidney functions deteriorated over time in rats fed fructose-rich diet. Ferroptosis was thought to be an important mechanism to consider in this deterioration. This study was supported by Trakya University Scientific Research Projects unit (TÜBAP 2021/149).

Keywords: Ferroptosis, High fructose diet, Oxidative Stress.

OC-44

Investigation of the Protective Effect of Nerolidol on Dehydroepiandrosterone-induced Polycystic Ovary Syndrome in Female Rats

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AIM: Polycystic ovary syndrome (PCOS) is the most common endocrine and metabolic disorder that affects women of reproductive age. Nerolidol (NRL), is a naturally occurring sesquiterpene alcohol, having the molecular formula of 3,7,11-trimethyl-1,6,10-dodecatrien-3-1. The aim of this study was to investigate the effects of NRL on oxidative stress, histological changes, apoptosis, and antioxidant activity in a rat model of dehydroepiandrosterone-induced PCOS.

METHODS: Pre-pubertal female Sprague–Dawley (SD) rats were randomly assigned into four groups (n=8/group), control, PCOS, P+ NRL, and NRL groups. Dehydroepiandrosterone (DHEA) was injected subcutaneously at 60 mg/kg daily for up to 21 days. NRL was orally administered at the dose of 100 mg/kg daily by gavages for 21 days after PCOS occurred. On the 42nd day, animals were sacrificed and various biochemical parameters related to oxidative stress, inflammation, apoptosis, and hormone levels were estimated in the blood and ovarian tissues. Histopathological analysis, ultrastructural analysis, and immunohistochemical analysis were also performed along with caspase-3 expression. BAX, P53, CASPASE 3, and BCL-2 gene expressions were detected in all experimental ovary samples with RT-PCR. The membrane array analysis detected chemokine, cytokine, and growth factor protein profiles of tissues.

RESULTS: NRL treatment in a rat model of PCOS significantly reduced the levels of the TBARS ($p<0.05$). NRL treatment resulted in a significant reduction in serum levels of AMH, T, and LH ($p<0.05$). Administration of NRL prevents biochemical and histopathological alterations. Proapoptotic genes were significantly reduced in NRL and P+NRL groups compared to the control. Anti-apoptotic genes were upregulated after NRL treatment.

CONCLUSION: The results of this study demonstrated that treatment with the potent antioxidant NRL can protect against biochemical alterations, histological damage, and apoptosis caused by PCOS in ovarian tissue.
Financial Disclosure: This study was supported by İnönü University Scientific Research Projects Coordination Unit (Project Number: TCD-2020/2090).

Keywords: Nerolidol, Polycystic Ovary Syndrome, Oxidative Stress, Apoptosis, Dehydroepiandrosterone.

OC-45

Effects of Cerebral Glucagon Administration on Blood Glucose Homeostasis in Rats

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AIM: Glucose homeostasis is the state of balance of hormonal and neuronal mechanisms that play a role in the control of glucose metabolism. The aim of our study is to elucidate the possible effect of 7-day intracerebral infusion (icv) of central glucagon on the regulatory role of pancreatic endocrine secretions in the brain.

METHODS: Fifty Wistar-Albino male rats were used in the study. The rats were divided into 5 groups (n=10) as Control, artificial Cerebrospinal Fluid (aCSF), Glucagon, pancreatic denervation (PD)+aCSF, PD+Glucagon. Glucagon and aCSF (1µg/10µl/min) were administered as icv for 7 days with an osmotic mini pump after PD. At the end of the study, serum glucagon, insulin and epinephrine levels were evaluated by ELISA and pacreas insulin/glucagon levels were evaluated by Western blot and immunofluorescence method from the taken tissues. Kruskal-Wallis test was used to compare the differences between the groups in statistical evaluations. $P<0.05$ was considered statistically significant.

RESULTS: The increase in blood glucose level and decrease in insulin levels in the glucagon group were statistically significant when compared with the control and aCSF groups ($p\leq0.05$).When insulin protein level in pancreatic tissue was compared with the control and aCSF groups, it was determined that there was a decrease in the glucagon and PD+aCSF group, and a significant increase in the PD+Glucagon group ($p\leq0.05$).When the glucagon protein level in the pancreatic tissue was compared with the control and aCSF groups, an increase in the Glucagon group and a significant decrease were determined in the PD+aCSF group ($p\leq0.05$). No difference was observed in the PD+Glucagon group.

CONCLUSION: Our study findings provide evidence that glucagon may have a much greater role in glucose homeostasis besides blood glucose and autocrine effects, and that it may have a role in both peripheral and central regulation of this activity by acting as a neurohormone in the brain.

Keywords: Brain, Glucagon, Glucose homeostasis, Insulin, Pancreas.

OC-46

Effects of High Intensity Interval Training (HIIT) on Skeletal Muscle Athrophy, Function and Myokine Profile in Diabetic Myopathy

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AIM: Diabetes is a chronic metabolic disease. Diabetic myopathy develops due to diabetes and causes functional limitations (increased atrophy, decreased strength, increased fatigue). HIIT is effective in both diabetic and healthy subjects. In our study,it is thought that HIIT will prevent the development of diabetic myopathy. It is aimed to examine the effects of diabetes and HIIT on myokine profile.

METHODS: 10-week-old Wistar albino 60male rats randomly divided into four groups: (1) Control (C), (2) Diabetes (DM), (3) Training (HIIT), (4) Diabetes+Training (DM+HIIT). For the diabetes model, single dose (60mg/kg) of Streptozotocin (STZ) was administered intraperitoneally. 1,3,7 days after, those with glucose values above 300mg/dl measured by glucometer from tail vein were considered diabetic. Maximal exercise capacity (MEC) of animals was determined by incremental load test. 8 weeks of HIIT (4 minutes 85-95% MEK, 2 minutes 40-50% MEK, 6 cycles, 5 days/week) was performed on a treadmill. In soleus and EDL, twitch values (60V-100Hz-0.5ms-2sec): Twitch amplitude (Ps), contraction time (CT), half relaxation time (DT50), maximum contraction rate, minimum relaxation rate), force-frequency measurements (60V-100Hz-0.5ms-5sec,10-30-50-70-100-120Hz), atrophy (wet/dry weight-moisture determination), sensitivity to fatigue (low frequency (LF) (soleus 60V-5Hz-0.5ms-8sec-30sec train period-6cycle and EDL60V-10Hz-0,5ms-8sec-30sec train period 6cycle), high frequency (HF) (soleus 60V-50Hz-0,5ms-8sec-30 sec train period 6 cycle and EDL60V- 100Hz-0,5ms-8sec-30 sec train period 6 cycle) evaluated by in vitro organ bath method and histologically (measurements of muscle-fiber diameter). IL-6, irisin, myonectin levels were measured in muscles and serum (AUHADYEK ethics committee permission, no: 2021-8-47).

RESULTS: In DM group, increased atrophy, fatigue sensitivity, inflammatory effects (IL-6 increase) seen in EDL due to diabetic myopathy were not observed in the soleus. The changes mentioned in EDL in DM+HIIT were significantly reduced compared to DM.Force-frequency and Ps increased significantly only in DM+HIIT compared to other groups.DT50 in soleus and EDL increased in DM compared to C,while it was found to be significantly higher in soleus in DM+HIIT compared to C.IL-6 increased in both serum and EDL in DM compared to C. IL-6 levels were decreased in DM+HIIT compared to DM.Irisin increased in soleus in both HIIT and DM+HIIT compared to C.Myonectin was found to be significantly higher in soleus only in DM+HIIT compared to other groups.

CONCLUSION: Our findings show that diabetic myopathy occurs earlier in glycolytic fast twitch fiber type (EDL)muscles than in oxidative-slow-twitch-fiber-type(soleus) muscles. It has been understood that HIIT prevents skeletal-muscle atrophy, increases fatigue resistance and has anti-inflammatory effect in diabetic groups. This study was supported by AUBAP (21B0230016).

Keywords: Diabetic myopathy, HIIT, IL-6, Irisin, Myonectin.

OC-47

Effects of High Fructose Corn Syrup Consumption on Age-Related Learning and Memory in Rats

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AIM: Fructose is a six-carbon monosaccharide found in fruits and vegetables.11%High fructose corn syrup(HFCS)(%11) was used to match the content of common beverages for human consumption.Is widely used in beverages and ready-to-eat foods.Here, we study the effects of HFCS consumption on metabolism and memory in young and elderly rats.

METHODS: After obtaining ethical approval(2020-11) in our study,60 Spraque-Dawley(SD) male rats of 2 months(young) and of 15 months (elderly) (Bahgat ve etc.) age were further grouped into:1) Young Control(YC),2)YHFCS+10 gr food group,3) YHFCS+20 gr food group,4) Elderly Control(EC),5)EHFCS+10 gr food group,6)EHFCS+20 gr food group(n=10/group).The rats were fed with standard food and water in a 12-hour light period for 16weeks,HFCS (11%) was given in the 12-hour dark period at night.Biochemical blood tests, body weight mass indexes (BMI),eight-armed radial arm maze test and locomotor activities were evaluated.Statistical analyses were performed with one-way ANOVA and analyzed with the lowest significant difference test (LSD test) in the post-hoc test. P<0.05 was considered significantly different.

RESULTS: BMI(g/cm2) (p=0.018), AST (IU/L) (p= 0.0248) and ALT (IU/L) (p=0.01) levels were significantly increased in EHFCS+10 gr food group compared to EC. While there was a significant increase in locomotor activity (p= 0.0031) between EHFCS+20 gr food and EC group, there was no difference in working and reference memory errors between the elderly groups. When compared to YC, glucose (mg/dL) (p=0.0003) was higher and AST(IU/L) (p=0.001), ALT (IU/L) (p=0.001) levels, working memory error (p=0.05) and reference memory errors (p=0.02) were lower in YHFCS+10 gr. YHFCS+20 gr food group had increased weight and locomotor activity (cm) (p=0.05), and decreased reference memory errors (p=0.02). YFMS consumption (11%), triglyceride (mg/dL) and cholesterol (mg/dL) levels were similar for all young and elderly.

CONCLUSION: In our study, chronic consumption of HFCS (11%) was found to increase in elderly groups compared to the control group, in body weight and liver enzyme levels. Compared to the control group, glucose and body weight increased, while liver enzymes decreased in the young groups. They made less memory errors than others. Consumption of 11%HFCS increased locomotor activity in all groups.

Keywords: Fructose, Corn syrup, Learning, Memory, Young, Elderly.

OC-48

Effect of Adropin Administration on Serum Oxidative Stress in Fructose Induced Metabolic Syndrome Model

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AIM: Metabolic syndrome (MS) consists of obesity, insulin resistance, hyperglycemia, dyslipidemia and hypertension. Oxidant-antioxidant system imbalance is amongst important causing factors for this syndrome. Adropin, a peptide synthesized by the liver, is found at low-levels in patients with MS, type 2 diabetes and hypertension. Negative correlation was found between adropin and oxidative stress in tissues. In the light of this information, aim of our study is to determine the effect of adropin treatment on metabolic parameters and serum oxidative stress in rat model of MS.

METHODS: This study was approved by the local ethics committee “Gazi Üniversitesi Hayvan Deneyleri Etik Kurulu”. 21 male Sprague-Dawley rats weighing 250-300 grams divided into 3 groups consist of Control(C), Metabolic Syndrom e(M) and Metabolic Syndrome+Adropin (MA). For MS groups, 20% fructose added into drinking water for 12 weeks. For MA group, 2.1 µg/kg/day intraperitoneal adropin treatment is administered for the last 10 days of the study. At the beginning and the end of the study; body weight, waist circumference and blood pressure were measured. At the end of the study, intraperitoneal-glucose-tolerance-test was performed. Rats were sacrificed with cardiac puncture under ketamine (45mg/kg-i.m.) and xylazine (5mg/kg-i.m.) anesthesia. Malondialdehyde (MDA), Glutathione (GSH) and Superoxide Dismutase (SOD) levels were measured in serum by commercial ELISA kits. Statistical analysis was performed using Kruskal-Wallis and Mann-Whitney-U tests. p<0,05 was considered statistically significant.

RESULTS: For group MS; body weight, waist circumference, blood pressure and glucose level at minute 15 in glucose-tolerance-test are increased significantly as compared to the control (p<0,05). This increase decreased by adropin treatment (p<0,05). With adropin treatment, increased MDA levels in group MS were decreased and decreased GSH and SOD levels in group MS were increased as compared to the control (p<0,05).

CONCLUSION: Adropin administration caused improvement in metabolic syndrome parameters and shown an effect towards the restoration of oxidant-antioxidant imbalance.

Keywords: Adropin, Fructose, Metabolic Syndrome, Oxidative Stress.

OC-49

Erythrocyte ROS Production and Apoptosis Increased in Preeclampsia

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AIM: Preeclampsia is a disease with increased blood pressure, protein excretion in the urine and/or edema that appears after the 20th week of pregnancy and can continue after birth. It is stated that one of the factors accused in the pathogenesis of preeclampsia is increment in the reactive oxygen species (ROS) production. The main reason of this increment is defects in the coupling mechanism of the endothelial nitric oxide synthase (eNOS) enzyme. Erythrocytes have an eNOS enzyme similar to that in endothelial cells and lead to ROS production. This study is aimed to examine how erythrocyte ROS production, apoptosis and eNOS activity levels change in preeclampsia.

METHODS: Packed of erythrocytes were isolated from two different groups; healthy and preeclamptic volunteers. Then packed erythrocytes were re-suspended in Hepes solution at a hematocrit of 0.01 %. Intracellular NO, ROS, Ca+2 and apoptosis levels, and eNOS activation were measured by flow cytometry. Student-t test was used for evaluating the results. Statistical significance was $p<0.05$. The investigation was approved by Antalya Training and Research Hospital Ethical Committee (Number: 069).

RESULTS: Intracellular Ca+2, ROS, and apoptosis levels increased in preeclamptic patients compared with the healthy group ($p<0.01$; $p<0.05$; $p<0.05$). Phosphorylated eNOS levels diminished in preeclamptic patients ($p<0.001$).

CONCLUSION: The results of the study suggest that in preeclamptic patients increased ROS production due to Ca+2 increment and eNOS phosphorylation decrement in erythrocytes induces apoptosis.

Keywords: Blood Pressure, Erythrocyte, Nitric oxide, Preeclampsia.

OC-50

Relationship Between Blood Neutrophil Amount and LDL and Estrogen

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AIM: Although impact of metabolic changes on neutrophil count is well defined, how changes in neutrophil count would affect lipid metabolism was not investigated. Thus, aim was to evaluate impact of changes in neutrophil number on blood cholesterol levels.

METHODS: To establish neutropenia and neutrophilia, two different types of recombinant G-CSF and anti-neutrophil serum (ANS) was subcutaneously injected into both young C57BL/6 male(n=12) and female(n=12) mice. To examine the possible underlying mechanism of relationship between neutrophil count and LDL levels, blood IL-17, G-CSF and liver HMG-CoA reductase enzyme activity were examined in male mice. To further evaluate the impact of sexes, blood samples were collected from male(n=12) and female(n=13) human subjects at two different time points (menstruation and late-follicular phase).

RESULTS: While any significant changes in neutrophil numbers increased total blood cholesterol levels in male mice, an increased total blood cholesterol level($p=0.0339$) was only occurred with increasing neutrophil count($p=0.006$) in female mice. Moreover, it was demonstrated that elevation in total cholesterol level in male mice was associated with LDL($p=0.0008$), but not HDL. There was a significant correlation between total cholesterol and LDL and neutrophils only in female mice ($p=0.0113$, $p=0.0242$ respectively), but not in males. In consistence with mice data, it was demonstrated in female subjects that when estrogen levels were significantly increased during menstrual cycle($p=0.0091$), neutrophil numbers were significantly decreased ($p=0.0034$), and cholesterol levels were significantly increased($p=0.0325$). And while there were no significant differences in G-CSF levels, a significant increase in IL-17 was observed only in ANS-given mice($p=0.0486$), and there was a significant decrease in HMG-CoA Reductase activity in both ANS-($p=0.006$) and filgrastim-injected mice($p=0.0096$) when compared to the control group.

CONCLUSONS: Concequently, it was demonstrated that any significant changes in neutrophil count directly affect LDL levels. Further, this interaction was observed during the menstrual cycle with fluctuating estrogen levels.

Keywords: Neutrophil, LDL, Estrogen.

OC-51

Stimulation of Estrogen Receptors Attenuates Oxidant Skin Injury in Hyperglycemic Rats with Incisional Wound

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AIM: In diabetic patients, wound healing process is impaired and delayed. Although widespread effects of estrogen on wound healing are known, their mechanisms are not clear. It was aimed to investigate possible therapeutic efficacy of estrogen receptor (ER) agonists and its mechanism in wounded hyperglycemic rats.

METHODS: Male Sprague Dawley rats were intraperitoneally administered with streptozotocin (STZ, 55 mg/kg), and rats with ≥200 mg/dL fasting blood glucose level measured on 3rd day were considered hyperglycemic. Fourteen days following STZ-application, under anesthesia, a 2x2cm2 skin incision was made between scapulae up to subcutaneous layer (n=40). Wound-induced hyperglycemic rats were divided into 5 groups; vehicle or ER-α-agonist PPT, ER-β-agonist DPN, non-selective ER-agonist estradiol (E2) or E2+non-selective ER-antagonist ICI-182780 were administered subcutaneously (each 1 mg/kg/day) for 3 days. In wounded-normoglycemic rats (n=8) and in "only-anesthetized" hyperglycemic (n=8) and normoglycemic (n=8) control groups, vehicle was administered for 3 days. On 4th day, skin samples were obtained following euthanasia. Histological evaluation was performed and levels of malondialdehyde, myeloperoxidase activity and luminol and lucigenin chemiluminescence (CL) levels (showing lipid peroxidation, neutrophil infiltration, free oxygen-radical formation, respectively) and antioxidant glutathione were measured. One-way ANOVA test was used for statistical analysis.

RESULTS: Compared to non-wounded control groups, microscopic damage score, myeloperoxidase activity, luminol- and lucigenin-CL levels, and lipid peroxidation were increased in skin samples of vehicle-treated normoglycemic and hyperglycemic wound groups ($p<0.05$-0.001) with no differences between hyperglycemic and normoglycemic groups. Microscopic damage scores were lower in PPT- and DPN-treated groups ($p<0.01$), and dermal luminol- and lucigenin-CL levels were reduced in all treatment groups ($p<0.001$). Wound-induced elevation in myeloperoxidase activity was not changed by any treatment, while glutathione levels were not different among groups.

CONCLUSION: Estrogen mediates the delimitation of oxidant damage at wound site and mediates the healing of diabetic wound mainly via the ER-α and ER-β receptors.
Keywords: Diabetic wound, Estrogen receptors, Oxidant damage, Wound healing.

OC-52

The Effect of High Salt Diet on Anxiety-Depression-Like Behaviors and Cognitive Function in Female and Male Mice

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AIM: Salt is an essential nutrient in our daily life. The World Health Organization recommends less than 5grams of salt per day. The average salt consumption in the world is 15.24grams and in Türkiye is 14.8grams. A high-salt diet(HSD) causes cognitive deficits by increasing hypertension and hippocampal oxidative stress. While most studies focusing on a HSD have been restricted to males, female-to-male comparative studies are few. Therefore, we investigated the gender-related effects of HSD on cognitive function, depression and anxiety.

METHODS: After ethical approval (2022/4-10), 14 female and 14 male mice (3 months,30-35gr) were divided into 2-subgroups for each gender (Control and HSD, n=7). It was assumed that females entered the same cycle on day 3 because of the Whitten effect. In the HSD(NaCl) application, mice were given feed with 4% and drinking water with 1% salt content ad-libitum for 16days. Open field test(OFT) was used to determine the level of anxiety; tail suspension test(TSD) and forced swimming test to determine depression level; the novel object recognition test(NORT) was used to determine cognitive function. Two-way ANOVA test was used for statistical analysis.

RESULTS: In female mice on HSD, compared with female control, the time spent in the center($p<0.001$) and the numbers of rearing decreased($p<0.001$) in the OFT; increase in sedentary time in the TSD($p=0.035$); in the NORT, a decrease in the time spent with the novel object($p<0.001$) was determined. No statistically significant difference in all tests was found in male mice on a HSD compared with male control.

CONCLUSION: HSD causes cognitive deficits by increasing hypertension. Obtained data show that a HSD causes anxiety and depression and decreases learning activity in female. It was concluded that females were more sensitive to HSD than males. These results can be explained by the fact that with HSD, females have a sharper increase in blood pressure than those observed males.

Keywords: Anxiety, Depression, Cognitive function, High salt intake

OC-53

Lactobacillus Rhamnosus Reduces Depression-Like Behavior, Neuron Damage and Neuroglia Activity

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AIM: Lactobacillus rhamnosus (LGG) has the ability to synthesize serotonin and GABA precursors at a high rate in the intestine. In this study, which was approved by Saü Hadyek (12.01.2022-07), it was aimed to examine the antidepressant effects of LGG probiotic bacteria. Serotonin-norepinephrine reuptake inhibitor venlafaxine and dopamine-norepinephrine reuptake inhibitor buprapion were used in drug groups.

METHODS: In the study, 35 8-week-old Wistar Albino rats were used (n=7). Study groups as control group (C), stress group (S), Lactobacillus rhamnosus (LGG) + stress group (LS), buprapion + stress group (BS), venlafaxine + stress group (VS); were formed. Chronic stress was applied for 6 weeks except the control group. Water for injection to the control and stress groups for the last 3 weeks, 15x108 ml/cfu/day LGG to the LS group, 20 mg/kg/day venlafaxine to the VS group, and 20 mg/kg/day buprapion to the BS group were applied by gavage. Behavioral tests were performed. The sucrose preference test was performed at 3-8 weeks. Histopathological evaluations were performed in the cerebral cortex. Values are expressed as mean ± S.E.M, $p<0.05$ was considered significant.

RESULTS: LGG probiotic bacteria decreased the immobility time in FST ($p<0.05$),In the elevated plus maze test, buprapion and LGG probiotic bacteria significantly increased the time spent by rats in the open arm compared to the stress group ($p<0.01$, $p<0.05$,respectively), the number of damaged neurons increased in the stress group ($p<0.001$), neuron damage caused by stress decreased by LGG,venlafaxine and buprapion treatment ($p<0.001$).The number of neuroglial cells gathered around the damaged neurons was significantly increased in the stress group ($p<0.001$). In LGG, venlafaxine and buprapion groups, this rate decreased significantly compared to the stress group ($p<0.001$). There was no statistical difference in sucrose preference test results.

CONCLUSION: These results show that LGG reduces depression-like behaviors, protects neuron cells and decreases neuroglia activity.

Keywords: Chronic Stress, Depression, Lactobacillus rhamnosus, Behavioral Tests, Hippocampus, Cerebral Cortex.

OC-54

Possible role of T3 hormone in Metaplasticity Disorder in Experimental Hypothyroidism Model

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AIM: Metaplasticity refers to the modulation of synaptic activity based on previous activity. It has been reported that experimental hypothyroidism induced in adulthood causes impaired hippocampal metaplasticity in rats. In this study, it was investigated which thyroid hormone derivative (T3 or T4) is responsible for these electrophysiological changes observed in hypothyroidism.

METHODS: Two-month-old Wistar albino male rats were used in the study; control group (KG; n=18) and hypothyroid group (HG; n=18). After stimulation of perforant pathway-dentate gyrus synapses with low frequency stimulation (LFS) consisting of 5Hz and 900 pulses, long-term potentiation (UDG) was induced by high-frequency stimulation (HFS: 4 X 100Hz) in control and hypothyroid rats which are induced by 6-n-propyl-2-thiouracil (0.05% PTU in drinking water for 21 days). Starting from the induction of metaplasticity, SF or T3 and T4 were infused intrahippocampally for 1 hour (Subgroups: CG-SF, CG-T3, CG-T4; HG-SF, HG-T3, HG-T4). Metaplasticity were evaluated as field excitatory postsynaptic potential (fEPSP) slope and population spike (PS) amplitude.

RESULTS: It was found that both EPSP slope and PS amplitude of hypothyroid and hypothyroid+T4 infusion group rats were significantly reduced compared to control and control+T4 infusion group rats (p's<0.05). It was also found that both EPSP slope and PS amplitude of hypothyroid group rats were significantly decreased compared to control, control+T3 and hypothyroid+T3 infusion group rats (p's<0.05). These findings show that hypothyroidism reduces hippocampal metaplasticity responses in young-adult rats, and T3 hormone infusion prevents this decrease, whereas T4 hormone has no effect.

CONCLUSION: This study revealed that hypothyroidism impairs metaplasticity in hippocampal perforant pathway-dentate gyrus synapses, and T3 hormone, but not T4 hormone, is responsible for this disruption.

This study was financially supported by TUBITAK (grant number: 220S857) and Erciyes University Research Found (grant number: TCD-2020-9261).

Keywords: Metaplasticity, Hypothyroidism, T3 hormone, T4 hormone, Hippocampus.

OC-55

Evaluation of Color Discrimination Ability in Patients with Transfusion Dependent Beta Thalassemia by Farnsworth Munsell 100 Hue Test

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AIM: It has come to our attention that color vision, which is reported to be impaired in transfusion-dependent beta thalassemia (TDβ-T) patients, is frequently examined with screening tests used for congenital color vision defects. We aimed to detailed examine color discrimination ability (CDA) in patients with TDβ-T by Farnsworth Munsell (FM) 100 hue test recommended for acquired color vision disorders.

METHODS: This prospective croOC-sectional study was conducted between January and June, 2022 in a tertiary hospital. Forty-two TBβ-T patients and 15 healthy individuals were included. All participants underwent a detailed ophthalmological examination. Subjects with any disease that may affect visual functions were excluded. Screening for congenital color vision deficiency was performed by the Ishıhara test. FM100 hue test is an arranging test based on ordering colored caps correctly and is evaluated on error scores. Total error score (TES), blue-yellow local error score (b-y LES), and red-green local error score (r-g LES) were calculated according to performed ordering in the study. SPSS 23 program was used for statistical analysis.

RESULTS: Eighty-three eyes of 42 patients (30.12±6.79 years) and 30 eyes of 15 healthy individuals (34.30±6.18 years) were included in the study. All patients were dependent on red blood cell transfusion every 2-3 weeks and were using iron-binding drugs. Hemoglobin levels were lower and ferritin levels were higher in patients compared to controls($p<0.001$). TES, b-y LES, and r-g LES were detected significantly higher in patients than in controls ($p<0.001$). TES; 63.35±31.60 vs 29.77±15.03, b-y LES; 33.26±18.24 vs 15.73±9.50 and r-g LES; 28.79±16.13 vs 13.23±7.47. b-y LES was significantly higher than r-g LES in patients ($p=0.015$), but no difference in controls.

CONCLUSION: The disease itself, tissue hypoxia, iron overload, or toxicity of iron-binding drugs may have affected color vision. More extensive studies are needed to understand the underlying mechanisms.

Keywords: Beta thalassemia, Color vision, Farnsworth Munsell 100 Hue Test.

OC-56

Cognitive Performance and Social Interaction in Nicotine-Preferred Rat Lines

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AIM: A nicotine-preferring (NP) rat line was developed to investigate the effects and new therapies for nicotine addiction. Aim of the present study was to investigate the changes in cognitive performance and social interaction of rats with nicotine-preference.

METHODS: Forty-eight Sprague-Dawley rats were assigned to four groups: Nicotine-preferring male (NPM), nicotine-preferring female (NPF), control male (CM) and control female (CF). New object recognition (NOR), object location recall (OLT) and Morris Water Maze (MWM) tests were used to evaluate the cognitive performance; three-chamber social interaction test (TCSI) was used to evaluate the social interactions. Data were analyzed with ANOVA tests using IBM SPSS 20.00 software.

RESULTS: NP rats had increased interest in objects ($F(3.38) = 5.128$ $P=0.030$) in the NOR familiarization session. All groups were more interested in the new object in the test session ($F(1.78)= 20.524$ $P=0.000$). Line differences were found in total time spent with the objects in the OLT familiarization session ($P=0.000$), time spent with the displaced object in test session ($P=0.000$) and in discrimination index ($P=0.028$). During MWM spatial learning acquisition period, time to reach the platform decreased by days. The effect of sex ($p=0.025$) and line ($p=0.009$) was statistically significant, but there was no interaction between them. In Duncan's test showed a significant difference between CF group and NPM and NPF groups. In probe trial, there was also a significant effect of line on path taken in the old quadrant ($p=0.001$).NP rats spent longer time in the old quadrant. No significant differences in line were found in social interaction and social novelty tests.

CONCLUSION: Nicotine-preferring rats have an advantage in detecting new objects and locations and they have better spatial memory. However, they displayed no significant change in social interaction and have no sex difference. We hope that these results will improve our understanding of addiction (project number: DESTEK BAP T TYL–2021–23456 EUHADYEK 2021-074).

Keywords: Memory, Nicotine, Learning, Sociability.

OC-57

Investigation of the Protective Effect of Treadmill Exercise on Molecular Pathways and Cognitive Behaviors in Alzheimer Disease Model

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AIM: It was aimed to investigate the protective effect of treadmill exercise on molecular pathways and cognitive behaviors in the Alzheimer'sdisease model induced by scopolamine.

METHODS: Male Balb/c mice (N=69) which was separated from their mothers on day21 were subjected to low-intensity treadmill exercise (45min/day, 5days/week, for 12weeks). In the last 4 weeks of the exercise, scopolamine was administered to some mice (2mg/kg, 0.1ml/bodyweight, once a day, i.p.) and same volume of saline (SF) was administered to the control group. Four different experimental groups(N=11-15) were formed (E-SF, E-SCOP, S-SF, S-SCOP). Emotional-cognitive behaviors were evaluated with openfield test using the parameters of time spent in the center, distance travelled, rearing, frequency of entry to the center, entry time to the center. Behaviors of mice also were evaluated with morriswatermaze test using the parameters of escape latency, swimming speed and time in target quadrant. Hippocampus and prefrontal cortex were isolated and BDNF, TrkB, p-GSK3ßSer389 levels were evaluated by Westernblotting, APP and Aß-40 levels were analyzed by immunohistochemistry. Ethics committee approval was received at the meeting No.5 dated 12.08.2020 of the local ethics committee of Cukurova University.

RESULTS: Scopolamine administration caused impairment in cognitive-emotional functions. Scopolamine caused a decrease in p-GSK3ßSer389, BDNF and TrkB levels in hippocampus. In prefrontal cortex, p-GSK3ßSer389 and BDNF levels decreased, while TrkB levels increased. It was found that APP and Aß-40 in hippocampus and prefrontal cortex increased in neuronal and perineuronal areas with scopolamine administration. It was found that long-term exercise had protective effects against impairment in cognitive-emotional functions. There was an increase in p-GSK3ßSer389, BDNF and TrkB levels in hippocampus in the exercise group. There were also increases in p-GSK3ßSer389, BDNF and TrkB levels in prefrontal cortex. It was observed that Aß-40 and APP were decreased in exercise groups.

CONCLUSION: Long-term treadmillexercise may have a protective effect against the impairment in cognitive-emotional behaviors induced by scopolamine. It can be suggested that this protective effect is mediated by increased BDNF level and GSK3ßSer389 phosphorylation.

Keywords: Alzheimer's disease, Amyloid beta, BDNF, Exercise, p-GSK3ßSer389, Scopolamine.

OC-58

Effects of Melatonin on Inflammation and Tissue Damage in Acute Kidney Injury

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AIM: The mediators secreted by the host in an increased and uncontrolled manner in response to inflammation in sepsis cause tissue damage and disruption of the oxidant balance. Acute kidney injury is one of the most common complications associated with sepsis. Although melatonin is one of the strongest known endogenous antioxidant, it is reported to be protective on damaged kidney tissue with its anti-inflammatory properties. In our study, we aimed to investigate the effects of melatonin on inflammatory and damage markers in serum and kidney tissue in rats with sepsis induced with lipopolysaccharide (LPS).

METHODS: Adult male Wistar albino rats were divided into 4 groups; Control, LPS (20mg/kg i.p.), Melatonin (10mg/kg i.p.x3), Melatonin+LPS. The rats were decapitated 6 hours after the first injection and samples were collected. Serum biochemistry parameters were evaluated with auto-analyzers. Kidney tissues were taken into 10% formaldehyde. Tumor necrosis factor-alpha(TNF-α), Interleukin-10 (IL-10), Matrix metalloproteinase-2 (MMP-2), MMP-9, chitinase-3-like protein (YKL-40), myeloperoxidase (MPO) and matrix metalloproteinase tissue inhibitor (TIMP-1) was performed using immunostaining antibodies. One-way analysis of variance and Tukey tests were used for statistical analysis.

RESULTS: In the LPS group, serum creatinine kinase, aspartate aminotransferase, alanine aminotransferase and blood leukocytes increased ($P<0.05$) and glucose levels decreased ($P<0.01$). In the kidney tissue, intense TNF-α, moderate MMP-2 and MMP-9, mildly intense YKL-40, MPO and IL-10 immunoreactivities were detected in LPS group. In M+LPS group, mild involvement of IL-10, MMP-2, MMP-9 and TIMP-1 was detected. No immunoreactivity was observed in the control and melatonin groups.

CONCLUSION: Melatonin effected in rats with LPS and acute kidney injury; We observed that increased cytokine and decreased the release of YKL-40, which is sepsis biomarker, partially corrected the tissue damage, and brought the serum biochemistry values closer to the normal. In our study, it was determined that melatonin prevents acute kidney damage due to sepsis.

Keywords: Melatonin, Sepsis, Kidney, Cytokines, YKL-40, Matrix Metalloproteinases.

OC-59

The Effect of Uridine on Inflammatory Mediators in REM Sleep Deprived Rats

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AIM: Sleep deprivation (SD) affects levels of inflammatory mediators that cause various effects on metabolism. Uridine, the main pyrimidine nucleoside in humans, has been shown to have anti-apoptotic and anti-oxidant as well as neuroprotective effects. Our aim is to investigate effects of uridine on inflammatory mediators in REM sleep deprived rats.

METHODS: Adult male Wistar albino rats (n=42) were randomized to 6 groups according to cages they were placed and uridine (1 mmol/kg)/Saline (1ml/kg) injections; CC+S: Saline treated control cage group, CC+U: Uridine treated control cage group, EC+S: Saline treated environmental control group, EC+U: Uridine treated control group, SD+S: Saline treated sleep deprivation group, and SD+U: Uridine treated sleep deprivation group. SD was induced by modified multiple platform method. A grid was placed on multiple platforms for environmental control cages. Rats were tracked for 96h and treated with U/S twice for 4 days and once on the 5thday intraperitoneally. Cytokine levels and mRNA expressions from hippocampi were analyzed by ELISA and RT-PCR methods. Groups were compared using ANOVA and post-hoc Tukey tests.

RESULTS: IL-1β($p<0.001$), IL-4($p<0.01$), IL-6($p<0.01$), IL-10($p<0.05$) and TNF-α($p<0.001$) levels increased in SD+S compared to CC+S. IL-1β($p<0.01$), IL-4($p<0.001$), IL-6($p<0.05$) and TNF-α($p<0.05$) levels increased in EC+S compared to CC+S. IL-1β($p<0.05$) and IL-4($p<0.01$) levels decreased in EC+U compared to EC+S. IL-1β($p<0.01$), IL-4($p<0.001$) and IL-6($p<0.001$) mRNA expressions increased in SD+S compared to CC+S. IL-1β($p<0,01$), IL-4($p<0,01$), IL-17A ($p<0,01$) and TNF-α ($p<0,05$) mRNA expressions increased in EC+S compared to CC+S. mRNA expressions of IL-1β ($p<0.001$) decreased; IL-4 ($p<0,01$) and IL-6($p<0,001$) increased in EC+U compared to EC+S. mRNA expressions of IL-1β($p<0.001$) decreased; IL-6($p<0,001$), IL-4($p<0,001$) and TNF-α($p<0,05$) increased in SD+U compared to SD+S.

CONCLUSION: We determine that SD ameliorates cytokine levels and mRNA expressions in rats. The effects of uridine on cytokine levels and mRNA expressions in REM sleep deprived rats were shown for the first time in our study (TÜBİTAK Project No:119S887).

Keywords: Anxiety, Cytokine, Learning-memory, REM sleep deprivation, Uridine.

OC-60

The Effect of Extra Virgin Olive Oil (EVOO) and Riviera Olive Oil on Anxiety-like Behaviours, Cognitive Functions and Neuroinflmmation in Adolescent Rats

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AIM: During adolescence, some factors such as neuroinflammation that occur in brain developmental process bring about changes in behavior and learning-memory functions. It is well-known that EVOO has positive effects on learning-memory functions and anxiety in elderly. However, the effects of both EVOO and ROO are not known during adolescence. This study aims to compare the effects of EVOO and ROO on inflammatory biomarkers (TNF- α and IL-10) in the hippocampus (HC) and prefrontal cortex (PFC), and blood lipids, anxiety-like behaviors and learning-memory in adolescent rats.

METHODS: 6-week-aged, 21-Sprague-Dawley-male-rats were divided into three-groups: (1) EVOO (n=7), (2) ROO (n=7), (3) Control group(n=7). Experimental groups were administrated with standard-chow(SD) with add EVOO (770 mg/kg polyphenol) and ROO (no-polyphenol-content) (10g EVOO or ROO/100g SD). While anxiety-like-behaviours were evaluated with elevated-plus-maze-(EPM) and open-field-test-(OFT), learning-memory functions were evaluated with Morris-water-maze-(MWM). TNF-α and IL-10 levels in PFC and HC, and blood triglyceride (TG), LDL and HDL levels were measured. One-way-ANOVA and post-hoc-Bonferroni-test and Pearson-correlation analysis were used for statistical evaluation.

RESULTS: While EVOO enhanced learning-memory functions, decreased anxiety-like-behaviors ($p<0.05$ for both of them). ROO decreased anxiety-like-behaviors ($p<0.05$). Compared to control, ROO decreased only PFC-TNF-α/IL-10-ratio($p<0.05$) whereas EVOO decreased inflammation-ratio in both PFC and HC ($p<0.01$ and $p<0.05$, respectively). EVOO reduced TG-levels and HDL/LDL-ratio ($p<0.01$ and $p<0.05$, respectively) while ROO only decreased TG-levels. A positive correlation was found between HC-TNF-α/IL-10 and anxiety-like-behaviors ($r=0.585$, $p=0.02$), and while a negative correlation between PFC-TNF-α/ IL-10 and decreased anxiety-like-behaviors ($r=-0.631$, $p=0.009$). While there was a negative correlation between TG-levels and learning-memory functions ($r=-0.551$, $p=0.041$), a positive correlation between TG-levels and anxiety-behaviors ($r=0.544$, $p=0.029$).

CONCLUSION: In conslusion, EVOO increased learning-memory-functions compared to ROO. Increased learning-memory functions due to EVOO was associated with decreased TNF-α/IL-10-ratio in HC, and TG-levels. EVOO and ROO decreased anxiety-like-behaviors. Decreased anxiety-like-behaviors in both EVOO and ROO was related to decreased TNF-α/IL-10 ratio in both HC and PFC, and blood-TG-levels.

Keywords: Extra virgin olive oil, Riviera olive oil, TNF-α/IL-10 ratio, Triglyceride, Anxiety ve cognitive function, Adolescence.

Poster Communications

PC-01

Effects of Hyperbaric Oxygen Therapy (HBOT) on Hemorheological Parameters in Patients with Chronic Wounds

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AIM: HBOT is effectively used in patients with chronic wounds. It has been reported that hemorheological parameters of chronic wound patients are negatively affected. These findings suggest that cardiovascular complications may occur in patients following HBOT. We investigated the effect of HBOT on hemorheological parameters in chronic wound patients.

METHODS: The study was approved by the ethics committee (number:147/2013). 25 patients (30-56, 11F/14M) without chronic disease were included. Routine care of the wounds continued throughout the study. According to the standard treatment procedure, 100% oxygen was administered at 2.4 ATA (1 session per day, 5 sessions per week). Blood was drawn before the initial therapy and after the 20th session and the initial values were considered as control. Whole blood viscosity at 8 different shear rates (SR) and plasma viscosity were measured with a cone/plate viscometer. Erythrocyte aggregation, erythrocyte deformability and osmotic deformability indices were measured using a laser applied refractometer (LORCA). Data were statistically evaluated using the Mann-Whitney U test and presented as mean±standard deviation.

RESULTS: The mean hematocrit values were 38.42±4.67 (28-45). Compared to the initial values after 20th therapy session; plasma viscosity and all SR values of blood viscosity corrected to 45% decreased significantly ($p<0.001$ and $p<0.05$, respectively). Erythrocyte aggregation parameters using both autologous plasma and dextran70 solution, significant and positive differences were observed ($p<0.001$ and $p<0.001$, respectively). There were no significant differences in erythrocyte deformability and osmotic deformability parameters.

CONCLUSION: Our results contradict with previous studies in that they showed that the parameters we investigated were not negatively affected by the treatment. On the contrary, it has shown that it has a positive effect on clinically important parameters such as erythrocyte aggregation. We think that these contradictions may be due to differences in clinical practice and experimental conditions and/or different responses in humans and animals.

Keywords: Chronic wound, Hyperbaric oxygen therapy, Blood viscosity, Erythrocyte deformability, Erythrocyte aggregation, Osmotic deformability.

PC-02

Effects of Epigallocatechin Gallate and Curcumin on Hydrogen Peroxide Toxicity to SH-SY5Y Cells

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AIM: Several studies have shown that plant polyphenols have positive effects on neurodegenerative diseases. Epigallocatechin-3-gallate (EGCG) and curcumin are antioxidant polyphenols. The aim of this study is to demonstrate the effects of EGCG and curcumin pre-treatment against hydrogen peroxide (H2O2) damage in SH-SY5Y cell line.

METHODS: Various doses of H2O2 were administered to the SH-SY5Y cell line for 1 hour in the study. The LD50 dose of H2O2 was determined as 100 µM. In order to determine the protective effects of EGCG and curcumin, 0.1 µM EGCG, 1 µM EGCG, 10 nM Curcumin, 50 nM Curcumin doses and their combinations were administered as a 24-hour pretreatment. It was exposed to 100 µM H2O2 for 1 hour at the end of the application. As a result of the applications, cell viability was determined by MTS test, and colony formation abilities were determined by clonogenic test. Caspase-3 ELISA was performed to assess the type of cell death. One-way ANOVA was used for statistical analysis.

RESULTS: Our results showed that 100 µM H2O2 manifested decrease approximately half of the cell population ($p<0.0001$). Cell survival and colony formation ability were significantly increased ($p<0.0001$) and active caspase 3 levels were significantly decreased ($p<0.0001$) when 0.1 µM EGCG or 10 nM curcumin treatment was applied 24 hours before 1-hour H2O2 administration. It was observed that the combination of these doses also showed protective effects on cell proliferation and colony formation ($p<0.001$) and decreased active caspase-3 levels significantly ($p<0.001$).

CONCLUSION: Our study revealed that H2O2 decreases cell viability by increasing apoptotic cell death. Doses of 0.1 µM EGCG, 1 µM EGCG, 10 nM Curcumin, 50 nM Curcumin and their combinations reduced the neuronal damage caused by H2O2. This shows that these agents can be used as protective agents against neurodegeneration.

Keywords: EGCG, Curcumin, H202, Neuronal toxicity.

PC-03

The Effects of Darbepoetin Alfa on the Changes Induced by Ethanol in Glucose Metabolism and Lipid Profile

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AIM: Ethanol leads to physiopathological disorders by affecting metabolic processes related to glucose metabolism and lipid profile. Darbepoetin alfa (DA) is an analogue of recombinant human erythropoietin (rHuEPO). In our study, we aimed to investigate the effects of darbepoetin alfa (DA) on the changes glucose and lipid metabolism and asprosin levels induced by ethanol in rats.

METHODS: 40 Wistar-Albino male rats were divided into four groups of control (C) (3.15 ml/kg isocaloric glucose solution, ig), ethanol (E) (3 g/kg 20% ethanol solution, ig), DA (0.25 µg/kg, ip) and E+DA. Fasting blood glucose (FBG) was measured on the first day, 15th and 30th days. On the 30th day, triglyceride, total cholesterol, HDL and insulin levels in serum and asprosin levels in plasma were measured. Liver tissues were investigated by histopathological methods.

RESULTS: FBG was significantly lower in E+DA group on the 30th day compared with C group ($p<0.05$). Serum insülin and triglyceride levels were significantly higher in E+DA group compared with C and E groups ($p<0.05$). There was no statistically difference between the groups in HOMA-IR, in the plasma asprosin levels, in the serum total cholesterol and HDL levels. Histopathologically, diffuse microvesicular fat accumulation in hepatocytes, and extensive dilatation and hyperemia in sinusoids were observed in E group compared with C group. In the E+DA group, these pathological findings were significantly reduced.

CONCLUSION: In our study, it was observed that ethanol had no effect on asprosin levels, insulin resistance and lipid profile depending on the ethanol dose and ethanol exposure time. In the E+DA group, the decrease in FBG within physiological limits is due to an increase in insulin level. In our study, there was an increase in serum triglyceride levels with the combined effect of ethanol and DA.

Keywords: Ethanol, Darbepoetin alpha, Asprosin, Glucose metabolism, Lipid profile.

PC-04

Synthesis of New Amino Acid Conjugates Containing Cinnamic Acid Derivatives and Investigation of Their Cytotoxic and Genotoxic Properties

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AIM: The aim of the study is to synthesize new amino acid conjugates and to investigate the effects of cytotoxicity and genotoxicity studies of these compounds on three different human cancer cells.

METHODS: The planned cinnamic acid derivatives were obtained by Claisen–Schmidt condensation, these compounds were reacted with three different amino acids using the benzotriazole method to obtain target compounds. The structures of all compounds were elucidated by FT-IR, 1H, 13C NMR spectroscopy. Cell viability of both cinnamic acid derivatives and target compounds against 3 different human cancer cell lines (human breast (MCF-7), human prostate (PC-3), and human colon (Caco-2) at 5 different doses was determined by MTT assay method. In order to understand whether all compounds that effective against cancer cells cause cell death through DNA damage, the cell death mechanism was elucidated using the comet assay method. Conformity to the normal distribution was determined by the Shapiro–Wilk test. Intergroup comparisons of quantitative variables were determined by the Kruskal–Wallis H test. When there were statistically significant differences between the groups, multiple comparisons were made with Bonferroni correction and Mann–Whitney U test. The data obtained from the comet assay were analyzed using one-way ANOVA, followed by post-hoc Tukey HSD test.

RESULTS: In general, the majority of the target compounds were effective in all cell lines, especially the leucine amino acid conjugate (Phenylbenzyl-CA-Leu-OH) bearing the Phenylbenzyl group showed activity at all doses (1, 5, 25, 50 and 100 µM) ($p < 0.05$).

CONCLUSION: The results of this study demonstrated that the tested compounds caused cell death by causing damage to the DNA of cancer cells.

This study was supported by Inonu University Scientific Research Projects Coordination Unit (Project No: TSG-2020-2183).

Keywords: Cinnamic acid, MTT assay, Comet assay, MCF-7, PC-3, Caco-2.

PC-05

Effects of Paclitaxel and/or Stattic Application on Cell Viability and Tumor Size in Triple Negative Breast Cancer

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AIM: Triple negative breast cancer (TNBC) is an invasive and metastatic cancer with aggressive progress. We aimed to investigate the antiproliferative and antimetastatic effects of Paclitaxel, used alone or in combination with Stattic, a Signal Transducer and Transcription Activator-3 (STAT-3) inhibitor, in experimental TNBC models in vitro and in vivo.

METHODS: Paclitaxel and Stattic were administered individually on 4T1 mouse TNBC cell line at varying concentrations for varying durations. Having its IC80 determined as 10 µM, Stattic was applied concomitantly with Paclitaxel administered at different concentrations for varying durations. Cell viability was determined by MTT assay. In vivo model was established by inoculating 4T1 cells subcutaneously into the mammary tissue of female BALB/c mice. Mice were randomly assigned into 9 groups (n=8, each) as: 1-Control+Saline, 2-Control+vehicle(DMSO), 3-Tumor+Saline, 4-Tumor+DMSO, 5-Tumor+Stattic (20 mg/kg), 6-Tumor+Paclitaxel (1 mg/kg), 7-Tumor+Paclitaxel (10 mg/kg), 8-Tumor+ Stattic+ Paclitaxel (1 mg/kg), 9-Tumor+ Stattic+ Paclitaxel (10 mg/kg). Saline, DMSO and Stattic were administered intraperitoneally every other day and Paclitaxel every third day. On day 24, mice were euthanized, and lung and tumor tissues were weighed and kept under convenient conditions until the time of histopathological and molecular analyses. The groups were statistically compared by Kruskal-Wallis/Wilcoxon tests. (Project: TSA-2021-19017, Ethical approval:2020/10-08).

RESULTS: Stattic reduced cell viability in vitro in a time-independent but dose-dependent manner when applied alone ($P<0.05$). Stattic+10 nM Paclitaxel application decreased cell viability significantly at 48 hours in comparison with that of higher concentrations of Paclitaxel used alone ($P<0.01$). Our in vivo findings revealed no differences between groups in terms of tumor diameter, weight and body weight. Lung weight averages were higher in all Stattic-received groups than Control+DMSO group ($P<0.05$).

CONCLUSION: Paclitaxel reduced cell viability at lower concentrations when co-administered with Stattic for a short duration. Prolonged exposure caused to increased metastasis and cell viability by inhibiting not only STAT3 but probably STAT1 as well, which has tumor suppressing activity.

Keywords: Paclitaxel, Stattic, STAT3, Triple Negative Breast Cancer.

PC-06

Cytotoxic and Genotoxic Effects of Nateglinide on A2780, LNCaP and Caco2 Cell Lines

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AIM: Cancer represents one of the leading causes of morbidity and mortality. Despite advances in cancer treatment, the low success rate and tumor recurrence make the discovery of new therapeutic agents important. Nateglinide is a new oral hypoglycemic agent with a carboxyl group and a peptide bond in its structure. In this study, we aimed to determine the cytotoxic and genotoxic effects of nateglinide on human ovarian cancer, human prostate cancer and human colon cancer cell lines.

METHODS: A2780, LNCaP and Caco2 cell lines were used in the study. After the cells were incubated with 1, 10, 100 and 1000 µM concentrations of Nateglinide for 24 hours, the cytotoxicity level in the cells was determined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method. According to the MTT assay results, the inhibitory concentration 50 (LogIC50) of Nateglinide was calculated in the Graphpad Prizm 8 program. Comet experiments were performed to determine the genotoxic properties of the concentrations showing cytotoxic effect according to the MTT assay results. Comparisons between groups were made using the Mann Whitney U test with Bonferroni correction.

RESULTS: Nateglinide 100 and 1000 µM doses significantly reduced cell viability of A2780, LNCaP and Caco2 cell lines ($p<0.05$). According to the comet assay results performed in A2780, LNCaP and Caco2 cell lines, as a result of the Comet analyzes performed at significant doses (100 and 1000 µM) of the drug, an increase in the tail lengths (TI), tail moments (TM) and a decrease in the head diameters of the cells were determined ($p< 0.05$).

CONCLUSION: The results of this study show that the tested Nateglinide has anticancer activity on A2780, LNCaP and Caco2 cells and causes cell death by damaging cell DNA.

Keywords: A2780, Caco2, Genotoxicity, LNCaP, Nateglinide, Cytotoxicity.

PC-07

Age-Related Characterization of Dental Pulp Mesenchymal Stem Cells

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AIM: Mesenchymal stem cells are cells that have the ability to self-renew and differentiate into various cells. Although dental pulp stem cells are one of the most important sources of easily available mesenchymal stem cells, they are known for their rapid proliferation and their potential to form mineralized tissue when differentiated with appropriate stimuli. Advances in stem cell biology and tissue engineering have paved the way for cell-mediated regenerative therapy options. There are studies showing that the number and functions of stem cells decrease with age. In our study, it was aimed to compare the ratios of dental pulp stem cells obtained from people aged 18-24 years, 25 years and older.

METHODS: From the obtained dental pulps, dental pulp stem cells were grown by cell culture and differentiated into adipogenic, osteogenic and chondrogenic cells. Dental pulps were compared with flow cytometry in terms of dental pulp mesenchymal stem cells. Approval for the study was obtained from the Ege University Faculty of Medicine Clinical Research Ethics Committee (18-1/26). The project was supported by Ege University BAP Coordination Unit.

RESULTS: Mesenchymal stem cell markers CD13, CD105 and hematopoietic stem cell marker CD 45 were evaluated. In the statistical analysis, no significant difference was found between the age groups.

CONCLUSION: Although more dental pulp stem cells were obtained in the 18-25 age group, no statistically significant difference was found.

Keywords: Mesenchymal Stem Cells, Dental Pulp Stem Cells, Flow Cytometry.

PC-08

Effects of Diisononil Phthalate on Different Types of Cancer Cell Lines

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AIM: Phthalates, as a class of endocrine disruptors, are widely used as plasticizers in consumer products, including building materials, medical supplies, and cosmetics. Diisononyl phthalate (DiNP) is one of most widely used primary phthalates in industry. Studies have shown that exposure to phthalates is associated with variety of disorders, most notably cancer. Compared with other phthalate groups, relationship of DiNP with cancer has not been fully elucidated. Therefore, we aimed to investigate effect of DiNP exposure cell viability in LNCaP, A2780, MCF-7 and Caco-2 cell lines.

METHODS: LNCaP, A2780, MCF-7 and Caco-2 cell lines were used in the study. Changes in cell viability were determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method after cells were incubated with DiNP concentrations of 1, 10, 100 and 1000 µM for 24 hours. After determining the dose-dependent effectiveness according to the MTT assay results, the inhibitory concentration 50 (LogIC50) value was evaluated in Graphpad Prizm 8 program. The genotoxicity level was analyzed with the COMET method by determining the effective doses as a result of the data obtained. Meanwhile, a reaction test was performed between DiNP and MTT chemicals. Comparisons between groups were made using the Kruskal-Wallis H test in IBM-SPSS 24 package program.

RESULTS: After 24 hours of DiNP incubation, viability levels of LNCaP, A2780, MCF-7 and Caco-2 cell lines were significantly decreased at certain concentrations (1000 concentration) ($p<0.05$). We performed Comet analysis at significant doses of the chemical and concluded that DiNP application caused DNA damage in LNCaP, A2780, MCF-7 and Caco-2 cell lines.

CONCLUSION: The fact that DiNP tested in this study exhibited an anticarcinogenic effect on LNCaP, A2780, MCF-7 and Caco-2 cells indicates that it has positive feature in addition to its other harmful effects DiNP. In this context, further research is needed.

Keywords: A2780, Caco-2, DiNP, Cancer, LNCaP, MCF-7.

PC-09

Trimebutin Demonstrate Antitumor Effects on Different Types of Human Cancer Cells

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AIM: Cancer is a major cause of death affecting millions of people and is caused by the uncontrolled growth and spread of abnormal cells. Anti-inflammatory drug intake has an important place among the pharmacological treatments recommended for cancer. Trimebutin, known for its anti-inflammatory activity, is widely used for the treatment of gastrointestinal disorders, including irritable bowel syndrome. Also, few data highlight that Trimebutin may act as an antitumor agent against lower gastrointestinal tract and brain neoplasms. Studies of in vitro and in vivo Trimebutin cancer studies on different types of human cancer cell lines are still limited. Therefore, we aimed to investigate the effect of Trimebutin exposure on cell viability in prostate (LNCaP), ovarian (A2780), colon (Caco2) and breast (MCF-7) cancer cell lines.

METHODS: In the study, the changes in cell viability for 24 hours by applying 1, 5, 25, 50 and 100 µM concentrations to Trimebutin LNCaP, A2780, Caco2, MCF-7 cell lines 3-(4,5-dimethylthiazol-2-yl)-2,5 -diphenyltetrazolium bromide (MTT) was determined by the assay method. After determining the dose dependent efficacy according to the MTT assay results, the inhibitory concentration 50 (LogIC50) value was evaluated in the Graphpad Prizm 8 program.

RESULTS: It was determined that there was a decrease in cell viability of LNCaP, A2780, Caco2, MCF-7 cell lines incubated with Trimebutin for 24 hours, and this decrease was significant at all applied concentrations of Trimebutin ($p<0.05$).

CONCLUSION: The results of this study show that Trimebutin tested has antitumor activity on LNCaP, A2780, Caco2 and MCF-7 cells.

Acknowledgements: This study was supported by Inonu University Scientific Research Projects Unit with the project number TSA-2022-2975.

Keywords: Trimebutine, Cancer, LNCaP, A2780, Caco2, MCF-7.

PC-10

In Vitro Investigation of the Effects of Desloratadine, an Antihistamine, on Different Types of Human Cancer Cell Viability

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AIM: Cancer is one of the diseases with the highest prevalence worldwide. Its incidence is increasing day by day. One of the leading causes of death worldwide is cancer. There are surgical and pharmacological treatment methods for cancer. However, more studies are needed to talk about a definitive and effective treatment. Therefore, research on anticancer agents continues. Recent studies have shown the anticancer activity of antihistamine group drugs. Studies on the effectiveness of Desloratadine, an important antihistamine, on cancer are very limited. Therefore, we aimed to examine the effects of Desloratadine on cell viability, DNA damage and apoptosis parameters of prostate (LNCaP), ovarian (A2780), colon (CaCo2) and breast (MCF-7) cancer cell lines.

METHODS: In this study, 1, 5, 25, 50 and 100 µM concentrations of the original raw material form of Desloratadine were applied to LNCaP, A2780, Caco2, MCF-7 cell lines. The effect of exposure to Desloratadine on cell viability was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay method. After determining the dose-dependent efficacy according to the MTT assay results, the inhibitory concentration 50 (LogIC50) value was evaluated in the Graphpad Prizm 8 program.

RESULTS: Desloratadine incubated with prostate (LNCaP), ovarian (A2780), colon (Caco2) and breast (MCF-7) cancer cells for 24 hours was found to cause significant decreases in cancer cell viability ($p<0.05$).

CONCLUSION: The results of this study show that Desloratadine has antitumor activity on LNCaP, A2780, CaCo2 and MCF-7 cells.
This study was supported by Inonu University Scientific Research Projects Unit with the project number TSA-2022-2975.

Keywords: Desloratadine, Cancer, LNCaP, A2780, Caco2, MCF-7.

PC-11

Evaluation of Lipocalin-2 and Metalloproteinase-9 Gene Expressions in Early-Stage Endometrial Cancer

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AIM: Increased lipocalin-2 (LCN-2) expression is observed in many cancer types. The aim of this study is to investigate the molecular mechanisms of LCN-2 in endometrial cancer and to evaluate the importance of biomarkers associated with these mechanisms in the diagnosis and treatment of endometrial cancer. We aimed to evaluate the gene expression of MMP-9, and LCN-2 in endometrial cancer, as matrix metalloproteinases (MMPs) and their physiological inhibitors play an important role in tumor cell invasion, angiogenesis, and growth.

METHODS: The study was conducted with 80 women who applied to İnönü University Turgut Özal Medical Center, Department of Obstetrics and Gynecology. 40 cancer cases diagnosed with endometrial cancer and 40 women who underwent surgery for benign endometrial pathology were included in the study. This study was carried out with the approval of İnönü University Malatya Clinical Research Ethics Committee dated 10.11.2021 and numbered 2021/197. Placental MMP-9 and LCN-2 gene expressions were analyzed by real-time polymerase chain reaction (RT-PCR). NGAL and GAPDH primers were synthesized and used as GAPDH housekeeping genes. Results were given as mean±SD.

RESULTS: Placenta MMP-9 gene levels were found to be statistically significantly higher ($p<0.0001$) in the patient group (0.57±0.11) compared to the control group (0.34±0.11). Similarly, a statistically significant ($p=0.0004$) increase was observed in placental LCN-2 gene expression in the patient group (0.74±0.08) compared to the control group (0.55±0.16).

CONCLUSION: Our results show that the expressions of both MMP-9 and LCN-2 genes are increased in the endometrial patient group compared to the control group. New approaches to suppress the synthesis of these genes, which trigger cancer aggressiveness and metastasis, will yield positive results in the treatment of endometrial cancer.

Financial Disclosure: This study was supported by İnönü University Scientific Research Projects Coordination Unit (Project code: TSA-2022-2776).

Keywords: Endometrial cancer, Gene therapy, Lipocalin-2, Metalloproteinase-9, Metastasis.

PC-12

Investigation of the Effect of Salvia Aytachii Vural & Adıgüzel on Blood Glucose Levels of Streptozotocin-Induced Diabetic Rats

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AIM: It is known that oxidative stress and inflammatory pathways play a role in the complications and pathophysiology of diabetes mellitus. Salvia aytachii (identified by Vural and Adıgüzel) is a perennial sage species belonging to the Lamiaceae family. This preliminary study was carried out to determine whether S. aytachii sage extract has a blood sugar lowering effect in streptozotocin-induced diabetes mellitus rats.

METHODS: 9 adult male Wistar-albino rats were used. Single dose 50 mg/kg of streptozotocin (STZ) was injected (i.p.) to induce diabetes. Blood glucose levels were measured 72 hours after the injection, and 250 mg/dL and above were considered diabetic, and rats were divided into 3 groups. Group I (STZ): STZ 50 mg/kg; Group II(SA100): STZ 50 mg/kg+100 mg/kg/day S. aytachii; Group III(SA200): STZ50 mg/kg+200 mg/kg/day S. aytachii. S. aytachii were administered by oral gavage for 8 days. OGTT (Oral Glucose Tolerance Test) test was performed on the first day of extract gavage and 24 hours before euthanasia. Statistics could not be made in the preliminary study because the number of animals was low.

RESULTS: At the 1st hour after the OGTT on the first day, the blood sugars of all 3 groups reached the highest level and then decreased. Especially at the 3rd hour, the blood glucose level of the SA100 group was lower than both the STZ group and the SA200 group. In the 8th day OGTT test, SA100 was more effective in reducing hyperglycemia compared to both groups. According to the OGTT results, the 2nd hour blood glucose of the STZ group increased by an average of 46 mg/dl compared to the 0th hour. Blood glucose level was decreased 34 mg/dl in SA100 group. SA200 group showed similarity to control.

CONCLUSION: Data suggest that S. aytachii extract at a dose of 100 mg/kg may reduce hyperglycemia in the STZ model.

Keywords: Diabetes, OGTT, Salvia aytachii, Streptozotocin.

PC-13

The Oxidant Effect of Topiramate, an Antiobesity Drug on the Liver

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AIM: Obesity is closely related to non-alcoholic fatty liver disease (NAFLD) and oxidative stress. Topiramate (TPM), an antiepileptic agent, is also used for obesity, while it is mainly known as an antioxidant some studies suggest the opposite. However, the effects of TPM on oxidant-antioxidant parameters in neither healthy liver nor NAFLD aren't known. Therefore, this study aimed to investigate the effects of TPM on both healthy and fatty liver.

METHODS: 24 Wistar albino rats were allocated into 4 groups as control (C), TPM, diet (D) and diet+TPM (DT). A high fat diet used for 6 weeks to develop NAFLD. Thereafter, TPM given for 3 weeks (100 mg/kg/day; po). Weekly weight and blood sugar follow-ups were taken; malondialdehyde (MDA), glutathione (GSH) levels and glutathione peroxidase (GPx) activity were measured. NAFLD activity score (NAS) was calculated by evaluating steatosis, infiltration and ballooning degeneration with H&E staining.

RESULTS: While diet increased both weight and blood sugar, TPM decreased them (C-D $p=0.037$; D-DT $p=0.003$). MDA levels increased in D, TPM and DT groups (C-TPM $p<0.0001$; C-D $p=0.035$), and GSH and GPx levels decreased (C-T $p<0.0001$ for GSH; C-D $p<0.0001$ & C-T $p=0.000$ & C-D $p<0.0001$ for GPx). In histological evaluations, diet-induced steatosis and ballooning didn't decrease after TPM administration (C-D steatosis $p=0.017$; ballooning $p=0.032$). Infiltration was higher only in the DT group compared to the control ($p=0.037$). Even though TPM alone caused some histological changes, there was no statistical significance in scoring.

CONCLUSION: Even though TPM elicits weight loss, it didn't reduce visceral steatosis and showed an oxidant effect in healthy liver tissue. Although the oxidant effect wasn't higher than that of TPM or diet alone in the DT group, histological damage was more apparent. Therefore, this study suggests that the use of TPM may be problematic especially in patients with liver disease.

Keywords: Nonalcoholic Fatty Liver Disease, Topiramate, Oxidative Stress.

PC-14

Peripheral Neuropeptide-S Administration Impairs Gastric Emptying and Motility through Nitrergic Pathway

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AIM: The expression of the neuropeptide-S (NPS) receptor (NPSR; formerly known as GPR154) has been demonstrated in gastrointestinal system (GIS) tissues suggesting that NPS/NPSR system may modulate digestive functions. This study aimed to investigate the action of peripheral exogenous NPS on (i) gastric motor functions and (ii) autonomic outflow.

METHODS: Effect of peripherally administrated NPS on gastric motility (GM) was assessed in anesthetized adult male Sprague Dawley rats through a pair of strain gage transducers sutured onto serosal surface of gastric antrum and pylorus. Spontaneous postprandial antro-pyloric contractions were recorded to assess the action of NPS (50 nmol, i.v.) or vehicle. Heart rate variability was analyzed to evaluate the effect of NPS on autonomic signalization. Additionally, effect of NPS (50 nmol, i.p.) on solid gastric emptying (GE) was measured in conscious and freely moving rats received vehicle, NPSR antagonist ML-154 (40 nmol, i.p.) or nitric oxide synthase (NOS) inhibitor L-NAME (10 mg/kg, i.p.). Data were analyzed by Mann-Whitney-U test.

RESULTS: Peripheral administration of NPS remarkably reduced the amplitudes of GM, while disturbing the coordination of antro-pyloric contractions suggesting that peripheral NPS could modulate GE rate. NPS did not affect sympathovagal balance indicates the peripheral NPC-induced gastroinhibitory action is solely local. Compared to the vehicle-injected control rats (66.91% ± 4.84, n=8), NPS significantly reduced solid GE (39.21% ±5.13, n=6, $p<0.05$). The NPC-induced delayed GE was significantly restored by preadministration of ML-154 (53.85% ± 5.10, n=8, $p<0.05$) and L-NAME (51.18% ±5.03, n=6, $p<0.05$).

CONCLUSION: The present findings indicate that peripheral NPS exerts an inhibitory action on gastric motor functions through mediation of NPSR and nitrergic pathway. Therefore, enteric NPSR appears to be a therapeutic target for treatment of GIS motility disorders.

Keywords: Neuropeptide-S, Gastric Emptying, Autonomic outflow, Gastric Motility, NPSR, Nitric Oxide.

PC-15

Dual inhibitory action of Neuropeptide-S on Gastric Smooth Muscle Contractility: The Role of Enteric Glial and Neuronal Cells

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AIM: Along with its specific receptor (NPSR), the novel brain peptide neuropeptide-S (NPS) is produced in alimentary tract. The present study aimed (i) to test NPS on contractility of isolated gastric tissues and (ii) elucidate the involvement of enteric neuronal and/or glial system in the action of NPS.

METHODS: Adult male Wistar rats were anesthetized and smooth muscle strips were then harvested from gastric corpus. After mucosa layer was removed, muscle strips were mounted in organ baths and mechanical activities were recorded via isometric force transducer connected to a data acquisition system. The effect of NPS (10-9 M-10-5 M) was tested on precontracted muscle strips elicited by bethanechol (10-5 M) or electric field stimulation (EFS; 4-16 Hz, 100 V, 10ms, 15 sec). Additionally, NPC-induced responses were monitored in the presence of NPSR antagonist ML-154 (10-6 M) or nitric oxide synthase (NOS) inhibitor L-NAME (10-4 M). Finally, NPS was applied after pretreatment of fluoroacetate (FA; 5x10-5 M) to exclude the contribution of enteric glial cells. Double immunofluorescence was performed in longitudinal muscle-myenteric plexus whole-mount preparations to determine whether NPSR is produced by myenteric neuronal and/or glial cells. All protocols were approved by Animal Ethical Committee of Akdeniz University (B.30.2.AKD.0.05.07.00/99). Non-parametric Mann Whitney-U test was used to determine the significance among the treatments.

RESULTS: Application of NPS caused a remarkable attenuation both in bethanechol- and EFS-induced contractions. The NPC-induced relaxation responses were significantly attenuated by ML-154 (43.2%, $p<0.01$, n=6) and L-NAME (38.2%, $p<0.01$, n=6). Pretreatment of FA blunted the action of NPS (34.1%, $p<0.05$, n=5). Double immunofluorescence analyses revealed colocalization of NPSR and NOS in myenteric neuronal cells; whereas NPSR is in close apposition with myenteric glial cells.

CONCLUSION: The present findings suggest the inhibitory action of NPS on gastric contractility which seems to be relevant with local neuronal and glial network.

Keywords: Neuropeptide-S, Isolated organ bath, Gastric corpus, Enteric glia, Myenteric plexus.

PC-16

Effect of KML29 and URB597 on Renal Ischemia Reperfusion Injury in Rats

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AIM: The endocannabinoid system is a physiological system that has been defined in the last 20-30 years. Anandamide and 2-arachidonoylglycerol (2-AG) have been identified as the most important endocannabinoid substances in the body. Anandamide is degraded by the fatty acid amide hydrolase (FAAH) enzyme, while 2-AG is degraded by the monoacylglycerol lipase (MAGL) enzyme. FAAH and MAGL enzymes are widely expressed in many tissues, including the kidney. Anandamide and 2-AG levels have been shown to be associated with ischemia-reperfusion (IR) injury. Although the protective properties of different FAAH and MAGL inhibitors against IR damage have been shown in various studies, the effect of MAGL inhibitor KML29 and FAAH inhibitor URB597 on kidney IR damage has not been investigated. In this study, we investigated the protective effect of MAGL inhibitor KML29 and FAAH inhibitor URB597 against kidney IR injury.

METHODS: 60 Sprague Dawley male rats were randomly divided into 6 groups (1. control 2. IR 3. KML29 4. KML29+IR 5. URB597 6. URB597+IR). The kidneys of the rats were bilaterally administered 45 minutes of ischemia and 24 hours of reperfusion. KML29 and URB597 were administered intraperitoneally to the treatment groups at the onset of ischemia. At the end of the experiment, histopathological damage and immunohistochemically caspase-3, tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β), interleukin-6 (IL-6) levels were measured in the kidney tissue.

RESULTS: Histopathological damage, caspase-3, TNF-α, IL-1β and IL-6 levels in the kidney tissue were decreased in the groups treated with KML29 and URB597 compared to the IR group ($P<0.05$).

CONCLUSION: In this study, we found the curative effect of MAGL and FAAH enzyme inhibitors KML29 and URB597 against kidney IR injury.

This work was supported by Yozgat Bozok University BAP (6602c-TF/20-353).

Keywords: Ischemia reperfusion injury, Kidney, KML29, URB597.

PC-17

A Novel Adipokine, Asprosin May Play a Key Function in Metabolism

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AIM: Impaired energy metabolism leads to many diseases, such as obesity, also may reduce the quality of life. Adipose tissue, one of the essential energy sources, is an effective organ in regulating energy metabolism. However, the function of asprosin, an adipokine secreted from white adipose tissue, in energy metabolism is still unknown. Therefore, our study was carried out to determine the effects of asprosin administration on some hormones related to energy metabolism in female rats.

METHODS: For experimental studies, 24 Sprague-Dawley female rats weighing 35 ± 2 g, 21 days old, were used and randomly divided into two groups as control and asprosin groups (n=12). Asprosin (500 ng/kg) was administered intraperitoneally to the animals in the asprosin group between 13.00-15.00 every day starting from the 21st day after birth. Similarly, physiological saline (1 ml/kg) was given to the control group. ELISA method was used to analyse ghrelin, GH (growth hormone), corticosterone, leptin and insulin hormones in serum from blood samples taken after decapitation at the end of the experiment. An autoanalyser was used for triglyceride. The experiment protocol was approved by Firat University Ethical Committee. The student's t-test was used for the analysis of the obtained data.

RESULTS: Asprosin administration significantly increased blood ghrelin, GH, corticosterone and glucose levels compared to the control group ($p<0.05$). However, no significant difference was observed in leptin, insulin and triglyceride levels.

CONCLUSION: The effects of long-term asprosin administration on appetite and energy metabolism in healthy female rats from the prepubertal phase were evaluated, and asprosin treatment significantly increased blood ghrelin, GH, corticosterone, and glucose levels in rats. Thus, asprosin may exert its effect on glucose metabolism by affecting some other hormones related to energy metabolism.

Acknowledgement: This study was supported by TUBITAK (project#220S744).

Keywords: Asprosin, Metabolic Hormones, Glucagon, Corticosterone, Ghrelin, Growth Hormone.

PC-19

The Effect of Cold on Angiogenesis in Cardiac Muscle of Hibernator Hamster and Non-hibernator Rats

Durmuş Deveci

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AIM: The fact that angiogenesis formation in the cardiac muscle of a hibernator and a non-hibernator group of mammals exposed to cold under the same conditions has not been studied in detail has led us to this study.

METHODS: Male Wistar rats (~270 g, n=6) and hibernator hamsters (~166 g) were divided into two groups. The control group was kept at room temperature (~21oC, n=6) and the cold exposed group (4oC) was kept in an environment with free access to food and water for 7 weeks. At the end of the experiment, the animals were sacrificed by overdose anesthesia and immediately afterwards their hearts were removed, weighed, and frozen in cold nitrogen gas. Sections taken with a cryostat were stained with alkaline phosphatase to count capillaries (CD, mm-2).

RESULTS: While the body weights did not change, it was observed that the ventricular weights increased significantly in both species. When looking at the ventricle as a whole, capillary density didn't change in rats, while capillarity significantly increased in the cold hamsters. When hamsters were compared with the control group, it was observed that the mean number of capillaries in both the whole ventricle muscle (2176±48 –2774±74, $P<0.001$, ANOVA) and in the epicardium, endocardium and papillary muscles increased significantly in those exposed to cold.

CONCLUSION: These results show; CD did not change in rats exposed to cold, while CD increased when both the entire ventricle (~27%) muscle of hamsters and the regions where it was studied in detail. Hypertrophy of the heart of hamsters and possibly prolonged exposure to cold resulted in vascular development as a preliminary to increase their oxygen carrying capacity before hibernation. In conclusion, the increase in heart rate, cold-induced other parameters and the increase in metabolic end-products, and ultimately the increase in angiogenic factors, may have stimulated angiogenesis.

Keywords: Angiogenesis, Heart, Hiernator, Nonhibernator, Cold Exposure.

PC-19

Asprosin Increases Sexual Instinct in Male Rats

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AIM: Asprosin is a novel discovered glucogenic adipokine synthesized from white adipose tissue during fasting. Also, asprosin has been shown to improve the sense of smell. In previous studies, it was revealed that the increase in oxytocin in the systemic circulation during ejaculation helps sperm release by stimulating contractions in the reproductive system, and therefore oxytocin has endocrine and paracrine roles on the reproductive system. Our aim was to reveal the effect of asprosin on sexual dysfunction in male rats for the first time with the non-contact erection (NCE) test.

METHODS: Control, sham, paroxetine, asprosin and paroxetine&asprosin groups (n=12) were randomly generated from 60 male Sprague-Dawley rats. The rats in the sham, asprosin and paroxetine&asprosin groups were implanted with a brain infusion kit and received a 28-day infusion (saline, asprosin 500 ng/kg). After NCE test, blood oxytocin levels were determined by ELISA method. One Way ANOVA test was used for the evaluation of the data.

RESULTS: As a result of the NCE test, there was no significant difference between the mean NCE numbers of the control, sham and paroxetine groups. However, when comparing the asprosin and the paroxetine&asprosin groups, the mean NCE numbers of the control ($p<0.05$), sham ($p<0.01$) and paroxetine ($p<0.01$) groups increment were observed. As the oxytocin values were examined, there was no significant difference between the control, sham and paroxetine groups. However, there was a significant increase in the asprosin and the paroxetine&asprosin groups compared to the control, sham and paroxetine groups ($p<0.01$).

CONCLUSION: Asprosin increased the number of NCEs by increasing the olfactory sensitivity, oxytocin level, and thus the sexual instinct in the sexual dysfunction model. We think that asprosin is a physiological mediator of penile erection and ejaculation by increasing oxytocin secretion in male reproduction.

Acknowledgement: This study was supported by TUBITAK (project no: 220S744).

Keywords: Asprosin, Scent, Oxytocin, Non-contact Erection Test.

PC-20

Asprosin May Play Important Roles in Spermatogenesis

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AIM: Asprosin, a fasting-related glucogenic hormone, is synthesized and secreted by white adipose tissue. It is known that asprosin can improve olfactory performance in rodents via OLFR-734. Moreover, odours play a vital role in sperm chemotaxis. Therefore, we aimed to investigate the effects of the asprosin hormone on male rat sperm.

METHODS: 21 days old, 24 Sprague-Dawley male rats (35g ± 2g) were randomly divided into two groups, control and asprosin (n=12). For ten weeks, the animals in the control group were given % 0,9 NaCl solution (1 ml/kg). The animals in the asprosin group were given asprosin (500 ng/kg) every day intraperitoneally. The right cauda epididymis of each animal was thoroughly dissected with the help of a scalpel in 1 ml of Tris buffer solution at 38°C, thus allowing the sperm to pass into this solution. Sperm motility, sperm concentration and proportions of morphologically abnormal sperm were determined from the obtained Tris buffer-sperm mixture. Testicular tissues fixed in Bouin's solution were washed with ethanol and then embedded in paraffin blocks. Sections of 5 µm thickness were taken from the paraffin blocks. Hematoxylin-Eosin and Masson's trichrome staining were applied to the preparations. Student t-test and Mann-Whitney U test were used for statistical analysis.

RESULTS: Chronic asprosin administration increased spermatozoon density ($p<0.001$). Asprosin did not affect the number of sperm tail anomalies and sperm motility. However, it decreased the number of sperm head anomalies ($p<0.01$). In the asprosin group, separations in the basement membranes of the seminiferous tubules were detected ($p<0.05$). Also, there was a decrease in seminiferous tubule diameters, and oedema (in the interstitial area) was detected ($p<0.05$).

CONCLUSION: Asprosin may affect sperm concentration directly and decrease head anomalies. As a result, asprosin may become a new treatment for oligozoospermia.
Acknowledgement: This study was supported by TUBITAK (project# 220S744).

Keywords: Asprosin, Sperm concentration, Morphology of sperm, Oligozoospermia.

PC-21

Protective Effect of L-carnitine on Liver, Kidney and Intestine Toxicity of Cadmium in Prepubertal Female Rats

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AIM: Cadmium is a toxic element with a half-life of more than 10 years that accumulates in tissues, especially in kidney and liver. Nickel-cadmium mixture taken into body with batteries, accumulators, cigarettes, water and food. Aim of this study was to investigate the effect of L-carnitine against cadmium-induced changes in liver, kidney and small intestine tissues in prepubertal female rats.

METHODS: 21-day-old female Wistar Albino rats were used in study. Control, CdCl2 (2mg/kg CdCl2 intraperitoneally), L-carnitine(LC) (300 mg/kg orally) and CdCl2+L-carnitine groups were formed. Sections were stained with H&E and Masson Trichrome. Histological scoring was performed in liver. Results were statistically evaluated with one-way analysis of variance using Graphpad Prism(Version9) program.

RESULTS: Necrosis, increase in connective tissue around the portal area, bile duct proliferation, sinusoidal congestion, increase in inflammatory cells were observed in the liver of the Cd group. Congestion in intertubular capillaries in kidneys, dilatation in tubules and also irregularity in villi structures in small intestines were detected. Structural changes in organs were found to be alleviated in cadmium group treated with L-carnitine. In inflammatory cell scoring of the liver, Cd with control(p:0.009), Cd with LC(p:0.004), in fibrosis scoring, Cd with control(p:0.002), Cd+LC with control(p:0.03), Cd with LC (p:0.006), also in necrosis scoring between control and Cd(p:0.001), LC and Cd(p:0.001), and between control and Cd(p:0.001), LC and Cd(p:0.02) groups in bile duct proliferation statistically significant increase was observed.

CONCLUSION: In conclusion medium-dose cadmium has toxic effects in liver, kidneys and small intestines of prepubertal female rats in subacute period, these effects are alleviated with L-carnitine. It is necessary to examine the effects of cadmium with advanced laboratory techniques to support the results.

Keywords: Cadmiyum, Intestine, Kidney, L-carnitine, Liver.

PC-22

The Effects of Irisin Hormone on Seminal Vesicle Fluid in Male Rats Administered Paroxetine

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AIM: It is known that antidepressants cause some negative effects in the reproductive system and especially in sperm parameters. It is stated that exercise is an effective factor on the transition to puberty, reproductive system and sexual dysfunction. Fructose, ions and molecules in the seminal vesicle fluid excreted the nutrition and mobility of the sperm. The aim of this study was to investigate the possible effect of irisin hormone on certain components of seminal vesicle fluid in male rats treated with paroxetine (antidepressant).

METHODS: In the study, 32 adult male Spraque Dawley rats were used. Rats were randomly divided into 4 groups as Control (C), irisin (I), paroxetine (P), and paroxetine+irisin (PI) (n=8). Paroxetine was given to the P and PI groups by oral gavage at a dose of 20mg/kg for 8 weeks. In the 4th week of the applications, irisin (100ng/kg/day) was administered to the I and PI groups by an osmotic pump as a subcutaneous infusion. At the end of the experiment, seminal vesicle fluids of sacrified rats were taken and analyzed (Advia 2400 analyzer and HPLC).

RESULTS: Calcium, magnesium and fructose levels were significantly decreased in the paroxetine group when compared to both the control group and irisin group, respectively ($p<0.05$). However, it was determined that fructose levels increased in paroxetine+irisin group compared to paroxetine group ($p<0.05$). In the irisin group, potassium and phosphorus levels were increased significantly compared to the control group ($p<0.05$).

CONCLUSION: The positive effect of irisin on fructose and some ion levels that decreased with paroxetine application suggests that this hormone may contribute to sperm vitality and motility. The increase of potassium and phosphorus levels caused by irisin hormone compared with the control group suggests that irisin has important effects on the reproductive system.

This work was supported by TUBITAK, Project No: 118S519.

Keywords: Paroxetin, Irisin, Seminal vesicle, Rat.

PC-23

Rotenone administration to the hypothalamus decreases the firing frequency of AgRP neurons without altering food intake in transgenic mice

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AIM: Agouti-related peptide (AgRP)-expressing neurons in the arcuate nucleus (ARC) of the hypothalamus are a major orexigenic population driving the food intake. Rotenone, which is a broad-spectrum pesticide and insecticide occurring in stems and seeds of several plants, is widely used in the mitochondrial energy dynamics research as it blocks and disrupts mitochondrial complex I and oxidative phosphorylation. In this study, we aimed to investigate the effect of intracranial rotenone administration to the ARC on food intake and electrophysiology of AgRP neurons.

METHODS: Male AgRP-IRES-Cre knock-in mice were infected with AAV-CAG-Flex-GFP virus tagging the AgRP neurons intracranially together with the injection of dimethyl sulfoxide (vehicle) or rotenone into hypothalamic ARC (posterior: -1.35 mm, lateral: ± 0.35 mm and vertical: 5.85 mm). Fifteen days after infection of the targeted neurons, animals were housed as single in caged and food intake was monitored for 25 days. At the end of experimental period, animals were sacrificed, and electrophysiological recordings were obtained ex vivo from the brain slices. Statistical analyses were conducted by using t-test.

RESULTS: Food intake of the animals after rotenone administration was not altered significantly, while the firing frequency of AgRP neurons were significantly reduced by intracranial rotenone administration ($p<0.05$).

CONCLUSION: Our results suggest that mitochondrial activity may be a regulatory factor for the hypothalamic AgRP neuronal activity in the regulation of energy metabolism.

Keywords: AgRP neurons, Electrophysiology, Food intake, Hypothalamus, Neuronal firing frequency, Rotenone.

PC-24

The Effect of Carotid Artery Cannulation And Femoral Artery Cannulation With The Cardiac Vagal Denervation On The Ischemia And Reperfusion Induced Arrhythmia

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AIM: Myocardial infarction in humans is one of the leading causes of sudden death. Experimental myocardial infarction has been produced by the occlusion of the left main coronary artery or other branches in animals. The carotid artery is cannulated to measure blood pressure in this model. Our hypothesis in this study is that the reflex sympathetic stimulation occurring in carotid artery cannulation may decrease arrhythmia. This study is aimed to investigate the effect of femoral artery cannulation, considered, to have low-baroreceptor stimulation and the effects of unilateral-vagal denervation on ischemia/reperfusion arrhythmias.

METHODS: In this study 58, 6-7 months-old male Sprague-Dawley rats were used; Four groups were produced. In the first group right carotid artery was cannulated and the right femoral artery was in the second. The left main coronary artery is ligated with the silk thread and reperfusion by loosening ligature to produce myocardial ischemia. In the others, vagal denervation is produced by cutting the N-Vagus. In sham operations, the nerve is just separated from the carotid artery. Blood pressure, heart rate, arrhythmia types, and durations were determined during ischemia/reperfusion. Statistical analyses were done by using one-way ANOVA with LCD posthoc test, one-tailed t-test, and Chi-squared test.

RESULTS: During ischemia/reperfusion, blood pressure and heart rate were lower in the femoral artery group than in the carotid artery group ($p<0,05$). The arrhythmia score was higher in the femoral group than in the carotid group ($p<0,01$). Unilateral-vagal denervation increased arrhythmias in the carotid group ($p<0.01$), but was ineffective in the femoral artery group.

CONCLUSION: The reflex sympathetic stimulation induced following carotid artery cannulation decreases the arrhythmia observed during ischemia and reperfusion. In the model of experimental myocardial infarction, femoral artery cannulation is more favorable to decrease the effect of baroreceptor stimulation on the ischemia-reperfusion-induced arrhythmias.

Keywords: Myocardial Ischemia, Reperfusion, Arrhythmia, Vagal Denervation, Baroreceptor

PC-25

Role of Erythrocytes from Pulmonary Arterial Hypertension Patients in ATP-mediated Vascular Relaxation Responses

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AIM: Pulmonary arterial hypertension (PAH) is characterized by increased pulmonary artery resistance. Although pathogenesis of PAH has not been fully elucidated, decreased NO bioavailability have shown to contribute the mechanism. Considering erythrocytes contain eNOS enzyme, the aim of this study was to examine ATP-mediated vascular relaxation responses in the presence of erythrocyte suspension obtained from healthy and PAH individuals and to reveal whether the erythrocyte eNOS enzyme has an effect on these responses.

METHODS: 8-10 weeks Wistar albino rats were used in our study (n=20). The study was approved by Akdeniz University Animal Experiments Local Ethics Committee. Blood samples were taken

from healthy individuals and PAH patients who applied to Akdeniz University Hospital Cardiology Clinic. Thoracic aorta segments obtained from healthy rats were placed in an organ bath, and vascular responses recorded in response to ATP (10-8-10-4 M) after precontraction in the presence of suspension containing erythrocytes from healthy individuals(n=8) and PAH(n=8) patients. Experimental protocols were repeated in the presence of non-selective eNOS inhibitor and eNOS substrate L-arginine. 'Repeated Measure 2-way ANOVA' test followed by Tukey post-hoc analysis was used. Statistical significance was $p<0.05$.

RESULTS: In the presence of erythrocytes obtained from healthy individuals, ATP mediated vasodilation responses were found to be significantly higher compared to Krebs solution ($p<0.001$). This increase in the vasodilation response was abolished in the presence of erythrocytes obtained from PAH patients ($p<0.001$). While L-arginine increased the vasodilation response, L-NAME abolished vasodilation responses in all groups.

CONCLUSION: Erythrocytes have incresead ATP-mediated relaxation responses in the aorta, and NO, derived from erythrocyte eNOS, may play an important role in this response. Due to decreased eNOS activity in PAH erythrocytes, increased vasodilation responses were abolished under PAH conditions. Therefore, reduction in erythrocyte-mediated NO may play a role in the pathogenesis of PAH, with increased vascular resistance.

Keywords: ATP, eNOS, Erythrocyte, Pulmonary arterial hypertension, Vasodilation.

PC-26

The Effect of Isatin on Cardiac Hemodynamic Function in Physically Active Rats

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AIM: Isatin (1H-indole-2,3-dione) has been proposed as an effective factor for muscle function and shows dose dependent different effects. This study aimed to determine the effects of low and high doses of isatin administration on cardiac hemodynamic changes, in an experimental model of voluntary physical activity.

METHODS: After ethical-approval, female rats were housed in cages with running-wheels. Control rats were kept in cages without a running-wheel during 28 days. In the last fourteen days of exercise, 20 mg/kg/day i.p isatin were given to the control-isatin-low-dose (CI-L) and physically active-isatin-low-dose (PAI-L) groups; 100 mg/kg/day i.p isatin were given to the control-isatin-high-dose (CI-H) and physically active-isatin-high-dose (PAI-H) groups; physiological saline was given to the control-vehicle (C-V) and PA-V groups. Daily physical-activity was recorded during isatin administration period. The hearts were extirpated and perfused ex vivo with a Krebs-Henseleit solution for 15 minutes. Left developed ventricular pressure, maximum and minimum rate changes of left ventricular pressure, and heart rate were recorded. Cyclic guanosine monophosphate (cGMP) levels were measured in the perfusate in groups.

RESULTS: In this study, no significant difference was shown in daily physical activity in the physically active groups in comparison to control group. Left ventricular developed pressure in the FAI-D group (69.75±17.49) were significantly lower than in both the KI-D (123.97±18.90) and FA-V (117.76±8.68) groups but similar to the FAI-Y (108.99±21.38) group ($p=0.017$ and $p=0.018$, $p=0.386$, respectively). Minimum rate changes of left ventricular pressure in the FAI-D group was found lower than CV, CI-L and CI-H groups ($p=0.036$, $p=0.016$ and $p=0.037$, respectively). Heart rate values were similar in groups. The cGMP level was higher in the PAI-H group than in the CI-H group ($p=0.001$).

CONCLUSION: The administration of isatin does not alter physical activity levels. However, isatin may have deleterious effect on ventricular contractility and relaxation function in female rats.

Keywords: Isatin, Heart, Isolated heart.

PC-27

Identification of Protein Interacting Partners of Na^+/K^+-ATPase Pump α1 Subunit by Proteomic and Bioinformatic Analysis in In-Vitro Hypoxic Cardiomyocytes

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AIM: Regular activity of Na^+/K^+-ATPase pump is essential for the function of the heart. Pump activity and subunits' expression decreases in ischemic heart diseases. However molecular mechanisms are not well known. This study aims to identify protein interacting partners of α1 NKA in in-vitro ischemic heart disease model by proteomic and bioinformatic analysis.

METHODS: H9c2 cardiomyocytes were used for the experiments. Cells were kept in 1% O_2+ 5% CO_2 for 24 hours as in-vitro ischemic heart model; normoxic cells were maintained in ~19% O_2 +5% CO_2. Immunoprecipitation experiments were performed by using same amounts of protein from total cell lysates; mixed with specific antibody against α1 NKA and Protein A Agarose beads. Each elution

fraction was analyzed by mass spectrometer three times, peptides identified at least in two replicates were included for the analysis. Proteome Discoverer 2.4 module was used for analysis of specific protein differences. Bioinformatic analysis was performed with Cytoscape software based on abundance ratio and coverage; functional enrichment analysis was performed with STRING DB. False discovery rate (FDR) was <0.05.

RESULTS: In normoxic and hypoxic cells α1 NKA non-specifically interacted with cell structure-cytoskeleton, muscle contraction-relaxation and focal adhesion associated proteins. Specifically, in hypoxic cells NKA β1, β3 interactions decreased compared to normoxic cells; proteins involved in glycolysis, cell metabolism such as GAPDH, LDH, PKM increased. Additionally, interactions with Hsp1,5, PDI, Hsp90aa1, Hsp47 related with endoplasmic reticulum (ER) homeostasis and ubiquitin-proteasome pathway increased.

CONCLUSION: This study identified new protein interacting partners of α1 NKA in cardiomyocytes that has not been previously reported. Specific interacting partners of α1 NKA in hypoxic cells emphasize that ER stress and ubiquitin-proteasome pathway may control cellular trafficking. Comprehensive analysis of α1 NKA interaction network is important for revealing molecular mechanisms in cardiovascular disease-hypoxia axis.
This study is supported by TÜBİTAK project no: 119S688.

Keywords: Cardiac ischemia, Hypoxia, Na^+/K^+-ATPase, Proteomic, Structural Bioinformatics.

PC-28

The Role of the Vascular Endothelial Layer in the Effect of Fospropofol on Vascular Tonus

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AIM: The tonus of vascular smooth muscles is among the factors controlling blood pressure via vascular resistance. As stabilisation and/or control of blood presure of the patients is crucial for tissue perfusion under general anaesthesia and sedation, the effect of the applied pharmacological agents on vascular smooth muscles is critical. In addition, endothelial damage and mal/dysfunction is frequent in patients with cardiovascular dieseases. On this background we aimed to investigate the effect of fospropofol, a water-soluble prodrug of propofol employed for induction of anesthesia and sedation.

METHODS: After the consent is obtained from the patients who will udergo coronary artery bypass graft (CABG) surgery, arterial rings (3mm) (n=15) were prepared from the discarded parts of the left internal mammary artery (LIMA) harvested for vascular greft. Full thickness endothelium-intact and mechanically destroyed endothelium-denuded rings were mounted in baths filled with Krebs' solution, gassed with 5% CO_2 and 95% O_2 at 37 °C. After equilibration for 60 min, maximum contraction response to KCl (120mM) for 10 minutes was recorded followed by cumulative dose-response curves with 10^{-7}-10^{-5} M fospropofol were obtained. The contraction response is presented as the percentage of KCl-induced contraction.

RESULTS: Both the endothelium-intact and endothelium-denuded rings were contracted when stimulated with KCl. Fospropofol decreased vascular tonus cumulatively at increasing doses in endothelium-intact rings, but not in endothelium-denuded rings. Vascular tone was different between the two groups at all doses applied ($p<0.05$).

CONCLUSION: Fospropofol, acts via endothelial transformation into the active substance propofol, can be preferred because of its lower risk of hypotension, especially in patients who are hypertensive, smoker, have valvular disease, and have a high risk of endothelial damage.

Keywords: Vascular tonus, Smooth muscle, Endothelium, Fospropofol.

PC-29

The role of opioid peptides in pulmonary edema

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AIM: Pulmonary edema (PE) is common in overdose of opioid derivatives. The mechanism of PO caused by opioids needs to be clarified. Disruption of alveolar sodium transport impairs fluid clearance (AFC), causing fluid accumulation in the alveolar space and PE. We tested whether opioids cause PE by disrupting AFC through epithelial sodium channels (ENaC).

METHODS: First we tested whether opioids could affect the AFC depending on the dose. An instillate containing 5% BSA and three different doses of morphine (0.1; 1; 10 µM) were instilled into the rats' lungs and bronchoalveolar lavage (BAL) samples were collected an hour later. AFC was calculated from the increase in the protein concentration in the BAL. Then the detection of opioid receptors involved with inhibition of AFC and whether their effect was on ENaC were tested. Antagonists specific to µ, κ and δ opioid receptors (10 µM) and/or amiloride (1mM), an ENaC inhibitor, were added to the instillate containing 10 µM morphine used in previous experiments. One-way ANOVA followed by Tukey test used for statistical analyses. $P< 0.05$ was accepted as significant.

RESULTS: AFC was significantly decreased in Amiloride and 10 µM Morphine groups compared to the control, 0.1 and 1 µM morphine groups ($p<0.05$). AFC was also decreased in all antagonist groups compared to the control and morphine groups ($p<0.05$).

Decrement of AFC in the δ opioid receptor antagonist group was even more than amiloride group (p<0.05). However, this decrease was not significant in the μ and κ opioid antagonist groups.

CONCLUSION: Opioids may cause edema by reducing AFC depending on the dose. However, this effect probably occurs via another pathway independent of sodium transport. On the other hand, μ and κ opioid antagonists disrupt AFC via ENaC and δ opioid receptors via another mechanism and contribute to the formation of edema.

Keywords: Opioid peptides, Pulmonary edema, Epithelial Na Channels.

PC-30

Muscle Damage and Oxidative Stress Responses Following a Single Bout of Downhill Running in Different Menstrual Cycle Phases

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AIM: This study aimed to investigate the muscle damage and oxidative stress (OS) responses after eccentric (downhill-running-DR) exercise in the follicular (FP) and luteal phases (LP).

METHODS: Thirteen women (age:20±2.0 years; menstrual cycle:27.9±2.4 days; VO2max:40.6±4.7 mL.kg-1.min-1) participated. The main exclusion criteria were using any hormone preparation or antioxidant supplement. Participants were tested in random order at different phases of the menstrual cycle (FF:6-13 days and LF:17-24 days) confirmed by hormone analysis. The tests were applied with an interval of 1-week. The 3-day-food consumption was analyzed. Active knee joint range of motion (AROM), active muscle soreness perception, and VO2max were determined on the 1st_day. 48h after the VO2max test, DR with –10% slope was performed at a speed coincide with 75% of their VO2max for 30min. Indirect muscle damage measurements and blood samples were obtained at rest (PRE) and immediately (POST), POST24h, POST48h, POST72h, and POST96h after the DR.

RESULTS: The estrogen (E2) and progesterone hormones were significantly higher in LP than FP; estrogen:148.8±69.7 vs. 45.6±17.9 pmol. L-1, progesterone:6.6±5.3 vs. 0.22±0.2 nmol.L-1, respectively (p≤0.001). There was no significant difference between phases in terms of vitamins A, C and E (p>0.05). No significant time-dependent changes within and between phases were observed in AROM (p>0.05). Muscle soreness didn't change in LP but significantly increased in FP (p<0.01). The oxidized protein carbonyl (PCO) values significantly increased following DR independently of the phases (p<0.05), reached the highest values at the POST96h (from 0.337±0.04 to 0.429±0.16 in FP; from 0.301±0.06 to 0.349±0.11 nmol/mg protein in LP). Moderate positive correlation was determined between %ΔE2 and %ΔPCO only in FP at the PRE-POST48h time interval (r=0.564; p=0.045).

CONCLUSION: The eccentric exercise protocol applied didn't cause serious muscle damage, but significantly increased the PCO concentration. The findings showed that the estrogen hormone doesn't prevent oxidative damage, but reduces the increase in oxidative stress.

Keywords: Muscle damage, Oxidative stress, Estrogen, Menstrual cycle, Eccentric Exercise.

PC-31

Investigation of Circadian Electrical Activity of Hypothalamic Arcuate Nucleus POMC Neurons in POMC-Cre Transgenic Mice

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AIM: Several hypothalamic neural circuits and peripheral hormones/factors play role in the regulation of energy homeostasis. Food intake is temporarily regulated by the brain during circadian cycle (~24 hour). Pro-opiomelancortin (POMC) neurons sense physiological energy state and regulate feeding, but the regulation of these neurons by the circadian rhythm is not fully elucidated. In our study, we aimed to investigate the daily electrical activity changes of these neurons using the electrophysiology patch clamp technique.

METHODS: Ten POMC-Cre transgenic mice were used in the study. Adeno-associated virus containing green fluorescent protein virus was intracranially injected into the arcuate nucleus of the hypothalamus to tag the arcuate POMC neurons and determine their electrical activity characteristics. After the injections, the mice were divided into two groups as fasted and fed. The mice fed with standard mouse chow and 16-hour fasted mice were decapitated at three different times of the day (10:00, 15:00, 18:00). Patch clamp technique was used to determine the electrophysiological changes in the POMC neuron activity. In addition, immunofluorescence staining was performed on brain sections obtained from mice using c-fos and POMC antibodies. Data were analysed using One-way ANOVA or Student's t-test, and p<0.05 was considered statistically significant.

RESULTS: When the electrical activity recordings taken from the brain slices at three different time points are compared, it is seen that the electrical activity of POMC neurons reaches the highest value at 15.00 hours and then decreases gradually (p<0.05). In addition, the activity of electrically altered POMC neurons was demonstrated by immunofluorescence staining as changes in c-fos activity.

CONCLUSION: In this study, daily electrical activity changes of POMC neurons were investigated ex-vivo for the first time with the patch clamp technique. These findings demonstrate that electrical activity of the POMC neurons required in the regulation of food intake change in a circadian-manner.

Keywords: Pro-opiomelancortin (POMC), Food intake, Circadian cycle, Electrophysiology, Immunofluorescence.

PC-32

Cerebellum and Oxidative Stress in Natural and Accelerated Aging Model

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AIM: Intracerebroventricular administration of galactose causes motor coordination deficiency by decreasing glutathione (GSH) level in the cerebellum. It has been shown that aging increases oxidative stress and Sirtuin 2 (Sirt2) expression in rat cerebellum tissue and Sirt2 inhibition has a protective effect in aging. In our study, we aimed to investigate the effect of AGK-2 administration, a specific Sirt2 inhibitor, on oxidative stress in an accelerated aging model with natural and D-galactose (D-GAL) administration.

METHODS: In the study, 7 groups were formed using 48 male rats of Wistar (W) and Sprague-Dawley (SD) species;1) Young-Control (3 months, n=6), 2) Young-AGK-2 (3 months, n=6), 3) Old-Control (22 months, n=6), 4) Old-AGK- 2 (22 months, n=6), 5) D-GAL (3 months, n=9), 6) Solvent+D-GAL (3 months, n=8), 7) Solvent+D-GAL+AGK- 2 (3 months, n=7). Control groups were given 4% DMSO+PBS, and experimental groups were given AGK-2 (10 µM/bw) subcutaneously (SC). For the accelerated aging model, D-galactose (150 mg/kg/day, SC) was administered for 10 weeks. Malondialdehyde (MDA) and GSH levels in cerebellum tissue were measured by spectrophotometric method. In the statistical analysis, one-way ANOVA (post-hoc LSD) was used to determine the differences between groups. The statistical significance level was set at $p<0.05$.

RESULTS: The D-GAL administration increased the cerebellum MDA level significantly compared to the young control group ($p<0.001$). In the D-GAL group, AGK-2 administration decreased the MDA levels and increased the GSH levels ($p=0.003$; $p=0.006$). D-GAL administration increased MDA levels more and decreased GSH levels significantly compared to aged rats ($p=0.006$; $p<0.001$). AGK-2 administration in natural aging was found to be more effective in increasing GSH levels compared to the accelerated aging model ($p<0.001$).

CONCLUSION: Both models compared increased oxidant stress in the cerebellum. AGK-2 application was found to be more effective than D-GAL on oxidant stress in natural aging.

Keywords: AGK-2, Accelerated aging, Cerebellum, D-galactose, Natural aging, Oxidative Stress.

PC-33

MOTS-c Levels in Acute Ischemic Stroke, Alzheimer's and Parkinson's Disease

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AIM: Mitochondial dysfunction is associated with the development of neurological diseases and neurodegeneration. Mitochondria produce various peptides that play a role in cellular functions and communication. MOTS-c (mitochondrial open reading frame of the 12S rRNA-c) is one of these peptides. In this study, we investigated whether plasma MOTS-c levels change in Alzheimer's-Parkinson's Disease (AD, PD) and acute ischemic stroke (AIS).

METHODS: Participants were divided into 4 groups as AD (n=32), PD (n=32), AIS (n=32) and control (n=30). Plasma MOTS-c levels of the participants were determined by the Enzyme-Linked ImmunoSorbent Assay (ELISA) method using commercial kits.

RESULTS: Plasma MOTS-c level was decreased in AIS and AD groups compared to control ($p<0.05$).

CONCLUSIONS: These results suggested that MOTS-c levels may have a role in the pathophysiology of AIS and AD. Further studies are required to understand the relationship of this peptide with AIS and AD. This work was supported by Yozgat Bozok University BAP (6602c-TF/19-345).

Keywords: MOTS-c, Acute ischemic stroke, Alzheimer's Disease, Parkinson's Disease.

PC-34

Right and Left-Hand Reaction Times to Regular and Irregular Auditory Stimuli in the Sympathetic Phase of Ultradian Rhythm in Right-handed Young People

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AIM: Ultradian rhythm can change the sympathetic and parasympathetic system activation by affecting cerebral lateralization. In this study, the reaction times (RTs) to regular and irregular auditory stimuli were tested and compared with resting period findings, by shifting of ultradian rhythm to sympathetic activation period.

METHODS: This study which received the necessary ethical permission was carried out with the voluntary participation of right

handed 23 female and 7 male students. After measuring participants' blood pressure, heart rate and nasal dominance in the resting period, right and left-hand RTs against auditory stimuli were measured. Sympathetic activation was provided by 5 minutes running of the participants on a treadmill after doubled the heart rate of the resting period. The sympathetic activation phase was confirmed by related tests and RT measurements were repeated. The data were analyzed using the paired t-test for time-dependent comparisons, as they have a normal distribution.

RESULTS: Right and left-hand RTs were shortened after sympathetic activation, compared to resting period in both stimulus types (P<0,05). In regular stimuli, although the right-hand RT is faster than the left, the difference is not significant neither in resting period nor in sympathetic activation. In irregular stimuli, the left-hand RT was faster than the right, both in the resting and sympathetic activation period (p<0,01).

CONCLUSION: In regular stimuli, the right hand may have an advantage over the left in the motor component of the reflex due to the learned automatic motor movement speed. However, in irregular stimuli, it was thought that the speed of the sensory component of the reflex, due to known speed of the right hemisphere in the process of processing non-verbal sounds increases with the involvement of attention also and the left hand shortens the RT to irregular stimuli in both resting and sympathetic processes.

Keywords: Ultradian Rhythm, Cerebral Lateralization, Nasal Cycle, Auditory Reaction Time, Sympathetic Activation, Acute Intense Exercise.

PC-35

Comparison the Respiratory Function Between Trained and Untrained 11-14 Aged Children

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AIM: This study aimed to compare various respiratory parameters between trained and untrained 11-14-aged girls and boys.

METHODS: A total of 253 students divided into 4 groups (trained boys: n=63; untrained boys: n=61; trained girls: n=65; untrained girls: n=64) participated. Subjects with any disease that could limit respiratory test performance were excluded. The study was approved by local Ethics committee and required permissions were obtained from National Education Directorate. All participants and their families were informed about the possible risks and benefits of the study and written consents were obtained. Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), peak expiratory flow (PEF), forced mid-expiratory flow rate (FEF25-75) and maximum voluntary ventilation (MVV) measurements were taken to determine the respiratory function using the Spirolab III device. During the spirometer measurements, the noses of the participants were closed with a latch, and the results were recorded by reading from the digital display of the spirometer. Spirometry measurements were taken when the participants were sitting. Statistical analysis was performed with One-way ANOVA, significance was accepted as p<0.05.

RESULTS: A statistically significant differences were determined for all respiration parameters (FVC, FEV1, PEF, FEF25-75% and MVV), except FEV1/FVC, between groups (p=0.005; p=0.004; p=0.021; p=0.016; p=0.004; respectively). Following the pairwise comparison (post hoc test: Tukey), the findings showed that the main difference was between trained and untrained girls. All examined variables were recorded significantly higher in thetrained-girls group. Such a difference was not found between the trained and untrained-boys groups.

CONCLUSION: Many studies have showed the positive effects of exercise programs on respiratory functions in individuals who have not yet completed their development. Although it's thought that growth may have an effect on respiratory parameters, research findings show that training has a positive effect on respiratory functions in girls who are disadvantaged in the society.

Keywords: Respiratory, Age group, Training, Sexes.

PC-36

Exam Anxiety Evaluation by Heart Rate Variability in University Students

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AIM: The majority of the previous research used questionnaire data to examine academic stress, however physiological reactions, such as changes in heart rate variability (HRV) is still relatively unexplored. Aim of this study is to evaluate the effects of exam stress on HRV parameters.

METHODS: 31 healthy volunteers (mean age:21±0.38) from medicine, nursing and physical therapy and rehabilitation departments participated to the study. Participants underwent 24-hour HRV recordings one day prior to and during written exams and another 24-hour recording during an exam-free day. Westside test anxiety scale, State Trait Anxiety Inventory 1-2, and Test Attitude Inventory were applied and anxiety scores were calculated. During the experiment, participants were assigned to two groups based on their anxiety scores: (i) participants with test anxiety (PTA+)(n=14) and (ii) participants without test anxiety (PTA-)(n=17). HRV parameters were compared between two

groups using the independent sample t-test and p<0,05 was considered statistically significant.

RESULTS: During the exam day, heart rate (HR), standard deviation of normal beats (SDNN), stress index, low-frequency and short-term detrended fluctuation analysis were significantly higher, root mean square of successive differences between regular heartbeats was significantly lower in PTA+ group (p<0,01) whereas total HRV did not differ between groups (p>0,05). However, during the exam free day only stress index was statistically higher in PTA+ group (p<0,05). In addition, participants in the PTA- group slept more and studied less before the exam compared to PTA+ group (p<0,05).

CONCLUSION: Being examined by others is a highly stressful event for the students. Our results showed that stress can alter heart rate variability parameters. Based on that finding we suggest that HRV may be a useful tool for evaluating the effects of stress and further investigation is required.
Keywords: Heart rate variability, test anxiety, Stress Detection.

PC-37

The Relationship Between Handgrip Strength and Fatigability with Cognitive Function in Individuals Over 65 Age

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AIM: The aim of the study is to investigate the relationship of handgrip strength and fatigability with cognitive functions in elderly individuals. The main hypothesis was determined as "There is a relationship between handgrip strength and fatigability with cognitive function in elderly individuals".

METHODS: The research was approved by Ethics Committee of Dr. Burhan Nalbantoğlu State Hospital (LBNDH) (06.01.2021-no. YTK.1.01). The sample consists of 89 individuals who applied to the LBNDH Physical Therapy and Rehabilitation Service between the ages 65-85 years. They also agreed to signed the informed consent form. Handgrip strength and fatigability was measured by BIOPAC USA Student Lab's and the cognitive functions were evaluated with Standardized Mini Mental Test (SMMT). Relationships between variables were examined by Pearson correlation and standard multiple regression analysis. The differences in cognitive functions were tested by Mann-Whitney and Kruskal Wallis tests.

RESULTS: As a result of the study, a moderate correlation was found between cognitive functions and grip strength (r= +0.31, p= 0.004). No statistically significant relationship was found between the fatigability index and cognitive functions. Cognitive functions were statistically significant according to gender (p=0.001), education (p=0.005) and employment status (p=0.000). Whole regression model was significant (F=12.236, p=0.001) and a unit change in the grip strength would cause an increase of 0.59 points in the SMMT score. In terms of education variable, the SMMT score of secondary, high school and university graduates was 2.28, 2.94 and 3.45 on average compare to primary school graduates. It can be said that 37% of the variance in the SMMT score is explained by the grip strength and education variable (R2=0.368).

CONCLUSION: Our results suggest that the decline in cognitive functions due to aging should be considered together with motor functions such as muscle strength and many individual variables.
Keywords: Handgrip Strength, Fatigability, Cognitive Function, Older Age.

PC-38

Effect of transcranial Direct Current Stimulation on Pain and Physical Functions in Individuals with Lumbar Spinal Stenosis: A Double-Blind Randomized Sham-controlled Study

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AIM: Lumbar spinal stenosis (LSS) is one of the most common reasons for spinal surgery in geriatric individuals. Transcranial Direct Current Stimulation (tDCS) is a neurophysiological treatment that was indicated to be efficacious in chronic pain syndromes. In this study, we aim to assess the efficacy of tDCS on pain and physical functions in individuals with LSS for the first time.

METHODS: In this double-blind study, 30 individuals with LSS (15 active, 15 sham) were administered 10 sessions of active/sham tDCS over the primary motor cortex consecutively on weekdays of 2 weeks. The pain was evaluated with the Visual Analogue Scale (VAS) and walking distance and duration were assessed with Self-Paced Walking Test before the first session, immediately after the last session and 3-months after the last session. Mann-Whitney U and Fisher's tests were utilized to assess baseline group differences and Friedman tests were utilized to assess treatment effect.

RESULTS: No baseline group differences were observed. Mean resting VAS (p<0,001), maximum resting VAS (p=0.001), mean VAS during walking (p<0.001) and maximum VAS during walking (p<0.001) were lower while symptomless walking duration after tDCS (p=0.004) and at 3-month follow-up (p=0.001), symptomless walking distance after tDCS (p=0.002), at 1-month follow-up (p<0.001) and at 3-month follow-up (p=0.006) were higher in the active tDCS group. No significant differences were found in other assessed variables.

CONCLUSION: Similar to other chronic pain syndromes, the present results highlight tDCS as a promising approach in LSS. Efficacy was considered to be achieved via both increased enkephaline release in descending pain modulatory pathway and increased emotional and cognitive control over pain. New studies evaluating treatment mechanisms using neuroimaging techniques are warranted.

Keywords: Lumbar Spinal Stenosis, Neurophysiology, Pain, Transcranial Direct Current Stimulation.

PC-39

Object Capturing with Photogrammetric Method and Use of Augmented Reality in Education of Heart Cycle and Heart Sounds

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AIM: Augmented reality have become widespread for medical education in recent years. Augmented reality provides the opportunity to add sound, 3D images and animations on the existing reality. The aim of this study is to create our own physiology educational material by preparing an application supported by augmented reality for better learning of the heart cycle and sounds.

METHODS: The "object capture" process was applied with Agisoft Metashape program to get 3D model of heart. For this, a sheep's heart was taken because of similarity to human heart. Totally 90 photographs were taken from 3 different axes by rotating 360 degrees on black background. The same process was repeated by taking frontal section to obtain the internal structure. After the photographs were converted into 3D models with the photogrammetric software program, they were brought into proportions suitable for human anatomy. Electrical activity, systole, diastole and blood filling were animated with Blender 3D animation program. Animation was converted to android application via Vuforia with Unity game engine. The program was activated by pointing the camera of the mobile device to the symbol placed in front of sternum of a real person. The heart animations were displayed inside the thorax. In addition to monitoring the movements simultaneously with heart sounds and Wigger diagram, theoretical information has been added to the application.

CONCLUSION: Distance education necessitated the inclusion of computer-assisted applications in education all over the world. In this sense, it is important that we can produce our own physiology education content in our country. This application, in which the heart cycle and heart sounds are presented with augmented reality, was made for this purpose. Further studies are planned in which students will be included after the addition of more detailed topics.

Keywords: Augmented Reality, Cardiac Cycling, Heart sounds, Object Capture, Simulation.

PC-40

Physiology Course Success Levels and Student Satisfaction in Face-to-Face and Distance Education Periods

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AIM: Face-to-face theoretical and applied education process is partly different than distant education. The aim of this study is to determine and compare the success level and satisfaction levels of the students who are engaged in Physiology course in face-to-face education and distance education period.

METHODS: The questionnaire data were collected from students in the Faculty of Health Sciences by the end of the term and after the permission of the ethics committee. The survey application was performed in classrooms and online as it was possible during the two periods with students in Physiology courses. All data was processed in digitized form.

RESULTS: 156 usual education period students and 133 distance education students completed the survey. Chi-square and unpaired t-tests were used for the given statistical analysis. Gender distribution ratios in both periods were found similar. There was a significant difference in terms of explaining the course objectives and using current tools/equipment ($p<0.05$), and those in the distance education period were found to be significantly higher in terms of the compatibility of the exam questions with the course content ($p<0.05$). The use of carefully prepared visual aids was found to be statistically higher in the distance education period ($p<0.05$). In terms of providing a suitable environment for asking questions freely, the rates in the distance education period were significantly higher ($p<0.01$). There was a significant difference between the two periods in terms of mean achievement (face-to-face: 70.26±9.71 and distance education: 73.17±9.19 SD).

CONCLUSION: Our results show that both education types can be applied successfully. Despite a difference in certain stages in the distant education process the learners' ability to obtain information and the level of success were not adversely affected. The supervised exam practice in the distance education period provides a testing environment under equal conditions.

Keywords: Face-to-face education, Distance education, Course Satisfaction Level.

PC-41

Determination of Nutritional Status and Protein-Energy Wasting in Patients with Diabetic Nephropathy

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AIM: The aim of this study is to evaluate the nutritional status of patients with stage 3 and 4 diabetic nephropathy (DN) and to explain the effect of DN stages on the prognosis of protein-energy wasting (PEW).

METHODS: Data from demographic characteristics, nutritional habits, anthropometric measurements, biochemical findings and food consumption records of 49 patients (25 DN stage 3; 24 DN stage 4) who were followed at Marmara University(M.U.) Pendik Training and Research Hospital, Department of Nephrology were collected. To evaluate the nutritional status of patients, Subjective

Global Assessment (SGA) screening tool and to determine the PEW, the criteria of the International Society of Renal Nutrition and Metabolism (ISRNM) were used. Statistical analysis was performed using SPSS 22.0 program. This study was approved by the M.U. Faculty of Medicine Clinical Research Ethics Committee (09.2018.800).

RESULTS: 56% of stage 3DN group and 66.7% of stage 4DN group have been diagnosed with diabetes for more than 15 years. Anthropometric measurements (total body weight,body muscle weight) were different between the groups($p<0.05$). The creatinine and microalbuminuria levels of the stage 3DN group were lower than the stage 4DN group; eGFR values were higher($p<0.05$). Energy (kcal/day), carbohydrate (g/day) and fat (g/day) intakes did not differ between the groups, while protein (g/kg) intakes were different($p<0.05$). In both groups, most of the patients had the SGA-A score (well-nourished). The PEW incidence was lower in the stage 3DN group ($p<0.05$). According to SGA data, the PEW incidence was found to be higher in patients with moderately-malnourished nutritional status (SGA-B score) ($p<0.05$).

CONCLUSION: In patients with stage 3 and 4DN, daily energy, protein and fat intakes are lower than recommended, but carbohydrate intakes are high. According to the ISRNM criteria, PEW is observed at a higher rate as the disease stage progresses.According to the SGA results, moderately-malnourished patients have a higher rate of PEW.
Keywords: Protein-Energy Wasting, Diabetic Nephropathy, Subjective Global Assessment, Diabetic Kidney Disease.

PC-42

Evaluation of Sarcopenia Parameters in Patients with Multiple Sclerosis

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AIM: Multiple Sclerosis (MS) is a central nervous system disease that causes muscle weakness, balance disorder and gait disturbance. Sarcopenia is a muscle disease with a decrease in muscle mass, muscle strength and function. The aim of our study is to reveal the sarcopenia parameters in MS patients living in the Turkish Republic of Northern Cyprus (TRNC) and how these parameters change with the “Expanded Disability Status Scale” (EDSS) score.

METHODS: 26 people participating in our study, who applied to the Physical Therapy Rehabilitation Department of Dr. Burhan Nalbantoğlu Hospital, were divided into 2 groups patients with MS (13) and without MS (13) matched for age and sex. The EDSS scores of patients with MS were between 1 and 5. Fatigue times, muscle strength, timed up and go (TUG) test and anthropometric measurements of all participants were recorded. Independent samples t test and Mann Whitney U test were used for statistical analysis. Statistical significance level was accepted as $p \leq 0.05$.

RESULTS: The TUG test results were significantly higher in the MS group (MS group 8,097 ± 3,029 sec, non-MS group= 5,565 ± 0,5994 sec, $p=0.002$), while the dominant (right hand) hand grip strength was also lower in the MS group compared with the non-MS group (MS group 17,64 ± 6,619 kg, non-MS group= 24,74 ± 6,983 kg, $p=0.0136$). Fatigue time recorded in the right ($p=0.009$) and left hands ($p=0.0185$) was significantly shorter in the MS group compared to the non-MS group. There was a statistically significant negative correlation between EDSS scores and right-hand fatigue time ($p=0.0265$).

CONCLUSION: The results of our study showed that sarcopenia criteria were getting worse in MS patients. We believe that MS patients can assist to retain their quality of life by exercising regularly and altering their diets before they get sarcopenic.
Keywords: MS, Sarcopenia, EDSS.

PC-43

The Effect of The Acetylcholinesterase Inhibitor Rivastigmine on the Pentylenetetrazole-Induced Kindling Model of Experimental Epilepsy

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AIM: Epilepsy is one of the most prevalent neurological diseases and has no known currently cure. The effects of acetylcholine mechanisms on epilepsy are contradictory in the literature and the effects of acetylcholinesterase inhibitor rivastigmine (RIVA) on epilepsy are unknown. The aim of this study is to investigate the effect of RIVA on the pentylenetetrazole (PTZ)-induced kindling model of experimental epilepsy.

METHODS: After the approval of the Animal Experiments Local Ethics Committee (OMU HADYEK 2022/35); firstly, Wistar albino rats weighing 245-265g were divided into four main groups: Sterile Physiological Saline (SPS)+PTZ (n=32) as a control group; 0.5mg/kg RIVA+PTZ (n=8); 1mg/kg RIVA+PTZ (n=8), and 2mg/kg RIVA+PTZ (n=8) to investigate the RIVA's effect on kindling: SPS; 0.5; 1, and 2mg/kg RIVA was administrated intraperitoneally 15 minutes before PTZ (35mg/kg) once every other day for 21 total injections. After the kindling procedure was completed, kindled animals in the control group were divided into four sub-groups considering the effects of these doses in the kindling process: SPS; 0.25; 0.5, and 1mg/kg RIVA, and these were delivered intraperitoneally 15 minutes before the acute PTZ (35mg/kg) application. The first myoclonic jerk latency and seizure scores (according to the Fischer & Kittner seizure scale) were observed and statistically analyzed with one-way ANOVA.

RESULTS: While the number of injections required for the kindling of the SPS+PTZ group was 14,12±1,02, the number of injections for

the 0.5mg/kg RIVA+PTZ group was 18,63±0,98 ($p<0.05$). 1 and 2mg/kg RIVA+PTZ groups were insignificant compared to the SPS+PTZ group. The first myoclonic jerk latency increased ($p<0.05$) and the seizure score decreased ($p<0.05$) only in the 0.5mg/kg RIVA+PTZ group compared to the SPS+PTZ group.

CONCLUSION: According to the data obtained, it was concluded that 0.5mg/kg dose of RIVA delayed the development of PTZ-induced kindling and showed anticonvulsant effect in kindled rats.

Keywords: Acetylcholinesterase, Epilepsy, Pentylenetetrazoel, Rivastigmine.

PC-44

Comparison of the Effects of Levetiracetam and Valproic Acid on Spike-Wave Discharges in WAG/Rij Rats with Genetic Absence Epilepsy

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AIM: Valproic acid (VPA) is the most commonly used drug in the treatment of absence epilepsy. However, VPA has serious side effects. In this study, we aimed to compare the effects of the second-generation antiepileptic drug levetiracetam (LEV) and VPA on absence seizures.

METHODS: All animal experimental procedures were approved by the OMU Animal Experiments Local Ethics Committee. 7-8 months old male WAG/Rij rats (n=21) were divided into three groups as control (sterile physiological saline; saline), LEV (100 mg/kg), and VPA (200 mg/kg). Tripolar electrodes were placed in all rats for electrocorticogram (ECoG) recording. One week after surgery, ECoG recordings of the rats were obtained for 3 hours before and after the first injection, and 24 hours after the 7th and 14th injections of the saline, LEV or VPA. One-way ANOVA and post-hoc Bonferroni test were used for comparisons between groups.

RESULTS: When the pre-injection periods were compared, there was no significant difference among groups. When the post-injection periods were compared, acutely administration of LEV and VPA significantly decreased the number of spike-wave discharges (SWDs) and the mean duration of SWDs compared to the control group ($p<0.001$). When the LEV and VPA records taken after acute, 7 days and 14 days injections were compared, there was no significant difference between the two groups in terms of the number of SWDs and the mean duration of SWDs ($p>0,05$).

CONCLUSIONS: While VPA is preferred as the first choice in the treatment of absence epilepsy, the use of LEV is more limited. Studies have shown that VPA has a higher hepatotoxic and hematologic side effects than LEV. From this point of view, we suggest that LEV may be the first choice in the treatment of absence epilepsy.

Keywords: Absence epilepsy, Electrocorticogram, Levetiracetam, Spike-wave Discharge, Valproic Acid.

PC-45

The Effects of Orexin Receptor Agonist Orexin-A in Wag/Rij Rats With Genetic Absence Epilepsy

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AIM: Orexin, a neuropeptide, regulates sleep-wake cycle, energy homeostasis, analgesia, learning, and memory. Orexins cause depolarization in neurons and increase in firing frequencies of neurons. In the present study, we aimed to investigate the effect of Orexin-A, an orexin receptor agonist, on absence epilepsy models of WAG/Rij rats.

METHODS: The rats were anesthetized with ketamine (90 mg/kg) and xylazine (10 mg/kg), and electrodes were placed after the coordinates were determined according to the bregma points of animals placed on the stereotaxic device. Records were taken from the operated animals after a 7-day recovery period. After 3 hours of baseline recording, 4, 8, and 16 µg doses of Orexin-A were injected intracerebroventricular (i.s.v.) and recorded for another 3 hours.

RESULTS: The number of spike-wave discharges (SWDs) ± SEM 140th minute value after DMSO was 66.6 ± 4.7 clusters/20 min. Orexin-A (4 µg, 1.33 µl) post-injection SWDs 140th minute value was 27.9 ± 8.7 and when compared with control group, it was observed that it decreased statistically from the 100th minute to the end of the recording ($p<0.05$). Orexin-A (8 µg, 2.66 µl) post-injection SWD's 140th-minute value was 17.9 ± 8.9 and post-injection from the 20th minute it was found to decrease the number of SWDs according to control group. Orexin-A (16 µg, 5.33 µl) post-injection SWDs 140th minute value 19.6 ± 6.0, and it was observed that the number of SWDs was statistically reduced compared to control group from the 20th minute after the injection.

CONCLUSION: Although the effect of 4 µg of Orexin-A has weak, all doses of Orexin-A showed anticonvulsant effects. Since there was no statistical difference in effect between 8 µg and 16 µg, the lower dose of 8 µg was accepted as the effective dose. The results of the study of Celli et al. support our study.

Keywords: Epilepsy, Orexin-A, {WAG/Rij} rat.

PC-46

The Effect of Magnesium Sulphate on Spike Wave Discharges in Genetic Absence Epileptic WAG/Rij Rats

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AIM: The aim of this study was to investigate the effect of acute administration of MgSO4 on spike-wave discharges (SWDs) in genetic absence epileptic rats.

METHODS: Male WAG/Rij rats (8-9 months old, 288±19 g, n=36) were randomly divided into six groups. Tripolar electrodes were placed on the skulls of all animals by stereotaxic device for electrocorticogram (ECoG) recording. After a seven-day recovery period, animals were attached to the data acquisition unit for electrophysiological recordings. After 1-hour of ECoG recording, the control group was given sterile physiological saline (the solvent of MgSO4). MgSO4 was administered intraperitoneally to other rats at the doses of 100, 200, 400, 600, and 800 mg/kg, and 2-hours of ECoG were obtained. The total number of SWDs for each group was compared statistically with the GraphPad Instant (v3.06) software in 15-minute periods. One-way ANOVA and after post-hoc Bonferroni tests were used for statistical analysis.

RESULTS: When the 1-hour period before the injections was evaluated, there was no significant difference among the groups. 800 mg/kg MgSO4 administered animals died. When 100 and 200 mg/kg MgSO4 administered, there was no significant difference in the total number of SWDs compared to the control group during 2 hours after injection ($p>0,05$). Administration of 400 mg/kg MgSO4 increased the total number of SWDs at the 30th and 45th minutes ($p<0.01$; $p<0.05$, respectively). When 600 mg/kg MgSO4 was administered, SWDs activity completely disappeared in the first 15 minutes ($p<0.001$), while an increase was detected in the total number of SWDs at 45., 60. and 75. minutes ($p<0.01$; $p<0.01$; $p<0.05$, respectively).

CONCLUSION: Studies have reported that MgSO4 activates GABA-A receptors, and also GABA-A receptor activation causes an increase in absence seizures. The present study suggests that MgSO4 increases absence seizures probably via GABA-A receptor activation.

Keywords: Absence epilepsy, Spike-wave discharge, Electrocorticogram, Magnesium Sulphate.

PC-47

N-Acetylcysteine Enhances the Antihyperalgesic Effect of Levetiracetam in The Posttraumatic Epilepsy Model

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AIM: Pain is an important clinical and social problem that affects the quality of life and has a cost to society in terms of economy and workforce. Traumatic brain injury (TBI) is one of the most common causes of chronic pain. In the present study, it was aimed to investigate the effects of the interaction of levetiracetam (LEV) and gabapentin (GBP) with n-acetylcysteine (NAC) on mechanical and thermal pain threshold in a model of subconvulsant pentylenetetrazole (PTZ) induced posttraumatic epilepsy (PTE).

METHODS: In the study, after 57 male Sprague-Dawley rats were divided into 7 groups, mild- TBI was performed to the animals except the control group (SBU HADYEK 2018-03/06). PTE model was created by applying subconvulsant dose of PTZ (30+15+15 mg/kg) intraperitoneally(i.p.) after mild-traumatic brain injury (TBI). Experimental groups with PTE were injected with 50 mg/kg/i.p. LEV, 100 mg/kg/i.p. GBP or the combination of these antiepileptic drugs with 100 mg/kg/i.p. NAC for 14 days. After drug administrations were completed, PTZ was given again in a subconvulsant dose and open field test for locomotor activity, dynamic and thermal plantar tests for pain threshold were applied respectively. Mann-Whitney U test was used after Kruskal-Wallis for statistical analysis.

RESULTS: According to the pain test findings, while the thermal pain threshold decreased significantly in the PTE group ($p<0.05$), it increased in the PTE+LEV, PTE+GBP and PTE+LEV+NAC groups ($p<0.05$, $p<0.001$ and $p<0.01$, respectively) was detected. While NAC alone was not effective on thermal pain threshold, it was determined that when applied together with LEV, it increased the thermal pain threshold more in the PTE+LEV+NAC group compared to LEV alone ($p<0.01$).

CONCLUSION: It was concluded that LEV and GBP exhibited antihyperalgesic effect in PTE model facilitated with PTZ, and NAC, which was used as an adjuvant, further strengthened the antihyperalgesic effect of LEV.

Keywords: Levetiracetam, N-acetylcysteine, Post-traumatic Epilepsy.

PC-48

Effects of Interaction of Clonazepam with Second-Line Antiepileptic Drugs Related to Treatment of Status Epilepticus on Motor and Cognitive Behaviors

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AIM: In the presented study, it was aimed to examine the effect of the interaction of clonazepam (CLZ), which is in the first step of the status epilepticus treatment algorithm, with the second-line antiepileptic drugs levetiracetam (LEV), lacosamide (LCM), valproic acid (VPA) and fosphenytoin (fPHT) on the motor and cognitive behaviors. In this way, it is aimed to the investigation of neuronal damage related to the status and polytherapy through motor and cognitive function tests in a possible polytherapy option.

METHODS: After the male Sprague-Dawley rats were divided into 6 groups (n=8), the experimental status epilepticus model induced by lithium/pilocarpine(5mEq/320mg/kg) was performed in 5 groups (SBU-HADYEK-2020-03/15). 30 minutes after the onset of seizures, groups with status epilepticus were given 1 mg/kg CLZ, 1+200 mg/kg CLZ+LEV, 1+50 mg/kg CLZ+LCM, 1+300 mg/kg CLZ+VPA or 1+100 mg/kg CLZ+fPHT. Physiological saline was applied to the control group. Between 15-18th days after the status and drug combination, open field tests for locomotor activity, rotarod for forced motor activity, radial arm maze for spatial memory, and passive avoidance tests for fear memory were performed, respectively. Mann-Whitney U test was used for statistical analysis of behavioral data.

RESULTS: While LCM and VPA applied together with CLZ did not have a negative effect on learning and memory performance, performance loss related to spatial memory was detected in the CLZ+fPHT group($p<0.05$). When compared with the control group, there was a decrease in forced motor functions in CLZ+VPA and CLZ+fPHT applied groups($p<0.01$). In addition, an increase in anxiety levels was detected in the CLZ+LCM and CLZ+VPA groups compared with the control group($p<0.05$).

CONCLUSION: It was observed that the combination of CLZ+LCM, one of the polytherapy options used to control experimental status epilepticus, did not adversely affect either motor functions or cognitive performance.

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Keywords: Antiepileptic, Klonazepam, Learning and memory, Motor behaviour, Status epilepticus.

PC-49

The Effects of GLP1 Analogue, Liraglutide on Mitochondrial Dynamics and Inflammation in the Rat Model of Lithium-Pilocarpine-Induced Temporal Lobe Epilepsy

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AIM: Mitochondrial stress and inflammation have been proposed to have central role in the pathophysiology of temporal lobe epilepsy (TLE). Anti-diabetic drugs, such as Glucagon-like peptide-1 receptor agonists (GLP-1RAs), have been shown to possess neuroprotective effects in several neurodegenerative diseases. The objective of the present study is to evaluate the possible effects of liraglutide, a GLP-1RA under phase-2 clinical studies, in rat model of TLE.

METHODS: Healthy control and epileptic Sprague Dawley adult (3 months old), male rats (200 – 300 g) treated with saline and liraglutide were used. TLE was formed by inducting status epilepticus (SE) with low-dose-repetitive-lithium chloride (3 mEq/kg)–pilocarpine hydrocholoride (20 mg/kg) intraperitoneal injections. Treatments were applied 3 hours after the SE to target the early stage of epileptogenesis. Intraperitoneal injections of liraglutide (300 µg/kg/day) or 0.9% saline (1 mg/kg/day) was continued for 3 days. Blood specimen and hippocampus tissues were collected. The changes in mitochondrial dysfunction (mitochondrial membrane potential, mitochondrial mass, and mitochondrial Sox levels) were evaluated in peripheral mononuclear blood cells. Inflammation markers (NRLP3, Caspase-1, IL-1β); antioxidant pathways (Nrf-2, phospho-Nrf-2) protein levels and mitochondrial dynamics were evaluated by western blot analysis on hippocampal tissues. Protocols have been approved by ACU-HADYEK (Approval number: HDK-2021-28). Statistical analysis was performed with GraphPad Prism 9. The mean value differences between the two groups were analyzed with student's t-test.

RESULTS: Liraglutide altered mitochondrial dynamics and antioxidant capacity in healthy control and TLE model of rats. Mitochondrial dynamics-related proteins showed that Pink1 and Mfn2 levels increased upon liraglutide treatment in the hippocampus of epileptic rats ($p<0.05$). Furthermore, inflammation markers such as NLRP3, IL-1β, and Caspase-1 decreased in liraglutide-treated epileptic rats ($p<0.001$; $p<0.05$; $p<0.0001$, respectively) whereas antioxidant phopsho-Nrf2 levels increased ($p<0.001$).

CONCLUSIONS: Our results suggest that liraglutide may provide potential beneficial effects for TLE through mitochondrial dynamics and anti-inflammatory pathways.

Keywords: Liraglutide, Epilepsy, Rat, Inflammation.

PC-50

TRPV1 Agonist Capsaicin Reduces Neurodegeneration in Alzheimer's Disease Model Induced with Okadaic Acid

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AIM: In recent years, it has been shown that Transient Receptor Potential Vanilloid 1 (TRPV1) channels, which are widely distributed in the central nervous system, play a role in many physiological and pathological processes in the nervous system. In this study, we investigated the effects of TRPV1 agonist capsaicin (CAP) and antagonist capsazepine (CPZ) in Alzheimer's Disease model induced with okadaic acid (OKA).

METHODS: 60 Sprague Dawley male rats were randomly divided into 6 groups. 1. Control group: no application was made. 2. Sham group: 5 µl of artificial cerebrospinal fluid (aCSF) was injected as bilateral ICV. 3. OKA group: 200 ng OKA dissolved in 5 µl aCSF was injected as bilateral ICV. 4. OKA+CAP group: Unlike the OKA group, 1mg/kg CAP injection was performed intraperitoneally for 13 days. 5. OKA+CPZ group: Unlike the OKA group, 1mg/kg CPZ injection was performed intraperitoneally for 13 days. 6. OKA+CAP+CPZ group: Unlike the OKA group, 1mg/kg CAP and CPZ injections were performed intraperitoneally for 13 days. Immunohistochemically, caspase-3, phosphorylated tau (ser396), amyloid beta, phosphorylated glycogen synthase kinase-3 beta-ser-9 (GSK3β-ser9), tumor necrosis factor alpha (TNF-α), interleukin-1 beta (IL-1β) levels were examined from the cortex and hippocampus regions of the brain. At the same time, histopathological examination was performed from the cortex and hippocampus regions.

RESULTS: CAP application decreased caspase-3, phosphorylated tau (ser396), amyloid beta, GSK3β-ser9, TNF-α, IL-1β levels, which increased with ICV OKA application in cortex and hippocampus ($P<0.05$). At the same time, CAP application reduced histopathological damage in the cortex and hippocampus ($P<0.05$).

CONCLUSIONS: In this study, we found that the administration of TRPV1 agonist CAP reduced neurodegeneration and neuroinflammation in the Alzheimer's Disease model induced by OKA.

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Keywords: Alzheimer's Disease, Okadaic Acid, Transient Receptor Potential Vanilloid 1, Capsaicin, Capsazepine.

PC-51

Effect of Forced Nicotine on Oxytocin and Vasopressine Levels in Striatum and Hippocampus in Nicotine Preferring Rat Lines

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AIM: This study aimed to determine the differences in hippocampal and striatal oxytocin and arginine-vasopressin (AVP) levels in Nicotine-preferring (NP) (male/female) and control (male/female) animals during chronic oral nicotine exposure.

METHODS: NP line is developed by selective breeding at Ege University Center for Research on Laboratory Animals. This study is a continuation project of previous project (TDK-2020-21454). Same animals were used in both projects; there were 4 groups (n=10/group): Control Male (CM), Control Female (CF), NP Male (NPM), NP Female (NPF). All groups received forced nicotine administration in drinking water for 4 weeks. In the previous project, we analyzed differences in empathy-like behavior of NP and control groups during baseline and chronic nicotine exposure. In this project, animals were decapitated following behavioral testing; striatum and hippocampus were dissected and stored at -80°C. Oxytocin and AVP levels in samples were measured by ELISA. One-way ANOVA and post-hoc Tukey tests were performed using SPSS for statistical analysis.

RESULTS: There were significant differences between the groups ($p<0.001$). Hippocampal oxytocin levels were higher in NPM compared to CM ($p=0.002$), in NPF compared to CF ($p=0.05$), in NPM compared to NPF ($p=0.05$), and in NPM compared to CF ($p<0.001$). Striatal oxytocin levels in NP were lower than controls ($p=0.05$). Striatal oxytocin levels in NPF were lower than CM ($p=0.02$). Hippocampal AVP levels in NP were higher than controls ($p=0.005$). Hippocampal AVP levels in NPM were higher than CF ($p=0.02$). Striatal AVP levels were not different between groups.

CONCLUSION: Alterations in brain oxytocin and AVP levels of NP animals may underlie the changes observed in empathy-like and social behavior of these animals. These differences may contribute to the susceptibility of NP rats to nicotine addiction.

Supported by Ege University, Scientific Research Projects Commission (TYL-2020-22397).

Keywords: Addiction, Hippocampus, Nicotine, Oxytocin, Striatum, Vasopressin.

PC-52

Interaction of Nitrergic and Cholinergic Systems on Anxiety and Depression-Like Behaviors in Diabetic Rats with Streptozotocin

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AIM: This study was planned to evaluate the effects of donapezil alone or through nitric oxide on anxiety- and depression-like behaviors in streptozotocin-induced diabetic rats.

METHODS: A total of 30 Wistar-rats were used in 5 groups in the study. Experimental diabetes was induced using streptozotocin (60 mg/kg). 30-days after induction, one group left as diabetic-control, while the other three-groups received 4 mg/kg donepezil for 20-days. One of the groups receiving Donapezil received 20 mg/kg L-NAME for 20-days, and the other 40 mg/kg i.p., L-arginine for 20-days. The open-field test (OF) was used to evaluate anxiety-like behaviors and forced-swimming test (FST) was used to evaluate depression-like behaviors. Obtained data were analyzed with one-way ANOVA and Tukey test. $p<0.05$ was considered significant.

RESULTS: The immobility times of all diabetic rats in the FST were found to be significantly higher than the control-group ($p<0.05$). While L-Arginine increased the immobility time ($p<0.05$), the effect of L-NAME was not statistically significant ($p>0.05$). In the OF, the time spent in the center and exploratory behavior of all diabetic rats were found to be lower than the control-group ($p<0.05$). However, there was no difference between the rats in the L-NAME and L-Arginine groups and the rats in the donepezil group ($p>0.05$). There was no significant difference between the groups in the number of line crossings in which locomotor activity was evaluated ($p>0.05$).

CONCLUSION: Rats induced diabetes by streptozotocin had increased levels of anxiety as assessed by OF and depression as assessed by FST. In our study, while donepezil did not have an effect on these parameters, an increase in depression-like behaviors was detected in the group receiving concomitant L-arginine. These findings may suggest that cholinergic and nitrergic systems may interact on depression-like behaviors in diabetic rats.

Keywords: Diabetes, Depression, Anxiety, Acetylcholinesterase, Nitric Oxide.

PC-53

The Relationship Between Parkinson's Disease and TRP Channels; Possible Therapeutic Effects of Carvacrol

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AIM: Parkinson's disease (PD) is a neurodegenerative disease characterized by degeneration of dopaminergic neurons. Carvacrol (CA) modulates Transient Receptor Potential (TRP) cation channels. In our study, the effects of CA on TRPC1 in dopaminergic neurons and TRPA1 in astrocytes and the role of these channels in PD were investigated in the model of Parkinson's induced by 6-hydroxydopamine (6-OHDA).

METHODS: Experiments were performed in 4 groups of male Sprague-Dawley rats. Groups; 1) Sham (Placebo Surgery), 2) 6-OHDA, 3) 6-OHDA+Vehicle (DMSO=Dimethyl sulfoxide), 4) 6-OHDA + CA (10 mg/kg). TRPC1 and TRPA1 immunoreactivity in brain tissue sections of 8 animals of each group was determined by immunohistochemical staining method. The SNpc and striatal areas of the brains of the other 8 animals in the groups were used for molecular studies.

RESULTS: the immunohistochemical analysis; there was a decrease in the number of TRPC1(+) dopaminergic neurons due to the Parkinson. This decrease in cell number was also observed in the DMSO and CA groups. However, dopaminergic neurons in the preparations of the CA group had a healthier appearance due to the neuroprotective effect of CA, and their cell integrity was preserved compared to the cells in the DMSO group. CA had no significant effect on gene expression and protein levels of dopaminergic neuron TRPC1 channels. While the number of TRPA1(+) cells in astrocytes decreased in the CA treatment group compared to the control group, gene expression levels increased significantly. As in TRPC1(+) dopaminergic cells, it was observed that cellular integrity was preserved by CA in treatment group astrocytes.

CONCLUSION: CA showed neuroprotective effect in the presented Parkinson animal model, TRPC1 is inhibited by CA in dopaminergic cells İn addition, CA activates TRPA1 channels, because of increased channel expression in astrocytes may be useful in neuron survival by triggering the neuromodulatory effects.

Keywords: Parkinson's Disease, TRP channels, Carvacrol, Neuroprotection.

PC-54

The Effect of Ginkgo Biloba on Hyperalgesia Induced by REM Sleep Deprivation

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AIM: Ginkgo-biloba extract contains ginkgo-flavone glycosides and has free-radical scavengers and platelet activating factor antagonist activity. Recent studies have also shown effects in modulation of pain. In this study, the antinociceptive effect of Ginkgo-Biloba was investigated in a model of REM sleep deprivation-induced hyperalgesia.

METHODS: After ethical approval, 40 female Wistar-Albino rats, 8-12 weeks old, were divided into five groups of eight animals each (PLS, placebo; GB30, Ginkgo-Biloba 30mg/kg; GB100, Ginkgo-Biloba 100mg/kg; GB300, Ginkgo-Biloba 300mg/kg and FLP40, flurbiprofen 40mg/kg). Flurbiprofen was added as a positive control. All groups were included in the 72-hour REM sleep-deprivation protocol with the modified multiple-pot technique and pain assessment was performed with hot-plate and tail-flick tests at the beginning, end and after drug administration of the sleep-deprivation period. Mean values for pain assessment were produced from triple-measurements and expressed in seconds. Drugs and placebo were administered by single-dose gastric-gavage after measurements after sleep-deprivation. In order to compare pre and post sleep-deprivation pain measurements between groups, the change from the first test to the post-test was calculated for each condition. Kolmogorov-Smirnov was used to determine the normal distribution of the groups, and one-way ANOVA and Post-hoc Tukey were used to determine the difference between groups in pain measurements.

RESULTS: Sleep-deprivation caused hyperalgesia in all groups. (Hot-plate time decreased at the stated rates: PLS=60.8%, GB30=65.8%, GB100=65.9%, GB300=67.5%, FLP40=70.8% ($p<0.05$); Decreases in tail-flick test: PLS=67.2%, GB30=67.7%, GB100=58%, GB300=71.4%, FLP40=64.6% ($p<0.05$). Ginkgo-biloba showed analgesic effect at all doses (Hot-plate:GB30=30%, GB100=28%, Tail-flick:GB30=24%, GB100=26.9%) ($p<0.05$). Especially at a dose of 300mg/kg, its effect was closest to flurbiprofen in the tail-flick test. (Hot-plate: GB300=43.5%, FLP40=94.8%, tail-flick GB300=43.7%, FLP40=48.5%) ($p<0.05$).

CONCLUSION: Ginkgo Biloba reduces the decrease in pain threshold due to sleep-deprivation and has an antinociceptive effect. We think that Ginkgo-Biloba has the potential to be added to the treatment in painful-symptoms associated with sleep-disorders.

Keywords: REM sleep deprivation, Hyperalgesia, Ginkgo Biloba.

PC-55

Effect of Ethyl Pyruvate on Sleep Deprivation-Induced Cognitive Dysfunction in Young Female Rats

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AIM: REM sleep deprivation (SD) affects various physiological processes such as learning and memory. The effect of ethyl pyruvate on cognitive functions has been studied in a limited number of studies and has not been investigated on sleep deprivation before.Therefore, the aim of our study was to investigate the effects of ethyl pyruvate treatment on learning and memory in female rats undergoing REMSD for 72 hours.

METHODS: 25 female Wistar albino rats aged 6months were divided into four different groups(7 sleep deprived rats, the others 6 rats).Control,wide platform(WP),SD,SD groups treated with ethyl pyruvate.WP group rats were placed in a tank with a large platform(13cm diameter) as environmental control of sleep deprivation.The rats in the WP group, which could sleep without falling into the water, remained in the tank for 72 hours.REMSD was created using the multi-platform(6.5cm diameter) method for 72 hours.Ethyl pyruvate treatment(50 mg/kg) was administered as a single daily dose(i.p) for 5 days.The Morris water maze(MWM) test was used to evaluate the effects of ethyl pyruvate on learning and memory.At the end of the experiment, the hippocampus and brain tissues of the rats were taken.

RESULTS: The results showed that the effects of SD on memory assessed by the MWM test were prolonged in the daily time to find the platform and shortened in the time spent in the platform area on the last day($p<0.05$).It also proved that SD increased MDA and nitrate levels in brain tissue and AchE activity in hippocampus tissue($p<0.05$).When the ethyl pyruvate treatment group was compared with the SD group, nitrate levels were found to be decreased($p<0.05$).Finally, it was found that there was no difference between the groups in terms of GSH and glycogen levels.

CONCLUSION: Our results show that ethyl pyruvate administered after 72 hours of REMSD has no effect on learning and memory in young female rats.

Keywords: Ethyl Pyruvate, Learning and Memory, REM Sleep Deprivation.

PC-56

The Effect of Morphine Dependence and Morphine Withdrawal on Neuritin and Some Markers of Neurogenesis in the Rat Hippocampus

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AIM: Neuritin, which was first identified in the rat hippocampal dentate gyrus, is known as the candidate plasticity gene 15. The effects of neuritin on neurite development, dendritic branching, synaptic activity and neuronal survival in the nervous system in some neurodegenerative diseases and psychopathologies have been determined. However, there is no research finding on how neuritin expression is affected in processes related to opioid addiction. In this study, we aimed to determine the neurogenesis status and neuritin gene expression level in the hippocampus in morphine-dependent and naloxone administered rats.

METHODS: Morphine addiction was constituted by subcutaneously administering morphine to adult male rats for 7 days in the study. In the morphine withdrawal group, in addition to morphine administration, naloxone was injected 1.5 hours after the last injection. Hippocampus tissues were removed from all animals. Neuritin and neurogenesis biomarkers such as doublecortin, brain-derived neurotrophic factor, NeuN and MASH1 gene expression levels were evaluated by using quantitative RT-PCR. One-way ANOVA was used for statistical evaluation.

RESULTS: The expression level of hippocampal neuritin in the morphine addiction group was significantly lower compared to control ($p<0.05$). Neuritin expression in naloxone group significantly increased compared to the addiction group ($p<0.001$). Brain derived neurotrophic factor, doublecortin and NeuN expression levels were significantly higher in the morphine withdrawal group compared to the addiction group ($p<0.05$, $p<0.001$ and $p<0.05$, respectively). There was no significant difference in MASH1 expression level.

CONCLUSION: The results of this study show that administration of naloxone significantly increases the return of hippocampal neurogenesis biomarkers in morphine-dependent rats. The fact that morphine addiction lowers the level of neuritin in the hippocampus and that morphine withdrawal significantly increases its expression suggests that neuritin may play a mediating role in the opioidergic modulation of neurogenesis and neuroplasticity in the hippocampal dentate gyrus.

Keywords: Hippocampus, Morphine addiction, Neuritin, Neurogenesis, Rat.

PC-57

On the role of cell death mechanisms in the pathophysiology of neuropathic pain: An in-silico study

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AIM: Neuropathic pain is caused by damage or injury to nerves that transfer information between the peripheral structures and spinal cord-brain. It is common and receives high research interest. However, the cellular mechanism of neuropathic pain has not been clarified yet. In addition to clinical studies, recent evidence indicates expectations from in silico analysis. Cell death and autophagy are recently discovered mechanisms involved. This study aimed to detect possible pathophysiological factors for neuropathic pain, by using bioinformatics tools, in the neuropathic pain rat model by Chung-method spinal nerve ligation.

METHODS: GSE38038 dataset obtained from the Gene Expression Omnibus database was re-analyzed in the R program. In the dataset, total RNA samples in dorsal root ganglia tissues from the neuropathic group (n=4) and control group (n=4) were recruited. Mann-Whitney U test and Benjamini-Hochberg correction analysis were performed in the data analysis, and adjusted p values <0.05 were accepted as significant.

RESULTS: Gene expression levels indicated that autophagy-related proteins (ATG4B, ATG7,12*), sequestosome-1 (SQSTM1), lysosomal membrane glycoprotein-2 (LAMP2*) [responsible for autophagy]; caspases (CASP1,3-8*, CASP9), B-cell leukemia-2 (BCL2), Bcl2-associated X protein (BAX*), tumor protein p53 (TP53*), somatic cytochrome C (CYCS), neuroblastoma ras oncongene (NRAS*) [for apoptosis]; tumor necrosis factor related genes (TNF, TNFRSF1A-B,11B,12A*, TNFSF13*), interleukins (IL1B,6*), toll-like receptor 4 (TLR4*) [for necrosis] and androgen receptor (AR), granzyme-B (GZMB*), cortactin (CTTN*) [for entosis] genes were up-* and down- regulated ($p<0.05$) in neuropathic group, compared with control group.

CONCLUSION: Results from this in silico preliminary study indicate imbalances in the expression levels (up- and down-regulation) of genes known to be involved in many cell death processes, implicating the involvement of impaired autophagic, apoptotic, necrotic, and entotic signaling in the pathophysiological mechanisms of neuropathic pain.

Keywords: Neuropathic pain, Autophagy, Apoptosis, Necrosis, Entosis, In silico analysis.

PC-58

Effects of Meteorin-Like Protein on Pain in an Experimental Diabetes Model

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AIM: Diabetes; It is a chronic disease that develops as a result of insufficiency or ineffectiveness of insulin secretion from the pancreas or disorders in the insulin molecule and progresses with neuropathic pain.Meteorin-like protein (METRNL), known to have neuroprotective effects, is thought to improve insulin resistance and be therapeutic for metabolic syndrome and type 2 diabetes.In addition, the role of METRNL in mitochondrial biogenesis shows that it may be effective on neuropathic pain, but its effectiveness is not fully known.Therefore, in our planned study, we aimed to investigate the effect of METRNL on pain threshold in an experimental diabetes model.

METHODS: In the study using 35 Balb-C mice, the animals were randomly divided into 5 groups (n=7).Diabetes model was created by administering a single dose of streptozotocin (200 mg/kg) to all groups by intraperitoneal (ip) injection.Pain threshold values were recorded with hot-cold plate and tail-flick tests of animals before and after diabetes was established.Animals in the control group were treated with ip solvent, while the other groups were administered 0.1, 1, 4 and 10 mg/kg METRNL,respectively.Tests were repeated after drug administration.In statistical evaluation,one-way analysis of variance with IBM SPSS 24 package program and post-hoc Dunnet's test following this analysis were used to reveal time-dependent differences between groups.

RESULTS: It was observed that the duration of stay in the hot plate tests of the animals in the METRNL groups increased (mean. 7 sec delay), the total number of foot lifts in the tail-flick test decreased (mean. 13) and the pain thresholds increased compared to the control group. This difference was determined to be significant at all doses of METRNL($p<0.05$).

CONCLUSION: The results of this study indicate that the tested METRNL may have analgesic activity on diabetic neuropathic pain.
Acknowledgment: This study was supported by the Scientific Research Projects Unit of Inonu University with the project numbered TSG-2020-2088.

Keywords: Pain, Diabetes, METRNL, Neuropathy.

PC-59

Investigation of the Effects of Meteorin-Like Protein in a Model of Neuropathy Induced by Sciatic Nerve Injury

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AIM: Neuropathic pain,which mechanisms such as mitochondrial dysfunction,oxidative stress,apoptosis and calcium signaling play a role in its pathogenesis,is a clinical finding that may develop due to nervous system lesions or disorders.It is stated that meteorin-like protein(METRNL) improves intracellular calcium signaling,lipid-induced inflammation and insulin resistance.We aimed to investigate the efficacy of METRNL,which also plays a role in mitochondrial biogenesis,but whose effectiveness is not fully known,on neuropathic pain and motor behavior induced by sciatic nerve damage.

METHODS: In the study conducted on 35 Balb-C mice, with the approval of Inonu University Animal Experiments Local Ethics Committee (dated 02.04.2020, decision number 2022/5-6, registration number 9742 HAYBIS), the animals were control, METRNL (0.1 mg/kg,1 mg/kg,4 mg/kg and 10 mg/kg) were randomly divided into 5 groups (n=7). Damage was created by clamping the right leg sciatic nerves of animals in all groups. Before and after the sciatic nerve injury, the pain threshold values of the animals were recorded with hot-cold plate and tail-flick tests, and motor activities with the rotarod test. The animals in the control group were administered intraperitoneally (ip) solvent, while the other groups were administered ip 0.1 mg/kg,1 mg/kg, 4 mg/kg, 10 mg/kg METRNL.Tests were repeated after drug administration. In statistical evaluation, one-way analysis of variance with IBM SPSS 24 package program and post-hoc Dunnet's test following this analysis were used to reveal time-dependent differences between groups.

RESULTS: It was observed that METRNL application increased the residence time in hot-cold plate, tail-flick and rotarod tests in animals with sciatic nerve damage, and increased pain thresholds and motor activities compared to the control group. This increase was found to be significant at all doses of METRNL ($p<0.05$).

CONCLUSION: The results of this study show that tested METRNL has positive efficacy on the model of sciatic nerve injury-induced neuropathy.

Acknowledgment: This study was supported by the Scientific Research Projects Unit of Inonu University with the project numbered TSG-2020-2088.

Keywords: METRNL, Neuropathy, Rotarod, Sciatic Nerve Injury.

PC-60

Investigation of the Antıconvulsane Effects of Venlafaxine in Experimental Penicillin Generated Epilepsy Model

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AIM: In this study, it was aimed to evaluate the antiepileptic activity of venlafaxine with electrophysiological and biochemical analysis methods. This study is the first to investigate the antiepileptic effects of venlafaxine in a penicillin-induced acute-epilepsy model according to the literature. The antiepileptic effects of venlafaxine were investigated, as it has less side effects and better tolerance than other antidepressants, increasing the rate of use.

METHODS: This study was approved by the BAİBU Animal Experiments Local Ethics Committee (Decision no: 2020/56). 35 Wistar Albino rats were divided into 5 groups. Rats were placed in stereotaxy device for electrocorticography (ECoG) measurement of the electrical activity of the brain. After five minutes of basal activity measurement, epilepsy was induced to rats with penicillin (500IU, 2.5µl, icv). After 30 minutes of recording, the control group was injected with saline, the positive control group was injected with 5mg/kg diazepam, and the experimental groups were injected with 50mg/kg, 100mg/kg, 150mg/kg venlafaxine (0.1ml, i.p.). ECoG recorded for ninety minutes and blood samples were collected by cardiac puncture method. Afterwards, experiment was terminated. The spike wave numbers and the amplitudes in records were compared in 5-minute segments. Also, the Total Antioxidant-Oxidant Level (TAS-TOS) and thiol-disulfite levels were determined by ELISA and electrolytes by ion-selective electron methods both in the serum, formed by centrifugation of blood samples.

RESULTS: Statistically, it was determined that 100mg/kg and 150mg/kg venlafaxine administration decreased spike wave numbers compared to diazepam and controls and kept the amplitudes similar to the diazepam group. Besides, it was observed that 100mg/kg and 150mg/kg venlafaxine administration increased TAS, calcium and magnesium levels compared to the control group.

CONCLUSION: In conclusion, venlafaxine showed antiepileptic property by decreasing spike wave numbers and antioxidant property by increasing TAS values. Venlafaxine may be an alternative and promising option in the treatment of epilepsy.

Keywords: Epilepsy, Venlafaxine, Electrocorticography (ECoG), Rat, Penicillin.