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Charité-Universitätsmedizin Berlin

D-10117 Berlin, Germany

Tel.: +49 30 450 528162

Fax: +49 30 450 7528972

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Proceedings of the 49th Turkish Physiology Congress

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Scientific Program

06 November Wednesday	07 November Thursday	08 November Friday	09 November Saturday
10.30 – 15.30 Registration	09.00 – 12.00 Scientific Program	09.00 – 12.00 Scientific Program	09.00 – 12.00 Scientific Program
15.30 – 16.15 Congress Opening Session	12.00 – 12.45 Poster Communications-I	12.00 – 12.45 Poster Communications-II	12.00 – 12.30 Poster Communications-III
16.15 – 16.45 Respect to Masters	12.45 – 13.45 Lunch	12.45 – 13.45 Lunch	12.30 – 13.30 Lunch
17.00 – 18.30 Opening Panel	13.45 – 18.00 Scientific Program	13.45 – 17.45 Scientific Program	13.30 – 15.00 Scientific Program
19.00 – 20.00 Opening Reception		17.50-18.50 AGM of the TFB	15.15 – 15.45 Awards & Closing Ceremony

06 November 2024 Wednesday

10.30 – 15.30	Registration
15.30 – 16.45	Salon A: Congress Opening Session Congress Opening TFBD Accreditation Report Respect to Masters (to the memory of Prof. Dr. Nuran Hariri & Prof. Dr. Kubilay Uzuner) Chair: Prof. Dr. Erdal Ağar
16.45 – 17.00	Coffee Break
17.00 – 18.30	Panel 1: The Last Century of Electrical Therapies in Heart Failure Oğuzhan Ekrem Turan, Emin Evren Özcan & Mehmet Birhan Yılmaz Chair: Prof. Dr. Bayram Yılmaz
19.00 – 20.00	Opening Reception (Palm Wings Ephesus Hotel)

07 November 2024 Thursday

09.00 – 10.30	Salon A: Oral Communications (OC01 – OC06) Chairs: Prof. Dr. Selim Kutlu & Doç. Dr. Erkan Kılınç Salon B: Oral Communications (OC07 – OC12) Chairs: Prof. Dr. Gülderen Şahin & Doç. Dr. Mümin Alper Erdoğan Salon C: Oral Communications (OC13 – OC18) Chairs: Prof. Dr. Mustafa Gül & Prof. Dr. Selda Kabadere
10.30 – 11.00	Coffee Break
11.00 – 12.00	Salon A: Conference 1: Targeting Senescence in the Repair of the Heart Georgina M. Ellison-Hughes Chair: Prof. Dr. Erdal Ağar
12.00 – 12.45	Poster Communications (PC01-PC40)
12.45 – 13.45	Lunch

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- 13.45 – 15.30 Salon A: **Symposium 1:** Angiogenesis in Physiologic and Pathologic Conditions and Vascularization in Tissue Engineering
Durmuş Deveci: A General Introduction to Angiogenesis, Metodology, Cases Where Angiogenesis Wanted and Unwanted
Ali Osman Saatçi: Clinical Applications of Anti-VEGF's in Ophthalmology
Ömer Kartı: Characteristics of Current Anti-VEGF Agents Used in Ophthalmology
Serkan Dikici: Construction of the Living Networks in Artificial Tissues: Vascularization in Tissue Engineering
Chairs: Prof. Dr. Özgür Kasımay & Prof. Dr. Fadıl Özyener
- 13.45 – 15.30 Salon B: **Panel 2:** The Sirtuin Family in Health and Disease
Gizem Dönmez Yalçın: The Investigation of SIRT4's Role in Brain Diseases
Arzu Keskin Aktan: The Relationship of the Sirtuin Family with Mitochondrial Dynamics and Inflammation
Kazime Gonca Akbulut: Role of the Sirtuin Family in Metabolic Regulation
Chairs: Prof. Dr. Hale Sayan Özaçmak & Prof. Dr. Gonca Akbulut
- 15.30 – 16.00 Coffee Break
- 16.00 – 18.00 Salon A: Oral Communications (**OC19 – OC26**)
Chairs: Prof. Dr. Lütfiye Kanıt & Prof. Dr. Cemil Tümer
Salon B: Oral Communications (**OC27 – OC34**)
Chairs: Prof. Dr. Mustafa Ayyıldız & Prof. Dr. Selma Arzu Vardar
Salon C: Oral Communications (**OC35 – OC42**)
Chairs: Prof. Dr. Süleyman Sandal & Doç. Dr. Ramazan Üstün

08 November 2024 Friday

- 09.00 – 10.30 Salon A: **Sempozyum 2:** Neurodevelopmental Research in Model Organisms
Şermin Genç: The Impact of Neuroinflammation on Neuronal Damage in the Neonatal Rodents Brain
Kemal Uğur Tüfekçi: The Effects of Oxidative Stress on Neurogenesis in Zebrafish
Arzu Çelik: In Vivo Modeling of Neurogenetic Diseases in Drosophila
Chairs: Prof. Dr. Ersin Koylu & Prof. Dr. Şermin Genç
- 09.00 – 10.30 Salon B: **Panel 3:** The Role of Multifocal Evaluations in Visual Electrophysiology in Diagnosis and Treatment
Hakkı Oktay Seymen: How Are Multifocal ERG and VEP Recordings Performed, and Why Do We Need to Evaluate the Findings?
Aykut Oruç: The Role of Specific Visual Electrophysiological Tests in Ophthalmological and Neurological Diseases
Kadriye Yağmur Oruç: Retinal Cell Network Electrophysiology
Chairs: Prof. Dr. Nevzat Kahveci & Prof. Dr. Hakkı Oktay Seymen
- 10.30 – 11.00 Coffee Break
- 11.00 – 12.00 Salon A: **Konferans 2:** Physiological Basis of Vestibular Function Testing
G. Michael Halmagyi
Chair: Prof. Dr. Ertuğrul Kılıç
- 12.00 – 12.45 Poster Communications (**PC41-PC76**)
- 12.45 – 13.45 Lunch

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13.45 – 14.45	Salon A: Oral Communications (OC43 – OC46) Chairs: Prof. Dr. Ahmet Ergün & Prof. Dr. Ayhan Bozkurt Salon B: Oral Communications (OC47 – OC50) Chairs: Prof. Dr. Nuran Ekerbiçer & Prof. Dr. Suat Tekin Salon C: Oral Communications (OC51 – OC54) Chairs: Prof. Dr. Vural Küçükataş & Prof. Dr. Bilge Pehlivanoglu
14.45 – 15.00	Coffee Break
15.00 – 16.00	Salon A: Conference 3: An Update on Renal Mineral Transport in Health and Disease Joost Hoenderop Chair: Prof. Dr. Fatma Töre
16.00 – 16.15	Coffee Break
16.15 – 17.45	Salon A: Symposium 3: Brain Organoids in Neuroscience Research Sinan Güven: Organoid Models for Brain – Ocular System Axis Özlem Yeşil Çeliktas: Human Organoids-on-Chips in Health and Disease Burak Derkuş: Modeling Pathogenic Microbiota-Driven Neurodegeneration in Cerebral Organoids Under In Vitro Conditions Chairs: Prof. Dr. Numan Ermutlu & Prof. Dr. Durmuş Deveci
16.15 – 17.45	Salon B: Symposium 4: A Scientific Journey from Physiology Laboratory to Clinics Berna Karakoyun: Oxidative Overview from the Physiology Research Laboratory to the Clinics Mehmet Koç: Investigation of Treatment Options in Acute and Chronic Kidney Injury Models Leyla Semiha Şen: The Bridge Between Physiology Laboratory and General Surgery Chairs: Prof. Dr. Berrak Yeğen & Prof. Dr. Berna Karakoyun
17.50 – 18.50	Salon A: AGM of the TFBD
20.00 – 23.30	Gala Dinner

09 November 2024 Saturday

09.00 – 10.30	Salon A: Oral Communications (OC55 – OC60) Chairs: Prof. Dr. Burcu Gemici Başol & Prof. Dr. Ayşe Çakır Salon B: Oral Communications (OC61 – OC66) Chairs: Prof. Dr. Sinan Canpolat & Doç. Dr. Emine Kılıç Toprak Salon C: Oral Communications (OC67 – OC71) Chairs: Prof. Dr. Abdülkerim Kasım Baltacı & Doç. Dr. Özgür Bulmuş
10.30 – 11.00	Coffee Break
11.00 – 12.00	Salon A: Conference 4: The GnRH Pulse Generator – Progress in Understanding the Neural Regulation of Fertility Allan Herbison Chair: Prof. Dr. Ahmet Ayar
12.00 – 12.30	Poster Communications (PC77-PC97)
12.30 – 13.30	Lunch
13.30 – 15.00	Salon A: Panel 4: Kinesiology and Biomechanics in the Past, Present, Future Evren Yaşar: Human Functional Bioengineering Berke Aras: The Concept of Ability Laboratory in the Current Physical Medicine and Rehabilitation Model

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Özlem Karasimav: Innovations in Sports Performance

Chairs: Prof. Dr. Yusuf Hıdır & Prof. Dr. Evren Yaşar

13.30 – 15.00

Salon B: Sempozyum 5: Living in Accordance with the Circadian Rhythm

Melek Bor-Küçükataı: Central and Peripheral Regulation Mechanisms of Circadian Rhythm

Özgen Kılıç-Erkek: Metabolic Effects of Chrononutrition

Emine Kılıç-Toprak: Circadian Rhythm and Exercise

Mustafa Çağlar Beker: Circadian Rhythm and Molecular Dynamics of Neuronal Injury

Chairs: Prof. Dr. Melek Bor-Küçükataı & Prof. Dr. Eylem Taşkın Güven

15.00 – 15.15

Coffee Break

15.15 – 15.45

Awards & Closing Ceremony

Conferences

Conference 1: Targeting Senescence in the Repair of the Heart

Georgina M. Ellison-Hughes

School of Basic and Medical Biosciences, Faculty of Life Sciences & Medicine, Guy's campus, King's College London, London, UK

Mammalian ageing is defined as a gradual loss of the capacity to maintain tissue homeostasis or to repair tissues after injury/stress. The adult heart is considered a post-mitotic organ, having a low cardiomyocyte turnover rate over the course of human lifespan, which decreases further with ageing. Like other tissues and organs senescent cells accumulate in the heart with ageing and in chronic disease, contributing to pathophysiology and deterioration. Regulation of cell senescence will impact the efficacy of reparative therapies, especially if most patients in need are of advanced age as occurs with heart disease and failure. Targeting cell senescence presents a promising therapeutic target to rejuvenate the heart's reparative potential.

We and others have shown that eliminating senescent cells using senolytics (Navitoclax, Dasatanib+Quercetin) or genetic (using INK-ATTAC+AP mice) clearance of senescent cells in aged mice alleviated detrimental features of cardiac ageing, including myocardial dysfunction, hypertrophy and fibrosis, and induced cardiac progenitor cell activation and cardiomyocyte renewal. We also show that D+Q senolytics ameliorate cardiac recovery and remodelling after injury in adult and aged mice.

A key feature of senescent cells is that they produce and secrete pro-inflammatory factors, termed the senescence-associated secretory phenotype (SASP). Long-term persistence of senescent cells and their SASP disrupts tissue structure and function with deleterious paracrine/autocrine and systemic effects. We show that the SASP decreases survival and proliferation of human cardiac progenitor cells, iPSC-derived cardiomyocytes and endothelial cells. Moreover, endothelial cells show impaired tube formation and migration. D+Q senolytics, by eliminating senescent cells and therefore abrogating the SASP, improves human CPC, iPSC-derived cardiomyocyte survival and proliferation, and endothelial cell survival, migration and tube formation.

In conclusion, targeting cell senescence using senotherapeutics can rejuvenate the reparative potential of the heart.

Conference 2: Physiological Basis of Vestibular Function Testing

G. Michael Halmagyi

University of Sydney, Royal Prince Alfred Hospital and IS Curthoys Psychology Department, Neurology Department, Sydney, Australia

The vestibular system senses and responds to head acceleration. Mechano-receptor hair cells in each of the 6 semicircular canals sense angular acceleration; those in the 4 otoliths sense linear acceleration. The responses of semicircular canals are polarized: each responds more during ipsilateral than during contralateral rotations, as a tandem pair with the contralateral semicircular canal. In contrast each otolith has oppositely polarized hair cells on each side of a central structure – the striola. Cochlear hair cells and vestibular hair cells work in a similar way.

Measuring human vestibular function is important in evaluating patients with vertigo or imbalance. Vestibular function is measured by the involuntary eye movement responses to vestibular stimulation: the vestibulo-ocular reflex (the VOR). Consider the VOR in relation to stimulus duration – long responses to long stimuli, versus short latency, short duration responses to short stimuli. Semicircular canal function has been traditionally measured by the magnitude and duration of nystagmus responses to long stimuli such thermal gradients, sinusoids of varying frequency and magnitude or velocity steps of whole-body angular acceleration. These measurements take minutes and are influenced by factors such as alertness and attention. Furthermore, with these stimuli it is difficult to calculate a useful input/output transfer function.

It is now possible to measure the VOR in response to short, fast head angular accelerations (head impulses). A reliable VOR input>output relationship (gain) can be calculated for each individual semicircular canal; the Head Impulse Test is now in routine clinical practice. It is a direct test of the short latency (<7ms) trisynaptic pathway from the hair cells of each semicircular canal to vestibular ganglion cells, to vestibular nucleus neurons then to brainstem ocular motoneurons.

Measuring short latency compensatory eye movement responses to stimulation of the otoliths by linear accelerations (the linear VOR) is more difficult as the whole body needs to be moved along a linear track. New evidence shows that some otolith receptors and afferents can be activated by sound or vibration and these stimuli have been used for clinical tests of otolith function (Vestibular Evoked Myogenic Potentials).

Conference 3: An Update on Renal Mineral Transport in Health and Disease

Joost Hoenderop

Radboud University Medical Center, Radboud Institute for Medical Innovation, Department of Medical BioSciences
Nijmegen, the Netherlands

The kidney plays a crucial role in the maintenance of the body mineral balance. Calcium and magnesium are essential ions in all organisms and participates in a large variety of structural and

functional processes. Of all minerals filtered by the glomerulus, the majority (99%) is reabsorbed. Magnesium deficiency is associated with a wide range of clinical effects including muscle cramps, fatigue, seizures and arrhythmias. Significant progress has been made into our understanding of the molecular mechanisms responsible for calcium and magnesium homeostasis. Members of the transient receptor potential channel (TRP) superfamily proved essential to the maintenance of divalent cation levels by regulating their absorption from renal and intestinal lumina. Current work focuses on the functional aspects of divalent transporters and regulatory proteins using a comprehensive approach that includes studies in epithelial cell lines, transgenic mice models and tubuloid lines. Flow has been demonstrated to be important to coordinate transepithelial calcium and magnesium transport. Kidney organoids and tubuloids are proved to be advanced in vitro models and have recently been described as promising tools to study kidney (patho)physiology. Recent developments have shown their application in disease modeling and drug screening.

In the lecture I will present newly discovered mechanisms that could provide potential pharmacological targets in the therapy of disturbances in mineral and water homeostasis. In the presentation a guided molecular tour along the nephron will be made detailing the contribution of the individual segments to the overall renal mineral handling.

Conference 4: The GnRH Pulse Generator – Progress in Understanding the Neural Regulation of Fertility

Allan E. Herbison

University of Cambridge, Department of Physiology Development and Neuroscience, Cambridge, UK

Fertility is critically dependent upon episodic gonadotropin hormone secretion. Recent studies using genetic mouse models have identified that a population of kisspeptin neurons located in the arcuate nucleus (ARN) represent the gonadotropin-releasing hormone (GnRH) pulse generator in both males and females. These cells exhibit abrupt periods of synchronised activity for 1-2 min that, in turn, activate GnRH neuron processes to release GnRH over a similar time scale to drive pulsatile luteinizing hormone secretion. The remarkable similarities between the activity patterns of mouse ARN kisspeptin neurons and early unidentified multi-unit recordings in the monkey infundibular nucleus, indicate that the kisspeptin pulse generator is highly conserved in mammals. Studies using in vivo CRISPR-Cas9 gene editing further demonstrate that the primary site of estrogen negative feedback in controlling GnRH secretion occurs through estrogen receptor alpha expressed by ARN kisspeptin neurons. These and other approaches in vivo are finally allowing the once enigmatic pulse generator to be characterized and explored.

Symposiums

Symposium 1: Angiogenesis in Physiological - Pathological Conditions and Vascularization in Tissue Engineering

Symposium 1.1: A General Introduction to Angiogenesis, Metodology, Cases Where Angiogenesis Wanted and Unwanted

Durmuş Deveci

Niğde Ömer Halisdemir University, Medical School, Department of Physiology, Niğde, Türkiye

This presentation will provide a general introduction to angiogenesis and discuss the situations where angiogenesis is desired and undesirable. In addition, in order to avoid possible errors in angiogenesis studies, especially in muscles, the importance of knowing the different muscle groups from which samples are taken, the locations where samples are taken, and the types and diameters of muscle fibers will be emphasized. In addition, some general information about angiogenic and antiangiogenic applications will be discussed.

There are several keywords that mean the formation of new blood vessels. Of these, angiogenesis reflects the formation of new capillary blood vessels from pre-existing ones, while arteriogenesis reports the formation of arteries. While vasculogenesis was previously reported to describe only the formation of vessels in the embryonic life stage, there have recently been studies reporting that vasculogenesis continues after postnatal life. In addition to all these, it is seen that vascularization, which forms the basis of many physiological and pathological events, is also called angiogenesis in one word.

The distance between a capillary vessel and a cell is approximately 100-300 micrometers and the exchange of substances between blood and tissue in these vessels shows how important angiogenesis is in growing and proliferating cells. While angiogenesis is beneficial in some cases (exercise) or diseases (coronary artery diseases and ischemic diseases in the legs, wound healing), it can be harmful or increase the severity of the disease in other cases (cancer, arthritis, retinopathy). While angiogenesis is encouraged in ischemic areas of infarction and peripheral arterial diseases by administering factors such as VEGF and FGF, angiogenesis is prevented in inflammatory diseases such as tumors and rheumatoid arthritis by administering endostatin, angiostatin and TSP-I. In addition, cyclic angiogenesis in the endometrium is also necessary for the formation and continuation of pregnancy. Hypoxia, ischemia, excessive force loading and exercise change the levels of angiogenesis and angiogenic factors in the plasma. These changes also vary depending on genetic polymorphism, as in the example of aspirin. Studies have shown that as the diameter of muscle fibers increases, whether in hypoxic or ischemic conditions,

their effects increase accordingly. Moreover, if the diameter of muscle fibers is large and at the same time there is an oxidative fiber area in the muscle, angiogenesis in those areas is clearly more evident. It is known that angiogenic and antiangiogenic factors are naturally present in the body of the living being and are secreted from different cell types. As a result of all these, it is necessary to be very careful while trying to turn the angiogenic balance in favor of the living being, as there is a possibility of undesirable situations. Deveci D, Marshall JM & Egginton S. (2001). Relationship between capillary angiogenesis, fibre type, and fibre size in chronic systemic hypoxia. *American J Physiology*, 28: H241-H252. Deveci D & Egginton S. (2002). Differing mechanisms of cold-induced changes in capillary supply in m. tibialis anterior of rats and hamsters. *J Experimental Biology*, 205: 829-840. Deveci D & Egginton S. (2002). Muscle ischaemia may be relieved by overload-induced angiogenesis. *Experimental Physiology*, 87: 479-488.

Symposium 1.2: Clinical Applications of Anti-VEGF's in Ophthalmology

Ali Osman Saatci

Dokuz Eylül University, Faculty of Medicine, Department of Ophthalmology, İzmir, Türkiye

Since the first anti-vascular endothelial growth factor (anti-VEGF) agent pegaptanib, an RNA aptamer, was approved by the US Food and Drug Administration (FDA) on 17 December 2004, several anti-VEGF agents have been administered intravitreally for various indications, including wet age-related macular degeneration, diabetic retinopathy, diabetic macular edema, retinal vein occlusion, myopic macular neovascularisation, retinopathy of prematurity and several other rare indications. Bevacizumab, ranibizumab, aflibercept (2 and 8 mg), brolucizumab and faricimab are currently in clinical use. However, new agents with more potent and lasting properties are being investigated, including gene therapies.

Symposium 1.3: Characteristics of Current Anti-VEGF Agents Used in Ophthalmology

Ömer Karti

Dokuz Eylül University, Faculty of Medicine, Department of Ophthalmology, İzmir, Türkiye

Vascular endothelial growth factor (VEGF) is produced by retinal pigment epithelium, vascular endothelial cells, pericytes, ganglion cells and Müller cells in response to ocular hypoxia and ischaemia in the eye. VEGF is a major cause of retinal and choroidal neovascularisation and vascular leakage leading to macular edema. The use of anti-VEGF therapies in ophthalmology has

revolutionised the treatment of common retinal diseases such as diabetic retinopathy, retinal vein occlusion and age-related macular degeneration. A number of important anti-VEGF molecules have been approved by the US Food and Drug Administration (FDA) for use in ophthalmology. Pegaptanib, an RNA oligonucleotide aptamer, is the inaugural anti-VEGF agent to be approved for ophthalmic use by the FDA. The molecule acts by binding to VEGF and inhibiting it. Ranibizumab is a recombinant, humanised fragment of the monoclonal antibody IgG1 that binds to and inhibits VEGF-A. Aflibercept, a fusion protein, is a soluble decoy receptor that has been demonstrated to exhibit a heightened affinity for binding with VEGF-A, VEGF-B, and placental growth factor in comparison to the body's native receptors. Brolucizumab is a single-chain variable antibody fragment. It consists of the variable regions of the heavy and light chains of immunoglobulins. Faricimab is the first bispecific monoclonal antibody that targets both VEGF and angiopoietin-2. Bevacizumab is an anti-VEGF drug originally developed for the treatment of cancer. It is a monoclonal antibody produced using recombinant DNA technology. It is widely used 'off-label' by ophthalmologists, although it is not FDA approved for ophthalmic use.

Symposium 1.4: Construction of the Living Networks in Artificial Tissues: Vascularization in Tissue Engineering

Serkan Dikici

Izmir Institute of Technology, Faculty of Engineering, Department of Bioengineering, Izmir, Türkiye

As the demand for innovative solutions in regenerative medicine rises, tissue engineering has emerged as a key bioengineering field, aiming to develop cell/biomaterial-based approaches to replace tissues and organs that have been damaged and lost their functionality due to injury, disease, or aging. The goal of a tissue engineer is to combine biological and engineering principles to create tissue substitutes under laboratory conditions that can anatomically and physiologically perform the primary functions of the tissue they are intended to replace or restore. Simple and thin tissue-engineered constructs can successfully integrate with well-vascularized implantation sites. However, the rapid neovascularization upon implantation is critical for the survival of thick and complex constructs due to the diffusion limits of oxygen and nutrients. The newly growing blood vessels from the host tissue into the scaffold post-implantation typically invade the tissue in response to signals secreted by the cells implanted within the scaffold, which are naturally secreted in response to hypoxia, acting as a "cry for help". However, this spontaneous blood vessel growth is generally limited to a few microns per day, meaning that the complete vascularization of an implant several millimeters in size can take several weeks.

In this context, tissue engineers have adopted various strategies to achieve rapid vascularization of their engineered constructs. Vascularization strategies in tissue engineering can be broadly categorized into three main approaches: (i) biomaterial and architectural design, (ii) molecular approaches, and (iii) cellular approaches. The biomaterial's properties, such as whether it is peptide or carbohydrate-based, synthetic or natural, hydrophilic or hydrophobic, mechanical compatibility, and pore and interconnect sizes, serve as the initial starting point for host blood vessels to readily invade the tissue-engineered construct. To shorten the time required for the formation of a functional vascular network within the scaffold upon implantation, pro-angiogenic constructs can be developed by functionalizing them using established pro-angiogenic factors or stimulation of these factors indirectly using alternative pro-angiogenic agents. As an alternative to biochemical functionalization of the constructs, pre-seeding of the scaffold with angiogenesis-associated cells to form a pre-vascularized structure prior to implantation is also a commonly preferred approach. Similar to in vitro pre-vascularization, the scaffold can be implanted into a more accessible in vivo site before the final implantation to achieve pre-vascularization, allowing the formation of a partially functional vascular network within the scaffold. This approach facilitates rapid integration with the host's vasculature after implantation, either through surgical or non-surgical (spontaneous) anastomosis, which is crucial for the long-term survival and functionality of the implanted tissue.

In summary, tissue engineering has been enhancing its clinical significance as an innovative alternative to transplantation surgery for nearly thirty years, with new developments emerging daily. Alongside countless scientific achievements in both in vitro and in vivo environments, the successful transition of tissue-engineered artificial tissues and organs from the laboratory to the clinic will only be possible through the successful adaptation of vascularization strategies in tissue engineering.

Symposium 2: Neurodevelopmental Research in Model Organisms

Symposium 2.1: The Impact of Neuroinflammation on Neuronal Damage in the Neonatal Rodents Brain

Şermin Genç

Izmir Biomedicine and Genome Center & Dokuz Eylül University, Faculty of Medicine, Department of Medical Biology, Izmir, Türkiye

Modeling neonatal diseases in rodents has been conducted for many years. Neonatal brain injuries such as Hypoxic-Ischemic Encephalopathy, Periventricular Leukomalacia (PVL), and neuroinflammation are modeled to shed light on the etiology and pathogenesis of these diseases. The use of genetically modified mice has facilitated the development of more targeted and effective treatment strategies. In my presentation, I will discuss our studies on neuroinflammation observed after lipopolysaccharide and bilirubin induction during the neonatal period, as well as the neuronal damage caused by this neuroinflammation.

A specific subtype of neuroinflammation, inflammasome activation, can lead to damage during early brain development. The inflammasome is a multiprotein complex that is part of the innate immune response mechanisms. After activation by external or internal stimuli, pro-inflammatory cytokines are released into the extracellular space, triggering a neuroinflammatory cascade, which leads to neuronal damage, developmental defects, and long-term cognitive, motor, and behavioral deficits. In the first of our studies, we detected increased microglial activation and inflammasome proteins, such as IL-1 β , caspase-1, and NLRP3, after bilirubin administration in neonatal mice. These changes were not observed in NLRP3 and caspase-1 knockout (KO) mice following bilirubin administration. Additionally, neuronal damage related with inflammasome activation in neonatal brains was demonstrated through immunofluorescence staining. The reduced inflammation and neuronal damage in KO mice confirmed that neuroinflammation is mediated by NLRP3 and caspase-1.

In another study, we examined inflammasome activation and perineuronal net damage in neonatal mice after LPS administration to induce inflammasome activation in the brain. Perineuronal nets are structures surrounding neurons, made up of components of the extracellular matrix, providing stability and regulating synaptic plasticity. Our study demonstrated that NLRP3 inflammasome activation induced by LPS causes damage to the perineuronal nets. The reduced perineuronal net damage in NLRP3 KO mice revealed that this damage is NLRP3 dependent.

In our third study, we investigated the effects of milk-derived extracellular vesicles (EVs) on brain damage in PVL. Breast milk contains many molecules that are important for the development

of baby and has healing properties for brain damage. In this study, EVs obtained from rat breast milk were administered intranasally to neonatal rats subjected to the PVL model. We found that breast milk-derived EVs inhibited astrocyte activation.

In conclusion, neuroinflammation plays a crucial role in the pathogenesis of brain damage during the neonatal period. Novel treatment approaches targeting neuroinflammation, without side effects, will help reduce brain damage.

Symposium 2.2: The Effects of Oxidative Stress on Neurogenesis in Zebrafish

Kemal Uğur Tüfekci

Izmir Demokrasi University, Centre for Brain and Neuroscience Research, Izmir, Türkiye

Izmir Biomedicine and Genome Center, Genc Neurodegeneration and Neuroprotection Laboratory, Izmir, Türkiye

Reactive oxygen species (ROS) are intracellularly generated and act as second messengers in essential cellular processes under physiological conditions. While the detrimental effects of high ROS levels due to oxidative stress are well known, how the developing brain responds to redox changes remains unclear. In our initial study, we explored in vivo microglial polarization and neurogenesis in zebrafish following hydrogen peroxide (H₂O₂) exposure. To quantify intracellular H₂O₂ levels in vivo, we used a transgenic zebrafish line expressing the Hyper protein, termed Tg(actb2:hyper)ka8. Subsequent in vitro experiments with N9 microglial coculture and conditioned medium were conducted to uncover the mechanisms driving changes in neurogenesis upon redox modulation. Both zebrafish and cell culture studies revealed that H₂O₂ exposure disrupted embryonic neurogenesis, promoted M1 microglial polarization, and activated the Wnt/ β -catenin pathway. Neural progenitor cell differentiation was significantly increased in H₂O₂-treated microglia compared to controls. Inhibition of the Wnt pathway prevented the effects of H₂O₂-treated microglia on neural stem cells. These findings highlight a strong interplay between microglia and neural progenitors mediated by redox state via the Wnt/ β -catenin pathway. In our second study, we aimed to elucidate the gene regulatory mechanisms of H₂O₂ treatment, focusing particularly on tRNA fragments, a subset of non-coding RNAs. In 48 hpf (hours post-fertilization) zebrafish embryos, H₂O₂ treatment upregulated 5'tRH-Gly-GCC, and in 72 hpf embryos, it led to increased levels of both 5'tRH-Glu-CTC and 5'tRH-Gly-GCC. Furthermore, inhibition of 5'tRH-Glu-CTC resulted in downregulation of α -III-Tubulin levels in H₂O₂-treated neural progenitor cells. Overall, our studies underscore the pivotal role of redox regulation in neural development, highlighting how oxidative stress can influence both microglial activity and neural progenitor differentiation through distinct molecular pathways.

Symposium 2.3: In Vivo Modeling of Neurogenetic Diseases in Drosophila

Arzu Çelik

Boğaziçi University, Department of Molecular Biology and Genetics, İstanbul, Türkiye

Neurogenetic diseases are conditions caused by mutations that disrupt the normal function of neurons, leading to various neurological and developmental disorders. One of the most effective ways to understand the molecular mechanisms underlying these diseases is through in vivo modeling, which allows for the examination of genetic changes within a living organism. *Drosophila melanogaster* (fruit fly) emerges as a powerful model organism in neurogenetic disease research due to its highly conserved genetic pathways, rapid life cycle, and the availability of advanced genetic tools.

In our studies, we investigate the functional consequences of specific gene mutations associated with neurological diseases in humans by using the *Drosophila* model. We induce mutations in the *Drosophila* genome and observe their effects on neuronal development, behavior, and lifespan. In my presentation, I will discuss the research we have conducted on two different genes. Our research contributes to a better understanding of the molecular and cellular pathways involved in neurogenetic diseases, providing new insights that could aid in the development of novel diagnostic and therapeutic strategies for these conditions.

Symposium 3: Brain Organoids in Neuroscience Research

Symposium 3.1: Organoid Models for Brain – Ocular System Axis

Sinan Güven

İzmir Biomedicine and Genome Center, İzmir, Türkiye
Dokuz Eylül University, Faculty of Medicine, Department of Medical Biology, İzmir, Türkiye

Organoids are 3D tissue equivalents that provide the structural and functional recapitulation of an organ that can be generated from stromal or pluripotent stem cells. Organoids provide in vitro venues to investigate molecular and mechanistic studies on target organ including realistic models for diseases and drug testing. Advances in stem cell research, bioengineering and organoid technologies lead the generation of diverse portfolio of organoids including brain, intestine, liver, kidney, stomach, lung, thyroid and lacrimal gland. Brain organoids (BOs) resemble embryonic development of the cerebellum and can be employed in understanding neurodegenerative diseases and brain research. Building and using powerful tools that organoids and assembloids offer the physiological and molecular mechanisms that govern the crosstalk between peripheral tissues. In this study, we will discuss

the human induced pluripotent stem cell-based organoids we developed for the ocular system and their interaction with the brain.

Symposium 3.2: Human Organoids-on-Chips in Health and Disease

Ozlem Yesil-Celiktas

Bioengineering Department, Faculty of Engineering, Ege University, Izmir, Türkiye
ODTÜ MEMS Center, Ankara, Türkiye

The central nervous system is highly compartmentalized and layered, containing diverse cell types with connectivity via axons and dendrites. Animal-based disease models have been used to study human brain function and related diseases. However, these approaches often lack human response. Microfluidic technology combined with tissue engineering has led to the development of organ-on-chips which are micro-engineered platforms that mimic physiological microenvironments and cultured tissues with vascular like structures [3]. Recent progress has made it possible to develop unique platforms for creating in vitro human neural models that emulates the in vivo conditions as much as possible. These technologies have established various in vitro neural models such as for cerebral cortex, blood-brain-barrier, neuroinflammation and Alzheimer's. At Biomimetic Microsystems Lab, we are tackling the challenges associated with fabrication and functionalization of organ-on-chips by designing innovative microfluidic platforms that recapitulate blood-brain-barrier (BBB) and brain parenchyma supported with extracellular matrix components under physiological conditions, both in healthy and diseased states. For that, we developed new protocols for maturation of cerebral organoids and differentiation of stem cells into neurons, astrocytes, oligodendrocytes, microglia and mast cells. By using these cutting-edge platforms, we aim to understand the fate of circulating particles in the peripheral blood, passage across the BBB and the effects on the brain tissue. Human organoid-on-chip models hold immense potential for revolutionizing biomedical research and accelerating drug development process.

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Symposium 3.3: Modeling Pathogenic Microbiota-Driven Neurodegeneration in Cerebral Organoids Under In Vitro Conditions

Burak Derkus

Ankara University, Faculty of Science, Department of Chemistry, SCRLab, Ankara, Türkiye

Organoids are micro-anatomical structures resembling organs, derived from pluripotent stem cells. In this study, our objective was to investigate the impact of distinct bacterial populations, specifically pathogenic microbiota (PM) and non-pathogenic microbiota (NM), on the phenotype of cerebral organoids (COs). To achieve this, we established COs and co-cultured them with PM and NM utilizing a transwell system, which comprises a two-compartment cell culture device separated by a 0.45 µm membrane. To evaluate the presence and architecture of tissues containing neural stem cells and neurons, we conducted immunofluorescent staining (Nestin, TUJ1, MAP2, GFAP) on COs. In addition, mRNA profiles were assessed to understand the effects of microbiotas on CO gene expressions.

Control COs (Cntrl_COs) exhibited the presence of Nestin+ and TUJ1+ cells, demonstrating the characteristic morphology of a Nestin+ cell-enriched ventricular zone and an outermost layer enriched with TUJ1+ neurons, consistent with the specific histological features of cerebral organoids. In COs co-cultured with NM (NM_COs), multiple ventricular regions displayed a lateral arrangement akin to that seen in Cntrl_COs; however, the outer region housing TUJ1+ neurons were notably broader. Conversely, COs co-cultured with PM (PM_COs) displayed ventricles arranged in a triangular or rectangular geometry rather than the longitudinal lateral arrangement witnessed in Cntrl_COs and NM_COs, and the regions containing TUJ1+ neurons exhibited signs of damage. Statistical analysis revealed no significant differences ($p>0.05$) in the quantity of Nestin+ cells across the three groups. However, the

density of TUJ1+ cells was highest in NM_COs and lowest in PM_COs ($p<0.05$).

Symposium 4: A Scientific Journey from Physiology Laboratory to Clinics

Symposium 4.1: Oxidative Overview from the Physiology Research Laboratory to the Clinics

Berna Karakoyun

University of Health Sciences, Hamidiye Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

When diseases reduce quality of life, therapeutic approaches come to the fore. The first step of these approaches is basic medical research, and the science of physiology serves as an important bridge between these basic medical and clinical research. The integration of scientific discoveries from studies in experimental medicine laboratories into clinical needs and applications is important in translational medicine. Experimental oxidant injury models mimicking different diseases are frequently created in physiology research laboratories and the efficacy of different therapeutic and/or prophylactic interventions are investigated on these models. In a healthy organism, oxidant production and antioxidant defense are in balance. If free radicals exceed homeostatic limits or antioxidants are insufficient, the resulting oxidative stress damages proteins, carbohydrates, lipids, nucleic acids and beneficial enzymes. Although there is increasing evidence that oxidative stress is indirectly/directly related to and responsible for the onset, progression and complications of diseases such as cardiovascular, renal, lung, liver, gastrointestinal diseases, neurodegenerative disorders, cancer and type-2 diabetes, the extent to which oxidative stress is involved in the pathophysiology of diseases is highly variable. The effectiveness of antioxidant defense is also limited by the role of oxidative stress in pathophysiology. This limitation is often overlooked when assessing antioxidant defense systems in clinical trials. The challenge is to determine the extent to which antioxidant strategies can be improved to ameliorate some symptoms but not the underlying cause of the disease. Perhaps a more effective strategy should aim to eliminate the damage caused as quickly as possible, rather than oxidative stress itself. Ultimately, maintaining the right balance of free radicals and antioxidants is the key to preventing and/or treating oxidant damage. Understanding this delicate balance is critical in developing innovative therapeutic strategies against oxidative stress-related diseases and guiding us towards better targeted treatments.

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Symposium 4.2: Investigation of Treatment Options in Acute and Chronic Kidney Injury Models

Mehmet Koç

Marmara University, Faculty of Medicine, Division of Nephrology, Istanbul, Türkiye

Animal models of acute kidney injury (AKI) and chronic kidney disease (CKD) provide information about the pathogenesis and treatment options for these diseases. It is well known that reperfusion following ischemia or exposure to nephrotoxic agents may cause tubular damage and further deterioration of the the injury is followed through accumulation of ions, generation of reactive oxygen species, endothelial dysfunction, platelet aggregation and immune system activation. Additionally, induction of inducible nitric oxide synthase by cytokines in the kidneys becomes abundant during ischemia-reperfusion injury (I/R) leading to further tubular cell injury. Obestatin, having anti-apoptotic and anti-inflammatuary actions, is shown to be protective against cardiac I/R injury in some studie. Obestatin also attenuated renal I/R injury and cisplatin nephrotoxicity by modulating oxidative stress, apoptosis, inflammation and nitric oxide metabolism. Similarly, stimulation of the cholinergic anti-inflammatory pathway by GTS-21, a selective agonist of $\alpha 7$ nACh receptor, also mitigated contrast induced nephropathy in our studies. Unilateral ureteral obstruction (UUO), an experimental model of CKD, is characterized by accumulation of leucocytes in the

interstitial area, tubular dilatation and atrophy, accumulation of collagen in the extracellular matrix leading to end-stage kidney disease in clinical practice. The neuropeptide nesfatin-1 is expressed in the neurons of the central nervous system. It reduced oxidative injury and neutrophil infiltration of the several models of tissue injury via its anti-inflammatory and antiapoptotic actions. Accordingly, we have demonstrated a protective effect of nesfatin-1 against UUO-induced renal fibrosis by reducing oxidative stress and inflammation.

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Symposium 4.3: The Bridge Between Physiology Laboratory and General Surgery

Leyla Semiha Şen

Marmara University Pendik Training and Research Hospital General Surgery Clinic, Istanbul, Türkiye

Experimental studies lead to a deeper understanding of diseases seen in the general surgery by explaining their pathophysiology

and forms the basis for development of new treatment modalities. Sometimes a new surgical technique or treatment method developed in experimental medicine, is being implemented in clinics as a new hope for treatment of patients. Therefore, the integration of scientific discoveries obtained as a result of research in physiology laboratories into clinical practice is very important in translational medicine which is an opportunity and bridge for scientists and clinicians in the transition of science from the bench to the patient, from the patient to the bench. Gastrointestinal and endocrine cancers; emergencies e.g. mesenteric ischemia and pancreatitis; life-threatening conditions concerning whole organism e.g. trauma, shock and sepsis are examples of diseases treated by general surgery. Also general surgeons must overcome hepatic ischemia and reperfusion injury occurring during liver surgery and transplantation; postoperative ileus; stress ulcers secondary to trauma, and problems of wound healing. In all these clinical conditions, free oxygen radicals are formed in the affected organ. If antioxidant mechanisms are insufficient to balance oxidative stress; depending on the severity of the oxidant damage, varying degrees of loss of function occur in the relevant organ. If oxidant damage cannot be limited to the affected organ with current treatment methods, other organs of the body are affected; than multiple organ failure may occur. The risk of multiple organ failure and death increases in clinical conditions where widespread oxidant damage affecting the whole body, such as trauma, shock, and sepsis. Therefore, it is crucial to develop new treatment methods using appropriate experimental models that can mimic these clinical situations. Collaborative research between physiology laboratories and general surgery departments has the potential to yield substantial advancements in human health outcomes.

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Symposium 5: Living in Accordance with the Circadian Rhythm

Symposium 5.1: Central and Peripheral Regulation Mechanisms of Circadian Rhythm

Melek Bor-Küçükataay

Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

The circadian rhythm is governed by the "central clock" located in the suprachiasmatic nucleus (SCN) of the hypothalamus. In addition to the SCN, molecular clock mechanisms found in almost all tissues, especially the brain, liver and skeletal muscle, constitute peripheral clocks. SCN signals send information to peripheral clocks via neurohumoral mechanisms. While the rhythm of the central clock is mainly regulated by light; factors such as food intake, physical activity, stress play important roles in regulating rhythms in peripheral clocks. Four basic proteins are involved in the regulation of circadian rhythm at the molecular level; these are brain and muscle ARNT like 1 (BMAL1), circadian locomotor output cycles kaput (CLOCK), PERIOD (PER) ve CRYPTOCHROME (CRY). BMAL1 is a transcription factor that forms a dimer with CLOCK, a histone acetylase which regulates gene transcription. CLOCK:BMAL1 dimerization causes transcription of PER, CRY, Retinoc Acid Receptor related Orphan Receptor (ROR) and reverse erythroblastosis virus (REV-ERB) known as orphan nuclear receptors. This transcription mediated by CLOCK:BMAL1 causes PER and CRY, known as repressors of the circadian mechanism, to accumulate in the cytoplasm throughout the day. PER and CRY combine in the cytoplasm and enter the nucleus, where they function as inhibitors of CLOCK:BMAL1. Thus, circadian rhythm regulatory proteins regulate their own transcription via negative feedback. CLOCK:BMAL1-mediated transcription, which is suppressed by the controlled degradation of PER and CRY in the cytoplasm, is reactivated, causing cycles in circadian gene expression. ROR and REV-ERB, which form the secondary transcriptional/translational cycle, together ensure the 24-hour rhythm by activating and repressing the transcription of the Bmal1 gene, respectively. Circadian rhythm and metabolic processes are closely related to each other. Modern lifestyle habits, characterized by exposure to unhealthy diets, long-term inactivity, irregular eating hours, emotional eating and late-night food consumption, cause chronic circadian disruption, leading to increased risks of diseases as obesity, hypertension, insulin resistance and dyslipidemia.

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Symposium 5.2: Metabolic Effects of Chrononutrition

Özgen Kılıç-Erkek

Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

Long-term circadian rhythm alterations increase the risks of metabolic diseases while timing of food intake within an eating window consistent with the circadian rhythm has been shown to improve metabolic conditions. Chrononutrition refers to food intake in line with the body's daily rhythms. This term emphasizes the idea that the timing of food is as important as the amount and content of food. Time-restricted feeding (TRF) is recommended for maintaining health and preventing obesity-related diseases. With TRF, daily eating time (the time between the first and last energy intake) is reduced from 12-14 hours to less than 10 hours. In order to promote health benefits, the feeding window should occur during the biologically active phase. Under conditions of high nutrient intake, mTOR stimulates protein synthesis and cell growth, whereas when cell energy reserves are low, AMPK represses mTOR to minimize energy consumption, activates SIRT1 and PGC-1 α , stimulating autophagy. Modern lifestyle is characterized by unhealthy diets, long-term inactivity, irregular eating hours, emotional eating and late-night food consumption. However, chronotype is one of the factors that affect individual circadian rhythm. Evening chronotype is characterized by nocturnal feeding, the risk of developing obesity and metabolic diseases. The modern lifestyle and evening chronotype cause disruption in circadian rhythm. Studies have shown that TRF applied in the active phase improve the rhythmicity of circadian clock genes (Bmal1, Clock, Per1/2/3, Cry1/2) via AMPK in the fasting state and mTOR in the fed state. TRF applied during the inactive phase can disrupt the synchronization of circadian clock genes. TRF affects by changing the peak time and amplitude of the expression of nucleus clock genes in hypothalamus, muscle and liver. TRF applied in the active phase may play an important role in reducing various metabolic risk factors by regulating phase shifts in the circadian rhythm.

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Symposium 5.3: Circadian Rhythm and Exercise

Emine Kılıç-Toprak

Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

The main regulator of circadian rhythm is the central clock located in the hypothalamus; peripheral clocks are present in almost every organ, especially in the liver and muscle. While the rhythm of the central clock is mainly regulated by light, the rhythms in peripheral clocks are regulated by neuronal and endocrine signals from the central clock and environmental zeitgebers (food intake, physical activity, stress). Exercise, an important non-photic zeitgeber, can regulate the internal rhythms of the organism; in this respect, it stands out as a non-drug approach for the prevention and treatment of circadian rhythm disorders. There is limited and partly conflicting results regarding the expression level of clock genes and related pathways in central and peripheral clocks in response to exercise. Since the skeletal muscle molecular clock largely regulates muscle substrate preference, storage and transport, metabolism, physical activity and feeding patterns are closely related. Furthermore, the type, intensity and duration of exercise are important when examining the relationship between exercise and circadian rhythms. It has been shown that BMAL1 and PER2 genes are up-regulated following acute exercise, and it is suggested that while a single exercise session has a lower effect on circadian rhythm, long-term, regular exercise may have a higher effect on circadian rhythm, including the expression of clock genes. Since the circadian rhythm of skeletal muscle is sensitive to the exercise clock, it has been reported that the metabolic effects of exercise in the active or inactive phase of life may be different from each other. Although the debate on the recommended time of day to obtain the best results from exercise continues, it is suggested that exercise in the inactive phase is characterized by marked upregulation of genes encoding proteins involved in inflammatory and apoptotic pathways in muscle, while exercise in the active phase is more related to growth factor pathways, causes an increase in the number of genes involved in glycolysis and may effectively regulate circadian rhythm. On the other hand, it has also

been suggested that time-restricted nutrition (TRF) and exercise may produce synergistic benefits by enhancing each other's effects on circadian rhythm when applied alone or in combination in the prevention and treatment of obesity and related diseases.

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Symposium 5.4: Circadian Rhythm and Molecular Dynamics of Neuronal Injury

Mustafa Caglar Beker

Istanbul Medeniyet University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

The circadian rhythm is an important mechanism that regulates the body's internal clock and controls many physiological processes, such as the sleep-wake cycle, hormone release, and metabolism. This rhythm ensures that biological processes are aligned with the day-night cycle through a transcription-translation feedback loop formed by the BMAL1, CLOCK, Per, and Cry genes. In addition, the nuclear receptor REV-ERB α/β is known to play a role in circadian regulation by binding to the promoter region of the BMAL1 gene. Recent studies have shown that circadian disruption triggers neurodegenerative processes such as stroke and increases cellular injury. Therefore, circadian disruption is considered an important topic in the investigation of the mechanisms of neurodegenerative diseases.

In our studies using C57BL/6 mice, it has been shown that neuronal injury mechanisms are differentially regulated through PI3K/AKT/mTOR and RAF/MEK/ERK signaling pathways after cerebral ischemia induced by middle cerebral artery occlusion at different times of the day. The effects of BMAL1, the main component of circadian rhythm, on DNA fragmentation and neuronal survival after stroke models performed both in vitro and in vivo, as well as the proteins with which it interacts directly or indirectly, were revealed by proteomic analyses using liquid chromatography-tandem mass spectrometry. Furthermore, the effects of increasing or decreasing the expression of the nuclear receptor REV-ERB α/β , a negative regulator of BMAL1, by lentiviral

vectors on cerebral infarct volume, cerebral oedema and blood-brain barrier permeability after ischemic stroke were demonstrated by large-scale molecular analyses. In conclusion, circadian rhythm disturbances not only trigger neurodegenerative processes but are also an important factor that increases cellular damage in the pathophysiological events that follow these processes. Therefore, it is thought that regulation of circadian rhythm, especially BMAL1, and REV-ERB α/β , may play critical roles in the prevention and treatment of neurodegenerative diseases.

Panels

Panel 1: The Last Century of Electrical Therapies in Heart Failure

Oğuzhan Ekrem Turan, Emin Evren Özcan and Mehmet Birhan Yılmaz

Dokuz Eylül University, Faculty of Medicine, Department of Cardiology, Izmir, Türkiye

Heart failure is a multifactorial and progressive disease that goes beyond pump failure. It represents end spectrum of cardiovascular disease with severely impaired quality of life and survival. Of note, heart failure manifests itself via electrical alterations at the subcellular, cellular, and structural levels, which deepen the vicious cycle yielding enormous morbi-mortality burden in clinical practice. In the last century, advances in physiology have enabled a better understanding of the mechanism of the disease and have allowed the development of non-pharmacological therapies. These therapies, aimed at correcting the disturbances in the heart's conduction system, have significantly improved patients' quality of life and survival rates. By the 1980s, implantable cardioverter defibrillators brought about a revolution, with the ability to detect life-threatening arrhythmias and provide shock therapy. These devices became a critical treatment option for these high-risk patients, reducing the risk of sudden cardiac death. During the same period, cardiac resynchronization therapy has also been developed for patients with heart failure with dyssynchrony. This therapy improved heart function by ensuring the coordinated contraction of both ventricles, leading to gains in life expectancy and quality. In recent years, the effectiveness of treatments and patient comfort have further increased due to the miniaturization of these devices and the addition of wireless technologies. Moreover, integrating artificial intelligence and telemetry into electrical therapies has made remote monitoring and adjustment of devices possible, offering personalized treatment options. In the majority of these patients, electrical abnormalities such as atrial and ventricular arrhythmias are present, which can either be a consequence or a cause of heart failure. With the advancement of modern technologies such as 3D mapping and catheter ablation therapies, which make cellular-level changes visible at the organ level, it has become possible to achieve permanent treatment of these electrical abnormalities driving the prognosis of heart failure.

Panel 2: The Sirtuin Family in Health and Disease

Panel 2.1: The Investigation of SIRT4's Role in Brain Diseases

Gizem Dönmez Yalçın

Aydın Adnan Menderes University, Faculty of Medicine,
Department of Medical Biology, Aydın, Türkiye

Sirtuins are a class of enzymes that target various proteins within the cell for posttranslational modifications such as deacetylation, ADP-ribosylation, sumolation etc. Sirtuins are known to have roles in neurodegenerative diseases, metabolism and cancer. They act as stress response genes and support pro-survival. Glutamate Transporter 1 (GLT-1) is the main transporter that absorbs the excessive glutamate and leads to the prevention of excitotoxicity in brain. Sirtuin 4 (SIRT4) was shown to have a potential protective role against excitotoxicity in previous studies. SIRT4 has been shown in previous studies to ADP-ribosylate GDH and regulate glutamate metabolism. In our recent study, the regulation of dynamic GLT-1 expression by SIRT4 was analyzed in glia (immortalized human astrocytes) and glioblastoma (U87) cells. We showed that GLT-1 expression is regulated differently in glia and glioblastoma cells. Small molecules that modify SIRT4 may be used to prevent excitotoxicity in glioblastomas.

Panel 2.2: The Relationship of the Sirtuin Family with Mitochondrial Dynamics and Inflammation

Arzu Keskin Aktan

Afyonkarahisar Health Sciences University, Faculty of Medicine,
Department of Physiology, Afyonkarahisar, Türkiye

Mitochondrial dynamics primarily involve the processes of fusion and fission and are crucial for maintaining cellular energy balance. Mitofusin 1 and 2 (MFN1/2) are the primary GTPases involved in the fusion of the outer mitochondrial membrane, optic atrophy 1 (OPA1) in the fusion of the inner mitochondrial membrane, and dynamin-related protein 1 (DRP1) in mitochondrial fission. Three members of the Sirtuin family (SIRT1-7), namely SIRT3, SIRT4, and SIRT5, are localized in the mitochondria. These mitochondrial sirtuins play a critical role in regulating mitochondrial dynamics in response to fundamental cellular stress conditions such as inflammation and oxidative stress, as well as aging. SIRT3 stimulates mitochondrial fusion by deacetylating OPA1, optimizes energy production, reduces reactive oxygen species production, and prevents cellular damage. SIRT4 promotes mitochondrial fusion through the negative regulation of fission proteins and the positive regulation of fusion proteins, maintaining cellular energy homeostasis during inflammation and regulating metabolic responses. Similarly, SIRT5 promotes mitochondrial fusion via MFN2 and OPA1, optimizing mitochondrial energy metabolism

during prolonged fasting and energy stress, thereby helping to reduce cellular damage.

The effects of other sirtuin family members, SIRT1 and SIRT2, on mitochondrial dynamics are associated with their roles in regulating mitochondrial biogenesis and quality control mechanisms. SIRT1 interacts with peroxisome proliferator-activated receptor gamma coactivator 1-alpha (PGC-1 α) to stimulate mitochondrial biogenesis, while SIRT2 influences mitochondrial dynamics through the deacetylation of DRP1. Nuclear-localized SIRT6 is involved in DNA repair and maintaining genomic stability, whereas SIRT7 regulates ribosomal RNA biogenesis and cellular stress responses. In conclusion, the relationship between the sirtuin family and mitochondrial dynamics helps maintain cellular energy balance, reduce oxidative stress, suppress inflammatory responses, and support cellular survival mechanisms. A better understanding of these mechanisms may contribute to the development of new strategies for the treatment of aging and various diseases.

Panel 2.3: Role of the Sirtuin Family in Metabolic Regulation

K. Gonca Akbulut

Gazi University, Medical School, Department of Physiology,
Ankara, Türkiye

Sirtuins, called longevity proteins, are members of the Nicotinamide Adenine Diphosphate (NAD)-dependent histone/protein deacetylase family, which can increase lifespan by maintaining genome stability and homeostasis. Sirtuin values increase in healthy children with higher consumption of fruits, vegetables and dairy products. It has previously been shown that SIRT1-3 and 6 decrease with aging. The correlation between education level and blood SIRT1 and SIRT6 mRNA levels suggests that SIRT1 and SIRT6 mRNA levels may be protective against premature aging.

Since NAD⁺ is an important cofactor in energy metabolism, sirtuins are also considered key sensors in cell metabolism. Since NAD⁺ is a strong regulator of glycolysis oxidation-reduction reactions, tricarboxylic acid cycle and electron transport chain metabolism, sirtuin activity has an important role in regulating metabolic activity. Metabolic control is provided by fatty acid oxidation and ketone body formation. Lipid and glucose metabolism and gluconeogenesis occur through PPAR γ , PGC-1 α , FOXO. While SIRT1 has an inhibitory effect on adipogenesis, SIRT7 activates it. With these properties, the sirtuin family is protective in diabetes, diabetic nephropathy, acute renal failure, liver damage and fibrosis, and obesity. While SIRT1 increases cell resistance in hypoxia, it reduces insulin resistance and lipolysis. SIRT1 prevents obesity while regulating food intake through hunger and satiety nuclei in the hypothalamus. Sirtuin members regulate bone

formation through estrogen and inflammation. SIRT1, SIRT3, SIRT6 slow down the aging process in endothelial aging and arterial hypertension with their vasoprotective properties. While SIRT1 and SIRT6 activate brown fat tissue in thermogenesis, SIRT 7 has the opposite effect. Again, SIRT1 and 6 have anti-inflammatory effects, while SIRT7 inhibits inflammation in white adipose tissue.

It is necessary to determine the biological regulation mechanism of drugs in different diseases and health conditions in the future, to use them as potential diagnostic and prognosis biomarkers for certain diseases with more comprehensive studies, and to evaluate their effectiveness with basic and clinical studies using agonists and inhibitors.

Panel 3: The Role of Multifocal Evaluations in Visual Electrophysiology in Diagnosis and Treatment

Panel 3.1: How Are Multifocal ERG and VEP Recordings Performed, and Why Do We Need to Evaluate the Findings?

Hakkı Oktay Seymen

Istanbul University-Cerrahpaşa, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

With the advancement of modern techniques, the detailed examination of the visual system and the evaluation of its physiological functions have become more precise and comprehensive. Two of these methods, multifocal electroretinography (ERG) and visual evoked potentials (VEP), play a significant role in both functional and structural analysis of the visual system and visual pathways. Multifocal ERG is a test that records the electrical activities of retinal cells and evaluates the functions of different retinal regions separately. This test is especially used to determine the physiological state of the macular and peripheral regions of the eye.

Multifocal ERG recordings are performed in four stages. The first stage is the preparation phase. Before starting the test, the patient's pupils are dilated, and local anesthetic drops are applied to the eyes to relax the patient. This step minimizes light reflexes and possible eye movements, ensuring accurate recordings. The second stage is the electrode placement phase. Electrodes are placed on the surface of the eye, as well as on the patient's face and head. These electrodes are necessary to record the electrical signals generated by the retina. The third phase is the test application phase. The patient watches varying light patterns that provide continuously changing light stimuli to the eye on a screen. These light patterns stimulate different regions of the retina, attempting to elicit electrical responses from each region. During the test, it is crucial for the patient to focus on a fixed point and minimize eye movements to ensure accurate test results. Additionally, the eyes are monitored by a camera within the recording system. The final phase is the recording phase. The

electrical responses obtained are recorded by a computer. These recordings are then analyzed by a specialist. Multifocal ERG allows for the examination of each retinal region separately, enabling the clear detection of any areas of vision loss if present.

VEP is a method that measures how well the visual pathways work in transmitting and processing visual information from the eye to the brain cortex. It evaluates the function of the nerve pathways from the optic nerve to the visual center in the occipital region of the brain. Like ERG recordings, VEP recordings are performed in four stages. The first stage is the preparation phase. The patient prepares to watch visual stimuli displayed on a screen in a dimly lit room. No medication needs to be applied to the eyes for these recordings. The second stage is the electrode placement phase. Electrodes are placed on the patient's scalp, especially on the occipital region. These electrodes record the brain's electrical responses to visual stimuli. The third stage is the test application phase. The patient is shown rapidly changing patterns, usually black-and-white checkerboards or flashlights, on a screen. The responses of the eyes to these visual stimuli are recorded. The fourth stage is the recording phase. The electrical responses transmitted to the brain's visual cortex are recorded. The timing of the signals transmitted to the brain is analyzed, and the information obtained about the nerve pathways is evaluated. Specifically, any delay or abnormalities in nerve conduction are checked.

As a result of the detailed examination of the retina and visual pathways through multifocal methods, ERG provides information about physiological and pathophysiological conditions in the retinal layer, while VEP allows for the evaluation of the visual pathways starting from ganglion cells, the optic nerve bundles, the brain regions involved in visual processing, and the visual centers the optic nerve reaches. Both tests allow us to assess the entire visual physiology. If there is a vision loss problem, these tests help determine the source of the loss. They make it possible to differentiate whether the problem lies in the retinas, optic nerves, or visual centers in the brain.

The system (Multifocal ERG and VEP), which provides highly valuable clinical information, is used in the following areas. First, it can be used in the early diagnosis of diseases. Functional disorders in the visual system can be detected before clinical symptoms appear. Diseases such as glaucoma, macular degeneration, or multiple sclerosis can be diagnosed early with these tests. This gives the physician the opportunity to intervene early, slowing or stopping the progression of the disease. The information obtained from the system can also be used to monitor the treatment process of the disease. In retinal diseases, especially multifocal ERG allows for a comparison of changes in the retina before and after treatment. Thus, the effectiveness of the treatment can be evaluated. In conditions like optic neuritis, whether there is an improvement in nerve conduction can be assessed with VEP recordings. When the electrical responses in damaged regions of

the retina decrease, ERG can predict whether the vision loss is permanent. The long-term consequences of delays in nerve conduction in the visual pathways are evaluated with VEP. While multifocal ERG precisely localizes which region of the retina has a functional disorder, VEP determines whether there is a disruption in the visual pathways and centers. In this way, it becomes possible to determine the stage of the disease and which region is affected.

Multifocal ERG and VEP play a critical role in the functional analysis of the visual system. These tests are used to reveal the physiology of the visual system between the retina and the visual centers, detect any functional disorders at any stage of the visual pathways, make an early diagnosis, monitor the treatment process, and predict the progression of the disease. Careful evaluation of these findings not only helps to understand the cause of vision loss but also provides an important source of information for offering patients individualized treatment plans. Therefore, the accurate and comprehensive interpretation of findings from multifocal ERG and VEP recordings is an area that requires expertise. The information obtained from the system is of great value in the management of diseases affecting the visual system.

Panel 3.2: The Role of Specific Visual Electrophysiological Tests in Ophthalmological and Neurological Diseases

Aykut Oruç

Istanbul University-Cerrahpaşa, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

Visual electrophysiology tests play an important role in the diagnosis and treatment follow-up of ophthalmological and neurological diseases. The most current of these tests that provide functional assessment of the retina and visual pathways are Multifocal Electroretinogram (mERG), Multifocal Visual Evoked Potentials (mVEP), Photopic Negative Response (PhNR), Flicker ERG, Sensory Electrooculogram (EOG) and Dynamic EOG. Multifocal ERG is the electrophysiological gold standard for early detection of Diabetic Retinopathy and treatment follow-up in Retinopathy of Prematurity (ROP) by evaluating retinal functions regionally. It is also important for the follow-up of the disease and the evaluation of treatment response.

Multifocal VEP is extremely guiding in the diagnosis of optic nerve diseases such as Optic Neuropathy, Multiple Sclerosis (MS) and glaucoma by evaluating the function of the visual pathways at the level of different visual cortex areas. Photopic Negative Response (PhNR) measures the function of retinal ganglion cells and optic nerve. It plays an important role in the early diagnosis and follow-up of diseases related to ganglion cell damage such as vitelliform diseases, Diabetic Retinopathy and glaucoma. Flicker ERG, on the other hand, evaluates the oscillatory potentials and frequency

spectrum ranges of retinal photoreceptors, especially cone cells, in detail and detects cone dysfunction especially in the early stages.

Sensory EOG is considered the gold standard in the differential diagnosis of diseases such as Retinitis Pigmentosa and cone dystrophies by evaluating the function of the retinal pigment epithelium (RPE). This test, which also plays a critical role in genetic retinal diseases, is of great importance in the early detection of RPE dysfunction. RPE dysfunction is a prominent finding in such diseases and Sensory EOG is an important tool in the diagnosis of these pathologies and in the process of monitoring the course of the disease. Dynamic EOG is used to evaluate eye movements and the interaction of the vestibular system with visual stimuli, especially in the diagnosis of balance disorders, nystagmus and vestibular diseases. Dynamic EOG also allows visual attention tests to be performed on patients by measuring how the eye adapts to rapidly changing environments. Each of these tests plays a key role in the early diagnosis of ophthalmological and neurological diseases and in monitoring the response to treatment.

Panel 3.3: Retinal Cell Network Electrophysiology

Kadriye Yağmur Oruç

Istanbul University-Cerrahpaşa, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

The complex and harmonious electrophysiological functioning of the cell groups in the retinal layers that provide the visual function of the eye forms the basis of the visual system. In this process, the retinal pigment epithelium (RPE), rod and cone photoreceptors, bipolar, horizontal, amacrine, ganglion and Müller cells play a strategic role. The retinal pigment epithelium (RPE) supports the survival and maintenance of functions of the adjacent neural retina by providing the necessary microenvironment for the photoreceptors to generate electrophysiological responses. When the RPE is stimulated by light, it gives electrophysiological responses just like the neural retina through the ion channels on it. The sensory electrooculography (sEOG) test is used to evaluate RPE functionality. Rod and cone photoreceptors are responsible for converting low and high light stimuli into electrical signals and transmitting these signals electrotonically to the lower layers. Light activates photopigments and causes hyperpolarization. It is possible to evaluate the responses of photoreceptors with electroretinographic tests (ERG).

Bipolar cells transmit the signals they receive from photoreceptors to ganglion cells. On-Bipolar and Off-Bipolar cells produce excitatory or inhibitory responses depending on the light intensity and provide the formation of contrast perception by separating the signals in the retinal circuit. While the functions of photoreceptors and On-bipolar cells are analyzed with the a and b waves, b/a ratio in ERG tests, Off-bipolar cell function is evaluated with c waves. The

feed-forward circuits of horizontal cells (GABAergic) regulate the interactions with neighboring rod cells and the feedback circuits (glycinergic) regulate the interactions between neighboring cone cells and provide lateral inhibition in the retina. It basically acts as a modulator that increases contrast sensitivity. Amacrine cells establish synaptic connections with ganglion and bipolar cells and control the input and output of electrical signals. GABAergic amacrine cells, which create hyperpolarization on off-ganglia, are key to processing peripheral vision. Glycinergic amacrine cells, on the other hand, regulate central vision by creating hyperpolarization on on-ganglia and bipolar cells. Ganglion cells are the main nerve cells that provides an output to the visual cortex and transmit visual information to the brain by generating action potentials. These cells are affected by both congenital and many sporadic diseases such as glaucoma and diabetic retinopathy, and pattern-ERG tests are used to evaluate their functions. Müller cells support the structural integrity of the retina by providing potassium siphoning. All these cell interactions ensure the continuity of the ocular circuit.

Panel 4: Kinesiology and Biomechanics in the Past, Present, Future

Panel 4.1: Human Functional Bioengineering

Evren Yaşar

Yozgat Bozok University, Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Yozgat, Türkiye

The field of Physical Medicine and Rehabilitation (PM&R) can be seen as a “human function engineer,” focusing on restoring and enhancing the body’s functional capacities. PM&R specialists are dedicated to regaining musculoskeletal, neurological, and cardiopulmonary functions. Today, the integration of robotic technology, artificial intelligence (AI), virtual reality (VR), and biomechanical analysis systems into rehabilitation has expanded PM&R’s scope, revolutionizing treatment methods.

Robotic rehabilitation, particularly exoskeleton devices, assists in regaining limb functions after stroke or spinal injuries. These devices support patient mobility and ensure maximum engagement throughout the rehabilitation process. Virtual reality and AI further enhance motivation, offering real-time analysis and personalized treatment based on individual movement patterns. This approach accelerates the rehabilitation process, yielding objective, measurable outcomes rooted in data-driven decisions.

In the future, PM&R specialists will embody the role of “human function engineers” even more profoundly, crafting treatments that enhance patients’ functional abilities. Real-time data tracking and analysis systems will tailor each patient’s treatment journey to their specific needs, creating uniquely effective pathways. This

engineering-based approach by PM&R specialists will extend beyond merely restoring current functions; it will also improve life quality and employ preventive strategies to minimize potential functional loss. Thus, PM&R will emerge as a pivotal field guiding individuals to reach their highest potential, offering significant functional gains and advancing human capability within the rehabilitative sciences.

Panel 4.2: The Concept of Ability Laboratory in the Current Physical Medicine and Rehabilitation Model

Berke Aras

University of Health Sciences, Ankara Bilkent City Hospital, Department of Physical Medicine and Rehabilitation, Ankara, Türkiye

In the field of Physical Medicine and Rehabilitation (PM&R), the concept of the “Ability Laboratory” refers to specialized areas created to assess, evaluate, and improve patients’ physical abilities. These laboratories are becoming increasingly significant in today’s rehabilitation models. Ability laboratories provide a comprehensive analysis of the movement capacities of patients, particularly those with neurological, orthopedic, and musculoskeletal disorders, thus enabling treatment processes to be more targeted and efficient. In ability laboratories, patients’ physical capacities are evaluated based on parameters such as strength, flexibility, balance, endurance, coordination, and gait. Advanced technologies are utilized in these evaluations. For instance, motion analysis systems objectively analyze patients’ gait and posture, identifying which muscle groups are weak or which movements are incorrect. Strength measurement devices are used to assess muscle power, while virtual reality (VR) applications help patients improve their balance and coordination skills. Ability laboratories are also supported by artificial intelligence (AI) and data analysis systems, providing opportunities for personalized treatment processes. The data obtained play a crucial role in setting rehabilitation goals and monitoring patient progress. Thus, a customized treatment program can be prepared according to each patient’s specific needs.

One of the world’s leading rehabilitation hospitals, the Shirley Ryan AbilityLab, offers one of the most comprehensive and advanced examples of the “Ability Laboratory” concept. Founded in Chicago in 2017, this center combines traditional hospital and research center models, becoming the first hospital to integrate rehabilitation processes directly with clinical and scientific research. Shirley Ryan AbilityLab aims not only to treat patients but also to maximize their functional capabilities. These laboratories are used as guides at every stage of the treatment process. Following the initial assessment, reevaluations are conducted as treatment progresses, and the treatment program is updated based on patient development. In conclusion, the concept of the

ability laboratory represents a modern approach within the PM&R field. These laboratories are specifically designed to enable patients to lead more independent and quality lives and reinforce PM&R's engineering-based role as a "human function engineer."

Panel 4.3: Innovations in Sports Performance

Özlem Karasimav

İzmir City Hospital, Department of Sports Medicine, İzmir, Türkiye

Sports performance analysis has evolved significantly from basic statistical analysis to complex predictive modeling and real-time decision-making systems, including artificial intelligence and sensorial systems. These advances in computerized power through sports biomechanics facilitate tracking the movements of athlete, analyzing performance, optimizing training loads, predicting the risk of sports injuries (and thus injury prevention), and also identifying the talents. Wearable technology and real-time feedback programs stand out as promising solutions for the partiality of precision and accuracy of conventional performance analyzing methods. Motion capture technology is the basis of these programs involving cinematographic, electromagnetic and computerized visual versions. Different sensor types are defined focusing on various purposes:

Inertial measurement units include accelerometers, gyroscopes, and sometimes magnetometers to measure acceleration, angular velocity, and magnetic field orientation.

Ultra-wide band sensors use radio waves to measure distances and track positions with high precision.

Local position measurement systems use radar wave reflections for positioning.

Global navigation satellite system sensors use satellite signals for precise positioning, suitable for large motion ranges.

The collected data through these sensorial systems are transmitted wirelessly to a central processing unit for real-time analysis or recorded for later-operation. The processing tracks the steps of calibration, filtering, pose estimation, zero-velocity updates and finally presents a kinematic model. This model provides valuable insights for performance optimization, technique improvement, and injury prevention with the advantage of being applicable to a wide range of sports types. Despite the advantages, each has also own limitations such as occlusion, fixed capture areas, the need for large-scale sport-specific datasets, electromagnetic interference and dis/harmony with environmental factors, shaping the goals of future perspectives. Artificial intelligence and sensorial systems seem to be an integral part of sports physiology and medicine, helping to enhance athletic performance and healthcare.

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Oral Communications (OC01 – OC71)

OC-01

Investigation of the Effects of Rivastigmine on Learning-Memory Impairment and Anxiety Accompanying with Age-Varying Seizure Severity in *Wag/Rij* Rats with Genetic Absence Epilepsy in Relation to Trpv1 Channels

Elif Türkdönmez Ak¹, Büşra Okuyucu², Gökhan Arslan², Erdal Ağar², Mustafa Ayyıldız²

¹Department of Physiology, Faculty of Medicine, University of Ordu, Ordu, Türkiye

²Department of Physiology, Faculty of Medicine, University of Ondokuz Mayıs, Samsun, Türkiye

AIM: Absence epilepsy and psychiatric disorders have a bidirectional relationship and also different severity at various ages. Also, recent studies have shown that Trpv1 channel expression is altered in the diseases mentioned. The present study aims to investigate whether rivastigmine (RIVA), an acetylcholinesterase inhibitor, affects age-related changes in spike-wave discharges (SWDs), learning-memory problems, anxiety, and changes in Trpv1 gene expression levels in *WAG/Rij* rats.

METHODS: In the study (OMU-HADYEK 2024/19), 5- and 13-month-old *WAG/Rij* (n=70) and only 5-month-old Wistar (n=14) male rats were used. Initially, electrophysiologic recordings were obtained from *WAG/Rij* rats after a single dose of 0.125 and 2 mg/kg injection and 24 hours after the end of the 14-day (long-term) administration of only 2 mg/kg dose to determine the effect of RIVA on SWDs. In the next step, both *WAG/Rij* and Wistar rats were subjected to y-maze and elevated-plus testing 24 hours after long-term administration. Following the behavioral tests, right-cortex and right-hippocampus of the rats were removed to used in the qPCR. Statistically, according to the results of Shapiro-Wilk test, t-test or one-way ANOVA test was applied.

RESULTS: RIVA showed similar effects in all *WAG/Rij* rats. 0.125 mg/kg was insignificant, whereas 2 mg/kg almost completely abolished SWDs (p<0.001) and reduced mean durations of SWDs (p<0.05). In the long-term; increased the number of SWDs and decreased the mean duration of SWDs (p<0.001), decreased short-term memory performance (p<0.05), and decreased anxiety (p<0.05). The Trpv1 gene levels; decreased in all *WAG/Rij* rat groups and increased in Wistar rats (p<0.001).

CONCLUSIONS: RIVA shows similar effects in all age groups: anti-epileptic at acute doses and pro-epileptic in long-term. RIVA negatively affected learning-memory while decreasing anxiety in *WAG/Rij* rats. Regarding Trpv1 gene expressions, *WAG/Rij* and Wistar rats showed opposing effects. We speculate that the effect of RIVA on absence seizures and accompanying memory impairment with anxiety may be Trpv1-channel related.

Keywords: Age, Absence epilepsy, Comorbidity, Spike-wave discharges, Rivastigmine, Trpv1-channel

OC-02

The Effect of Venlafaxine on Seizure Activity in Genetically Absence Epileptic *WAG/Rij* Rats: The Role of Adrenergic Receptors in This Effect

Burcu Hatipoğlu¹, Gökhan Arslan¹, Ayhan Bozkurt¹, Yonca Betil Kabak², Sinem İnal², Erdal Ağar¹, Mustafa Ayyıldız¹

¹Department of Physiology, Faculty of Medicine, University of Ondokuz Mayıs, Samsun, Türkiye

²Department of Pathology, Faculty of Veterinary Medicine, University of Ondokuz Mayıs, Samsun, Türkiye

AIM: To investigate the effects of venlafaxine on spike-wave discharges (SWDs) in *WAG/Rij* rats, the role of adrenergic receptors in this effect, and the impact of venlafaxine on GABA-A receptor $\gamma 2$ (GABAAR $\gamma 2$) subunit expression in brain tissues.

METHODS: Male *WAG/Rij* rats (n=102) aged 8-9 months were divided into 16 groups. Tripolar electrodes were implanted to rats for obtaining electrocorticogram (ECoG) recordings. The control group received sterile saline, while the venlafaxine groups received 12.5, 25, and 50 mg/kg doses of venlafaxine intraperitoneally. To investigate the role of adrenergic receptors, the non-specific alpha adrenergic receptor blocker phentolamine (10 and 30 μ g) and the non-specific beta adrenergic receptor blocker propranolol (30 μ g) were administered intracerebroventricularly before venlafaxine. Additionally, atomoxetine, a norepinephrine reuptake inhibitor, was used to determine the effects of increased norepinephrine. The long-term effects of venlafaxine (14 days) on absence seizures and GABAAR $\gamma 2$ subunit expression in the somatosensory cortex, hippocampus, and thalamus were also analyzed.

RESULTS: Single dose of 25 mg/kg venlafaxine decreased the number of SWD for 75 minutes, while 50 mg/kg venlafaxine decreased it for 90 minutes. The combination of venlafaxine (50 mg/kg) and phentolamine (10 μ g) enhanced the duration of venlafaxine's effect. The effect of venlafaxine did not change when combined with propranolol. Atomoxetine increased both the number and mean duration of SWDs at the doses of 12 mg/kg and 24 mg/kg. Long-term venlafaxine administration decreased both the number and mean duration of SWDs. According to western blot and immunohistochemistry analyses, GABAAR $\gamma 2$ subunit expressions decreased only in the thalamus.

CONCLUSIONS: Our results suggest that the adrenergic system does not play a role in the antiepileptic effect of venlafaxine. Additionally, the antiepileptic effect observed with long-term venlafaxine administration may be due to the decreased expression of GABAAR $\gamma 2$ subunit in the thalamus.

Keywords: Absence epilepsy, GABA-A receptor, Phentolamine, Propranolol, Spike-wave discharge, Venlafaxine

OC-03

Effect of Cardioselective Beta Blocker Metoprolol on Epileptiform Activity Induced by Penicillin in Rats

Ali Koray Kaya¹, Fatih Mehmet Gökçe², Sinan Saral²

¹Kutahya Health Sciences University, Faculty of Medicine, Department of Physiology, Kutahya, Türkiye

²Recep Tayyip Erdoğan University, Faculty of Medicine, Department of Physiology, Rize, Türkiye

AIM: Limited information is available on the effects of the cardioselective beta-blocker metoprolol, which is commonly used in the treatment of cardiac and hypertensive problems in epilepsy patients, on epileptic activity. The aim of this study is to shed light on the clinical review of metoprolol treatment in patients with epilepsy by determining whether its effects on epileptic activity are proconvulsant or anticonvulsant.

METHODS: For this purpose, fourteen male Sprague-Dawley rats were divided into two groups with 7 rats in each group. The first group (SHAM group) received a single dose of penicillin (500 IU, 2.5 µL, i.c.) and 0.9% saline (0.5 mL, i.p.). The second group (Treatment group) received a single dose of penicillin (500 IU, 2.5 µL, i.c.) and metoprolol (0.5 mL, 50 mg/kg, i.p.). Metoprolol was administered 30 minutes after the penicillin injection, as the epileptic spikes were expected to become prominent. Each rat was fixed in a stereotaxic apparatus and ECoG recordings were taken for 240 minutes with electrodes placed on the brain tissue. The evaluation of the recording data was based on the frequency and amplitudes of the epileptic spikes. The average frequency was calculated as spikes/min, and the average amplitude was calculated as µV in 10-minute periods and included in the statistics.

RESULTS: The two independent groups, SHAM and Treatment, were statistically compared based on the average spike frequency and amplitude values in 10-minute periods, and no statistically significant result was obtained.

CONCLUSIONS: In conclusion, further studies focusing on different dose ranges and cellular mechanisms in the brain are needed to fully understand the effect of metoprolol on epileptic activity.

Keywords: Epilepsy, Metoprolol, Penicillin, Rat

OC-04

The Effects of Prebiotic and Probiotic Supplements Administered with Lacosamide on Epileptic Seizures in a Post-traumatic Epilepsy Model

Uğur Aykın, Cumaali Demirtaş, Sezin Kiroğlu Uzun, Mehmet Yıldırım

University of Health Sciences, Hamidiye Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

AIM: Although there is currently no effective treatment for post-traumatic epilepsies, numerous studies in recent years have shown a relationship between dysbiosis and epilepsy. This study aims to investigate the contribution of prebiotic, probiotic, and synbiotic supplements to the effectiveness of lacosamide (LCM) on epileptic seizures in a rat model of post-traumatic epilepsy (PTE).

METHODS: Traumatic brain injury was induced in Sprague-Dawley rats using the weight-drop method, and EEG electrodes were implanted. Seven days later, a PTE model was induced with intraperitoneal injections of subconvulsant doses of pentylenetetrazol (PTZ, 30+15+15 mg/kg) at 30-minute intervals (SBÜ HADYK 2023-09/03). Subconvulsant PTZ injections were repeated four times at one-week intervals, and behavioral parameters related to epileptic seizures were recorded along with EEG. Starting before the first PTZ application, 30 mg/kg LCM or LCM combined with 1 g/kg inuline, 10 x 10⁹/kg VSL#3, or a combination of 1 g/kg inulin + 10 x 10⁹/kg VSL#3 were administered orally via gavage for 28 days. Data were statistically analyzed using the Kruskal-Wallis test followed by the Mann-Whitney U test.

RESULTS: When comparing the group treated with LCM and probiotics to the group treated with LCM alone, it was found that probiotics led to a reduction in total seizure duration (p<0.05), and an increase in the subconvulsant PTZ dose required to initiate seizures and seizure onset latency (p<0.05).

CONCLUSIONS: It was concluded that probiotics in the form of VSL#3 administered with LCM enhanced the antiepileptic drug efficacy against epileptic seizures related to PTE facilitated by PTZ.

Keywords: Lacosamide, Post-traumatic epilepsy, Prebiotic, Probiotic

OC-05

Investigation of Behavioral Properties of Dentate Gyrus Prodynorphin Neurons in Alzheimer's Model Transgenic Mice

Habibe Gören¹, Yavuz Yavuz¹, Bayram Yılmaz²

¹Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

² Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Alzheimer's Disease (AD) is marked by cognitive decline and abnormal protein accumulation. The opioid system, particularly prodynorphin (Pdyn) neurons, plays essential roles in various processes; however, its role in AD is poorly understood. This study investigates the relationship between DGPdyn neurons and AD, crucial for learning and memory.

METHODS: The experimental design included control (GFP-PBS and GFP-A β), chemogenetic activation (hM3D-PBS and hM3D-A β), chemogenetic inhibition (hM4D-PBS and hM4D-A β), optogenetic (GFP-PBS, ChR2-PBS, ChR2-A β) groups. Alzheimer's Disease (AD) was modeled by administering amyloid beta (A β) 1-42 intracerebroventricularly to 3-4 month-old male Pdyn-Cre mice. DGPdyn neurons were selectively activated and inhibited using chemogenetic and optogenetic techniques. Following manipulations, animals were taken into behavioral tests: Open Field (OF) for locomotor activity, Elevated Plus Maze (EPM) for anxiety-like behavior, and Novel Object Recognition (NOR) for memory. Statistical analysis was performed using Two-way ANOVA and Tukey's and Bonferroni's tests, with $p < 0.05$ considered significant.

RESULTS: In the PBS group, chronic inhibition and activation of DGPdyn neurons significantly decreased center entries in the OF test ($p < 0.05$). In contrast, in the A β group, only chemogenetic activation of DGPdyn neurons resulted in a significant reduction in center entries ($p < 0.05$). Additionally, inhibition of DGPdyn neurons in the PBS group impaired novel object exploration, negatively affecting both short-long terms ($p < 0.01$).

CONCLUSIONS: These findings suggest that A β accumulation may disrupt synaptic transmission in DGPdyn neurons, thereby impacting locomotor activity. DGPdyn neurons likely play a critical role in memory and cognitive processes, with their functions altered by the presence of amyloid beta.

Keywords: Alzheimer's Disease, Prodynorphin Neurons, Optogenetics, Chemogenetics

OC-06

Evaluation of the Effect of Asprosin on Pain and Behavioral Functions in a Mouse Model of Experimental Migraine

Çağdaş Kocal¹, Muhammed Adam², Orhan Sayın³, Ahmet Sait Bozyıl³, Ferah Bulut², Mehtap Pervin³, Mete Özcan², Sibel Özcan¹

¹Firat University, Faculty of Medicine, Department of Anesthesiology, Elazığ, Türkiye

² Firat University, Faculty of Medicine, Department of Biophysics, Elazığ, Türkiye

³Firat University, Faculty of Medicine, Department of Physiology, Elazığ, Türkiye

AIM: Migraine is a type of headache that is localized on one side of the head and recurs periodically. The endocrine system, particularly adipose tissue, plays crucial role in pain perception and modulation. Dysregulations in the endocrine system and interactions between hormones and pain have been associated with the development of chronic pain conditions. The aim of this study is to investigate the effects of asprosin, an adipokine synthesized from adipose tissue, on pain and behavioral functions in mice with an experimental migraine model.

METHODS: In this study, male Balb/C mice weighing 25-30 grams were used. To induce migraine pain nitroglycerin (NTG) was administered intraperitoneally (i.p), and sumatriptan was given to the treatment group. The mice divided into four subgroups: healthy control group, NTG group (10 mg /kg), NTG+asprosin group (10 μ g /kg), and NTG+sumatriptan group (300 μ g /kg) (n = 10 per group). Pain response was assessed using periorbital von Frey test. Behavioral functions such as motor coordination, anxiety and depression, learning and memory were evaluated using rota-rod, open field and novel object recognition test respectively. Statistical analysis of group differences was performed using One-Way ANOVA and post-hoc Tukey test.

RESULTS: In mice with migraine induced by NTG, decrease in periorbital mechanical threshold values compared to baseline values was observed. In the groups treated with sumatriptan and asprosin this effect of NTG was reversed and increase in periorbital mechanical threshold values was noted. Similarly in other behavioral test, the negative effects of migraine were mitigated by asprosin. However, the ameliorative effects of asprosin on these behavioral outcomes were not statistically significant.

CONCLUSIONS: This study suggests that asprosin may elevate pain threshold and contribute to improvements in locomotor activity and behavioral functions in mice with a migraine model. Further studies are needed to precisely elucidate the effects of asprosin on pain and behavioral functions.

Keywords: Asprosin, Migraine, Pain, Sumatriptan

OC-07

Protective Potential of Boron-Based Compounds in In Vitro Nephrotoxicity Model Induced by Gentamicin in Monkey Kidney Epithelial Cell Line

Nilgün Oksak¹, Mustafa Ünal Boyraz², Akın Yiğit³, Ahmet Kılıç⁴

¹ Harran University, Faculty of Health Sciences, Department of Physiology, Sanliurfa, Türkiye

² Harran University, Faculty of Veterinary, Department of Histology and Embryology, Sanliurfa, Türkiye

³ Harran University, Faculty of Veterinary, Department of Genetics, Sanliurfa, Türkiye

⁴ Harran University, Faculty of Arts and Sciences, Department of Chemistry, Sanliurfa, Türkiye

AIM: Gentamicin (GM), which is frequently used due to its wide range of activity and low cost, causes nephrotoxicity. In patients treated for more than one week, nephrotoxicity was found in 30% of cases. Several substances have been shown to protect against nephrotoxicity. Boron-containing compounds with anti-microbial, anti-oxidant, anti-cancer, and anti-arthritis effects have recently been used as therapeutic candidates in the medical and pharmaceutical sectors. The objective of this study was to examine the nephroprotective impact of boron compounds (T1B1 and T1B2) in an in vitro gentamicin-induced nephrotoxicity model.

METHODS: The Vero cell line, a monkey kidney epithelial cell used for in vitro nephrotoxicity, was divided into four groups: control, GM, GM/T1B1, and GM/T1B2. The GM group was treated with gentamicin IC50 dose only (50% inhibition of cell viability; 6000 µg/mL) for 72 hours. The GM/T1B1 and GM/T1B2 groups were treated with the gentamicin IC50 dose for 24 hours, and then T1B1 and T1B2 compounds were added to the same cell medium and incubated for 48 hours more. After incubation, cell viability and apoptic changes were determined by the MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) test and DAPI staining, respectively. The data was examined using a one-way ANOVA test with a significance level of $p < 0.05$.

RESULTS: T1B1 and T1B2 boron compounds significantly increased cell viability in Vero cells after in vitro gentamicin-induced nephrotoxicity ($p < 0.05$). As a result, cell viability increased from 50% to 94% with the T1B1 compound and 86% with the T1B2 compound. Furthermore, DAPI staining microscopic imaging demonstrated that these compounds diminished apoptotic indications, including cell and nucleus shrinkage and chromatin network condensation.

CONCLUSIONS: In conclusion, this study revealed for the first time that T1B1 and T1B2 compounds may exert nephroprotective effects against gentamicin-induced nephrotoxicity. After this study, an investigation will be conducted to ascertain the nephroprotective effect of these compounds in vivo.

Keywords: Boron compounds, Nephrotoxicity, Kidney epithelial cell line, Nephro-protectant

OC-08

Effects of Apelin-13 in Diabetic Kidney Injury: Analysis of Histological and Biochemical Markers

Melisa Bilaloğlu¹, Ayşe Arzu Yigit¹, Fatma Helvacioğlu², Ece Yıldırım Özkaya², Sevtap Kılınç¹

¹ Başkent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

² Başkent University, Faculty of Medicine, Department of Histology and Embryology, Ankara, Türkiye

AIM: The mortality due to kidney damage secondary to diabetes is notably high, accounting for nearly half of all chronic kidney disease cases. This study evaluates the effects of apelin, a hormone expressed in vascular endothelial and adipose tissues, on histological changes, oxidative stress, and inflammation markers in rats with diabetes-induced kidney damage.

METHODS: Thirty-two male Wistar albino rats were divided into sham, Diabetes, Apelin, and Diabetes+Apelin groups. Diabetes was induced with a single dose of 45 mg/kg intraperitoneal streptozotocin (STZ). Apelin groups received 50 µg/kg apelin-13 intraperitoneally for seven days, while the control group received saline. Post-treatment, left kidneys were analyzed histologically with hematoxylin and eosin staining, and right kidneys were assessed for total oxidant capacity (TOC), total antioxidant capacity (TAC), interleukin 1β (IL-1β), and tumor necrosis factor (TNF-α). Serum urea and creatinine levels were also measured. Statistical analysis was performed using JAMovi program, with $p < 0.05$ considered significant.

RESULTS: Tnf-α level was significantly higher in the diabetes group compared to the sham group ($p = 0.012$). While TAC level decreased significantly in those receiving only apelin compared to the sham group ($p = 0.039$), it was observed that apelin intervention in diabetes significantly increased TAC level compared to the diabetes group ($p = 0.014$). There was no significant difference between the groups in terms of urea, creatinine and IL-1β levels. Histological analysis revealed increased tubular dilation, epithelial shedding, brush border and nuclear loss in the diabetes and apelin groups compared to the sham group ($p < 0.05$).

CONCLUSIONS: Short-term apelin treatment did not significantly mitigate diabetes-induced renal damage. Degenerative changes in the diabetes groups were also observed in the apelin-only group, particularly in glomeruli and renal tubules. These results suggest the need for further research into the long-term effects of apelin on kidney function.

Keywords: Apelin, Oxidative stress, Inflammation, Kidney injury, Diabetes

OC-09

Investigation of the Effect of Metformin on Rat Bladder Smooth Muscle and the Mechanisms Mediating This Effect

Pelin Türkan¹, Gökçe Sevim Öztürk Fincan², Ayşe Meltem Sevgili¹, Burak Kayabaşı¹, Tilbenur Akyol², Sibel Dinçer¹

¹Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Gazi University, Faculty of Medicine, Department of Medical Pharmacology, Ankara, Türkiye

AIM: The effects of metformin on detrusor smooth muscle tissue are not yet fully understood. This study aims to investigate the in vitro effects of metformin on detrusor smooth muscle tissue and the possible mechanisms mediating these effects. Additionally, it seeks to contribute to the literature for its potential use in treating various diseases associated with bladder dysfunction.

METHODS: Bladder strips isolated from 12 male Wistar Albino rats were placed in an organ bath containing aerated Krebs solution and attached to a force transducer to record isometric contractions. Metformin (10^{-4} M– 3×10^{-3} M) was cumulatively applied in the presence of guanethidine and indomethacin to evaluate its effects on Electrical Field Stimulation (EFS)-mediated contraction responses in rat bladder detrusor strips. The effect of metformin (3×10^{-3} M) on carbachol-induced contraction responses was also assessed. The effect of metformin was re-evaluated in the presence of dorsomorphin (10^{-5} M, an AMP-activated protein kinase [AMPK] inhibitor), Y-27632 (10^{-5} M, a Rho-kinase inhibitor), or N(ω)-nitro-L-arginine methyl ester (L-NAME) (10^{-4} M, a Nitric Oxide Synthase [NOS] inhibitor). Data obtained from the experiments were analyzed using the SPSS 20 statistical program with Mann-Whitney U and, where appropriate, Wilcoxon tests. Results were expressed as mean \pm standard error of the mean (SEM), with $p < 0.05$ considered statistically significant.

RESULTS: Metformin did not affect EFS-mediated contraction responses. However, in the presence of dorsomorphin, an AMPK inhibitor, metformin significantly reduced contraction responses only at a concentration of 3×10^{-3} M ($p < 0.05$). The presence of the Rho-kinase pathway inhibitor Y-27632 and the NOS inhibitor L-NAME did not alter the effect of metformin. Metformin led to a reduction in cumulative carbachol-induced contraction responses in all tissues ($p < 0.05$).

CONCLUSIONS: Metformin exhibits its relaxant effects on bladder detrusor smooth muscle tissue primarily through direct smooth muscle contraction-relaxation pathways, independent of neural stimulation.

Keywords: Metformin, Detrusor, Contraction, AMPK, Rho-kinase, L-NAME.

OC-10

Phoenixin-14 Administration Acts Protective Role in Rats with Experimental Acute Kidney Injury Model

Samet Öz¹, Mehmet Refik Bahar², Güldeniz Şekerçi³, Aslı Çetin⁴, Suat Tekin³

¹Osmaniye Korkut Ata University, Vocational School of Health Services, Veterinary Medicine Department, Osmaniye, Türkiye

²Osmaniye Korkut Ata University, Faculty of Health Sciences, Department of Nutrition and Dietetics, Osmaniye, Türkiye

³Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

⁴Inonu University, Faculty of Medicine, Department of Histology and Embryology, Malatya, Türkiye

AIM: Acute kidney injury (AKI) caused by ischemia-reperfusion (IR) injury is characterized by inflammation and oxidative stress. Phoenixin-14 (PNX-14) is a recently discovered neuropeptide. The peptide is thought to be secreted in peripheral tissues and may exert anti-inflammatory effects. This study was conducted to investigate the effects of PNX-14 in rats with ABH model.

METHODS: In the study, 40 male Wistar Albino rats (ethics committee 2024/14-2) were divided into 4 groups as control, I/R, PNX-14 (50µg/kg) and PNX-14 (100µg/kg) (n=10). While no surgical procedure was performed in the control group, both kidneys of the animals in the other groups were subjected to ischemia for 45 minutes and reperfusion for 24 hours. In the PNX-14 (50µg/kg) and PNX-14 (100µg/kg) groups, two different doses of PNX-14 (50-100µg/kg) were administered intraperitoneally before ischemia. At the end of the experiment, the animals were sacrificed and kidney tissues were removed. MDA, SOD, CAT and GSH levels were determined in the kidney tissues. In addition, histopathologic examinations in kidney tissue were determined by immunohistochemical method. Comparisons between groups were made using Mann Whitney-U test with Bonferroni correction in SPSS program.

RESULTS: PNX-14 decreased MDA level ($p < 0.05$) and increased GSH, SOD and CAT enzyme activities ($p < 0.05$) in the kidney tissue of ABH groups. On the other hand, histological evaluation showed that the kidney tissue in the control group had a normal histological appearance, whereas in the IR group, compared to the control group, degeneration in the tubules and glomerular structures of the kidney tissue; dilatation, hemorrhage, mononuclear cell infiltration, fluid accumulation in the tubule lumen, shedding of tubule epithelial cells, vacuolization and vascular congestion in the tubules were observed. These findings were decreased in PNX-14 (50µg/kg) and PNX-14 (100µg/kg) groups ($p < 0.05$).

CONCLUSIONS: As a result of the study, PNX-14 administered intraperitoneally had protective effects against IR-induced ABH by activating antioxidant systems.

Keywords: Acute Kidney Injury, Ischemia-Reperfusion, Oxidative Stress, Phoenixin-14

OC-11

Effects of Melatonin on Trace Element and Electrolyte Levels in Acute Kidney Injury

Gülten Ateş Uluçay¹, Hatice Yorulmaz², Elif Özkök³, İ. Ertuğrul Yalçın⁴, Şule Tamer⁵

¹ Istanbul Yeni Yüzyıl University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

² Halic University, Faculty of Health Sciences, , Istanbul, Türkiye

³ Istanbul University, Aziz Sancar Institute of Experimental Medicine, Department of Neuroscience, Istanbul, Türkiye

⁴ Bahçeşehir University, Faculty of Engineering and Natural Sciences, Department of Civil Engineering, Istanbul, Türkiye

⁵ Istanbul University, Medical Faculty, Department of Physiology, Istanbul, Türkiye

AIM: Acute kidney injury is a case that occur due to many reasons such as sepsis, obstruction, nephrotoxic substances. The factor that causes apoptosis, necrosis and ferroptosis along with the nephron damage has been investigated but has not been elucidated yet. Melatonin is a powerful endogenous antioxidant and has many pleiotropic effects such as anti-inflammation. It protects from cell deaths due to iron accumulation such as ferroptosis and scavenges free radicals. Trace elements participate in enzyme structure as coenzymes. Therefore, they play an important role in antioxidant enzymatic reactions. Electrolytes affect the distribution of body fluids that change in the provision of homeostasis in septic shock. In this study we aimed to investigate the effects of melatonin on trace element and electrolyte in renal tissue in rats induced with lipopolysaccharide (LPS).

METHODS: Adult male Sprague dawley rats were divided into 4 groups; control, LPS(20 mg/kg i.p.), melatonin(10 mg/kg i.p.x3), melatonin+LPS. Rats were decapitated 6 hours after the first injection and blood samples were collected from the heart. Blood urea nitrogen (BUN) values were evaluated by auto-analyzers. Sodium, potassium, calcium, magnesium, iron, copper, zinc and selenium tissue element levels were measured by inductively coupled plasma optical emission spectroscopy technique(ICP-OES). One-way analysis of variance and Tukey tests were used for statistics.

RESULTS: It was observed that sodium, potassium, magnesium, calcium, iron, copper, zinc and selenium levels increased significantly in the LPS group compared to the others ($p<0.0001$). A significant increase in BUN levels was observed in the LPS group compared to the others ($p<0.01$).

CONCLUSIONS: We suggest that sepsis causes trace element and electrolyte accumulation caused to imbalance in oxidant/antioxidant levels in kidney tissue and melatonin may have scavenged free radicals with its antioxidant effect and increased the use of elements such as zinc and selenium.

Keywords: Sepsis, Acute kidney injury, Melatonin, Electrolytes, Trace element

OC-12

Effects of Ischemic Pre-conditioning and Boldine on Renal Ischemia Reperfusion Induced Remote Brain Injury

Esra Tekin¹, Gülay Kip², Ayşegül Küçük¹, Zeynep Yiğman³, Mustafa Kavutçu⁴, Mustafa Arslan²

¹Kutahya Health Sciences University, Faculty of Medicine, Department of Physiology, Kutahya, Türkiye

²Gazi University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Ankara, Türkiye

³Gazi University, Faculty of Medicine, Department of Histology and Embryology, Ankara, Türkiye

⁴Gazi University, Faculty of Medicine, Department of Medical Biochemistry, Ankara, Türkiye

AIM: One of the organs most affected by renal ischemia reperfusion (I/R) injury is brain. The aim of current study is to evaluate the effects of boldine and ischemic pre-conditioning on renal I/R induced brain damage via apoptotic, pyroptotic and inflammatory pathways.

METHODS: 5 groups (n=6) were created with rats: sham, renal I/R, pre-conditioning+renal I/R, boldine+renal I/R and boldine+pre-conditioning+renal I/R. 45 minutes of ischemia and 24 hours of reperfusion were applied. Pre-conditioning was performed with 3 sets; 2 minutes ischemia/5 minutes reperfusion. Boldine was applied intraperitoneally at dose of 20 mg/kg/day during 7 days. Total brain Bax, Bcl-2, cleaved caspase 3, Nrf2, NLRP3 and Gasdermin D levels were evaluated by Western blot. IL-2, TNF- α , IL-6 and IL-10 levels were evaluated by ELISA. Hematoxylin-eosin staining was performed and p53 and NF- κ B expressions were evaluated immunohistochemically. Kruskal Wallis and post hoc Mann Whitney U test with Bonferroni correction was applied.

RESULTS: Bax/Bcl-2 ratio increased in other groups compared to sham, and decreased with boldine and pre-conditioning ($p<0.05$). Cleaved caspase 3 increased in other groups compared to sham ($p<0.05$). While Nrf2 was low, NLRP3 was high in I/R group ($p<0.05$). Gasdermin D was similar in all groups ($p>0.05$). IL-2 was found to be high in I/R group, while IL-10 was low ($p<0.05$). TNF- α and IL-6 did not statistically significant ($p>0.05$). Tubular necrosis, cytoplasmic vacuole formation and hemorrhage were reduced by boldine and pre-conditioning ($p<0.05$). Number of degenerated neurons in somatosensory cortex, which increased in I/R, was reduced by boldine ($p<0.05$). p53 and NF- κ B increased with I/R and decreased with boldine and pre-conditioning ($p<0.05$).

CONCLUSIONS: The decrease in apoptotic, pyroptotic and inflammatory markers were evaluated as positive effects of boldine and pre-conditioning. It was concluded that boldine may be a potential treatment and/or prophylaxy agent.

This study was supported by Gazi University (TGA-2023-8829).

Keywords: Renal ischemia reperfusion injury, Boldine, Brain, apoptosis, Pyroptosis, Inflammation

OC-13

Effect of Cumulative Zinc Doses on Papillary Muscle Contractions and the Zinc Finger Protein ZEB1

Nilufer Akgun Unal¹, Aylin Ustun², Omer Unal³, Rasim Mogulkoc⁴,
Abdulkarim Kasim Baltaci⁴

¹Ondokuz Mayıs University, Faculty Medicine, Department of Biophysics, Samsun, Türkiye

²Selcuk University, Vocational School of Health Services, Department of Medical Services and Techniques, Konya, Türkiye

³Kirikkale University, Faculty of Medicine, Department of Physiology, Kirikkale, Türkiye

⁴Selcuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: In this study, we aimed to investigate the effect of cumulative ZnCl₂ doses on myocardial papillary muscle contractions isolated from rat hearts in vitro and the roles of ZEB1, a zinc finger protein, in this effect.

METHODS: The project protocol for the study carried out on female Wistar rats was approved by the local experimental animal ethics committee. A total of 20 female rats were randomly selected and divided into 4 equal groups. Control Group: Myocardial papillary muscle contraction recordings were taken in the animals in this group without zinc administration in Krebs solution. 1µM/L ZnCl₂ Group: The group in which myocardial papillary muscle contraction was recorded by administering 1µM/L ZnCl₂ into Krebs solution. 10 µM/L ZnCl₂ Group: The group in which myocardial papillary muscle contraction was recorded by administering 10 µM/L ZnCl₂ into Krebs solution. 100 µM/L ZnCl₂ Group: The group in which myocardial papillary muscle contraction was recorded by administering 100 µM/L ZnCl₂ into Krebs solution.

RESULTS: In the 100 µM zinc chloride group, when compared to all other groups, including the control group, there was a decrease in contraction force in both frequency-dependent parameters and pre-waiting stimuli (p<0.05) and an increase in contraction times (p<0.05). These data indicate that RyR2-mediated Ca-homeostasis is closely associated with increasing zinc doses (especially at the 100 µM zinc chloride dose). Secondly, the levels of ZEB1, a zinc finger protein, were significantly lower in the 100 µM/L ZnCl₂ group compared to the other groups (p<0.05); This suggests that high doses of zinc may be associated with increased Ca, which triggers ROS production.

CONCLUSIONS: Our data indicate that in vitro zinc administration may have a dose-dependent effect on myocardial papillary muscle contractions, with the aim of understanding zinc concentrations in the heart and uncovering new mechanisms involved in the regulation of Ca dynamics in cardiac tissue.

Keywords: Zinc, ZEB1, Papillary muscle, Oxidative stress, Excitation-contraction coupling

OC-14

Effects of GLP-1 Receptor Agonist on SIRT-1/PGC-1α Signaling Pathway in Isoprenaline-Induced Takotsubo Cardiomyopathy in Ovariectomized Female Rats

Sefa Özdoğan¹, Nazmiye Sultan Özdoğan², Naile Eriş Gündül³, Ahmet Avcı³, Hale Sayan Özçmak¹

¹Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Physiology, Zonguldak, Türkiye

²Bursa Uludağ University, Faculty of Veterinary Medicine, Term IV Student, Bursa, Türkiye

³Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Cardiology, Zonguldak, Türkiye

AIM: Takotsubo syndrome (TTS) is a temporary acute heart failure condition caused by oxidative tissue damage from catecholamines released due to severe stress. It commonly occurs in postmenopausal women and those with diabetes. GLP-1 has been shown to impact glucose homeostasis and reduce cardiac ischemia-reperfusion injury. This study aims to assess the effects of liraglutide, a GLP-1 analogue, on cardiac oxidative stress, sirtuin-1 (SIRT1), PGC-1α levels, and echocardiographic outcomes in TTS. **METHODS:** Female rats underwent bilateral oophorectomy to model surgical menopause and were divided into three groups: Oophorectomy (OVX), TTS, and TTS+Liraglutide, then monitored for 6 weeks. TTS was induced in the TTS and TTS+Liraglutide groups with a 150 mg/kg dose of isoprenaline. Liraglutide was administered subcutaneously at 150 µg/kg/day starting 3 days before TTS induction and continued for 5 days. Echocardiography was performed at 2, 24, and 48 hours post-isoprenaline to evaluate heart function. At 48 hours, rats were sacrificed and heart tissues collected. Cardiac SIRT1 and PGC-1α levels were measured using ELISA, while oxidative stress parameters, malondialdehyde (MDA), reduced glutathione, and nitrate levels were assessed spectrophotometrically. Statistical analysis utilized Kruskal-Wallis and Dunn tests.

RESULTS: In the echocardiographic evaluations performed at 2 and 24 hours in the TTS and TTS + Liraglutide groups, it was observed that ejection fractions (EF) decreased statistically significantly compared to the control and liraglutide groups (P < 0.05), and EF returned to normal after the 48th hour. In addition, while ST segment elevations were detected in the ECG in the TTS group, liraglutide application was effective in preventing ST segment elevations (p<0.05). MDA levels in heart tissue were found to decrease in the TTS+Liraglutide group compared to the TTS group (p=0.049). While SIRT1 and PGC-1α levels were lower in the TTS group compared to other groups (respectively p=0.008 and p<0.001), an increase in these parameters was observed with liraglutide treatment (p=0.047). No significant results were found in heart weight/body weight and blood glucose levels.

CONCLUSIONS: Liraglutide pretreatment was observed to be effective in reducing the impairment of myocardial functions in a rat model of TTS-like cardiomyopathy, primarily by increasing SIRT1 and PGC-1α and reducing oxidative stress.

Keywords: GLP-1, Heart failure, Sirtuin-1, PGC-1α, Takotsubo syndrome

OC-15

Nesfatin-1 Alleviates Gastrointestinal, Cardiovascular and Nervous System Injury in Ovariectomized Rats: Role of Vagal Afferents

Merve Meriç Kahraman¹, Zarife Nigar Özdemir Kumral¹, Beyza Tarhan², Birsu Barın², Zeynep Berre Atılğan², Zeynep Elif Cıdık², Feriha Ercan³, Berrak Yeğen¹

¹Marmara University, Faculty of Medicine, Physiology Department, İstanbul, Türkiye

²Marmara University, Faculty of Medicine, İstanbul, Türkiye

³Marmara University, Faculty of Medicine, Histology and Embryology Department, İstanbul, Türkiye

AIM: Hormonal changes during menopause negatively affect female health. Nesfatin-1 (NES) expression varies by estrus cycle stages. This study aimed to investigate therapeutic potential of NES on menopause-induced gastrointestinal, nervous and cardiovascular system alterations and involvement of vagal afferents in NES-induced protective effects.

METHODS: Under anesthesia, female Sprague-Dawley rats underwent ovariectomy (OVX; n=12), sham-surgery (SX, n=12) or OVX+vagal afferent denervation with perivagal capsaicin (1%; OVX+VD; n=12). After recovery, rats were injected subcutaneously with NES (0.2 µg/kg/day) or saline for 25 days. Memory functions were evaluated with passive avoidance test, anxiety levels were measured using hole-board test. After sacrifice, serum HDL and LDL levels were measured. Aortic contractility was examined in organ bath. Myeloperoxidase (MPO) activity, malondialdehyde (MDA), glutathione (GSH), superoxide dismutase (SOD), and catalase (CAT) levels were measured in heart, liver, and brain tissues. Microscopic damage scores were assessed with Hematoxylin-Eosin-stain. Statistical analyses were performed using one-way ANOVA.

RESULTS: Liver SOD levels were lower in OVX groups compared to SX (p<0.05). Cardiac CAT levels in OVX (p<0.05) and OVX+VD (p<0.001) groups were reduced compared to SX group, while NES treatment replenished CAT levels in both OVX groups (p<0.05). Brain SOD levels were lower in OVX (p<0.01) and OVX+VD (p<0.05) groups compared to SX. NES treatment also restored brain SOD levels. Histological evaluations of liver showed moderate inflammation in OVX and OVX+VD groups, but very mild inflammation in NES groups. OVX-induced histological cardiac damage was normalized in OVX+NES, OVX+VD, and OVX+VD+NES groups. Aortic endothelial damage by ovariectomy was rectified in NES-treated groups. Reduced aortic contraction-relaxation responses in OVX group was improved with NES treatment, except in OVX+VD+NES group.

CONCLUSIONS: At post-menopausal state, NES increased antioxidant activity in the liver, brain, and heart and preserved normal histological structures, while menopause-induced disruption in aortic function was improved by NES via vagal afferent activation.

Keywords: Menopause, Nesfatin, Vagus

OC-16

Investigation Of Oxidative Stress, Inflammatory Response and Cardioprotective Effects of Antidiabetic Liraglutide and Empagliflozin in Experimental Diabetic Rats

Cemre Uçar Ekin¹, Hüda Oflazoğlu Diken¹, Nazan Baksi²

¹ Dicle University, Faculty of Medicine, Department of Physiology, Diyarbakir, Türkiye

² Dicle University, Faculty of Veterinary, Department of Basic Sciences, Medicine Department of Laboratory Animals, Diyarbakir, Türkiye

AIM: This study aimed to investigate and compare effects of antidiabetic drugs liraglutide and empagliflozin on oxidative stress, inflammation markers, and cardiovascular complications in rats with induced diabetes mellitus (DM).

METHODS: 37 male Wistar Albino rats were divided into four groups: Control (n=7), DM control (n=10), DM + Liraglutide (0.6 mg/kg, subcutaneous), DM + Empagliflozin (30 mg/kg, oral gavage). Diabetes was induced using 110 mg/kg intraperitoneal nicotinamide followed by 60 mg/kg streptozotocin. Treatment was administered for 8 weeks, after which final weights and fasting blood glucose levels were measured. Blood samples were taken from the caudal vein under anesthesia, and levels of tumor necrosis factor-α (TNF-α), interleukin-1 (IL-1), malondialdehyde (MDA), superoxide dismutase (SOD), advanced glycation end products (AGEs), and insulin were determined. Heart and coronary artery tissues were also examined histopathologically.

RESULTS: Compared to healthy controls, DM control group exhibited significantly increased levels of FBG, AGE, IL-1, TNF-α, and MDA (p<0.01), while insulin and SOD levels were significantly reduced (p<0.01). Both liraglutide and empagliflozin treatments brought blood glucose levels closer to those of controls. Both drugs significantly decreased levels of TNF-α, IL-1, and AGEs (p<0.01) and also reduced serum MDA levels (p=0.03, p<0.01). SOD levels increased in treatment groups (p<0.05), only liraglutide treatment led to an increase in insulin levels (p<0.01). Histopathological analysis revealed that both drugs significantly improved structural changes, fibrosis, and inflammation caused by DM, with empagliflozin demonstrating a more pronounced positive effect on the myocardium compared to liraglutide.

CONCLUSIONS: Liraglutide and empagliflozin positively influence cardiovascular complications induced by DM. By alleviating oxidative stress and inflammation, they help preserve cardiac and coronary artery structures. It can be concluded that both drugs may prevent the development of cardiovascular complications in diabetic patients. This study was supported by Dicle University Scientific Research Projects Coordination with project number SBE.22.002.

Keywords: Diabetes mellitus, Cardioprotective effect, Liraglutide, Empagliflozin

OC-17

Investigation of The Effects of Granulocytes on Hemostasis by Optical Aggregometer and Thromboelastogram

Fatma Özer¹, Öznur Gürel¹, Sueda Güneş¹, Didem Çakırsoy Akyöney², Digidem Yoyen-Ermis³, Engin Sagdilek⁴

¹Bursa Uludag University, Institute of Health Sciences, Department of Physiology, Bursa, Türkiye

²Bursa Uludag University, Institute of Health Sciences, Department of Medicine-Immunology, Bursa, Türkiye

³Bursa Uludag University, Faculty of Medicine, Department of Immunology, Bursa, Türkiye

⁴Bursa Uludag University, Faculty of Medicine, Department of Biophysics, Bursa, Türkiye

AIM: The term "immunothrombosis" indicates that hemostasis process affects function of the immune system and that immune system components contribute to thrombosis. In many studies, it is observed that platelet-leukocyte aggregates increase in the blood, especially in inflammatory events, and even the importance of parameters such as amount and size of these aggregates in the prognosis of cardiovascular diseases is emphasized. In this study, effects of granulocytes on hemostasis were studied with aggregometry and thromboelastogram.

METHODS: Granulocytes were separated from whole blood samples. Three different conditions of granulocytes were studied: 1-immediately after separation. 2-incubation without stimulation with lipopolysaccharide for 4 hours. 3-incubation with stimulation with lipopolysaccharide for 4 hours. Granulocytes were added to platelet-rich plasma, and the effects on platelet aggregation were studied in an aggregometer and on hemostasis in a thromboelastogram. Paired t-test and Bonferroni Test was used for comparisons.

RESULTS: In the 0th hour experiments, granulocytes significantly decreased their maximum aggregation values in ADP and collagen-stimulated aggregations compared to the control group. No effect was observed on ADP and collagen-stimulated aggregations of 4th hour stimulated and unstimulated granulocytes. In thromboelastogram experiments, 0th hour and unstimulated granulocytes did not affect hemostasis parameters, while stimulated granulocytes activated hemostasis and created a hypercoagulable state.

CONCLUSIONS: It was found that granulocytes inhibit platelet aggregation immediately after separation from whole blood, and when stimulated with LPS, a hypercoagulable state was observed in the thromboelastogram. It was observed that granulocytes may have different effects on platelets depending on time and stimulation status. It was observed that granulocytes may also be effective in the coagulation process with thromboelastogram. The finding of opposite results between the aggregometer and thromboelastogram suggested that the measurement system in thromboelastogram should be considered more accurate and reliable because it simulates in-vivo conditions better and is more compatible with other hemostasis tests and clinical situations.

Keywords: Granulocyte, Platelet, Hemostasis, Aggregometer, Thromboelastogram

OC-18

Investigation of the Efficiency of Platelet-Rich Plasma (PRP) Against Central Effects of the Experimental Aluminum Toxicity

Duygu Seren Özyilmaz, Enver Ahmet Demir, Okan Tutuk, Cemil Tümer

Hatay Mustafa Kemal University, Faculty of Medicine, Department of Physiology, Hatay, Türkiye

AIM: Aluminum (Al), it affects numerous cellular processes responsible for cellular organization and cellular transmission in the central nervous system. It also inhibits long-term potentiation. It causes learning disabilities and impairs working memory. This study aimed to investigate the effectiveness of allograft platelet-rich plasma (PRP) against the behavioral and cognitive consequences of experimental Al toxicity.

METHODS: Thirtyfour male Wistar albino rats were divided into 4 groups (Control n=7, AlCl₃ (n=9), AlCl₃+PRP (n=9), PRP (n=7). For the experimental Al toxicity model, intraperitoneal injections (saline [0.5 mL] or AlCl₃ [75mg/kg]) were administered on the first and eighth day of the experimental procedure. Oral gavage (saline [0.5 mL] or AlCl₃ [75mg/kg]) was applied for the remaining 12 days of the experimental procedure. PRP was administered intravenously (0.15 mL) to AlCl₃+PRP and PRP groups throughout the experimental procedure. In this context, locomotor activity, exploratory behavior, anxiety-like behavior and perceptual memory, as well as spatial learning and memory performances of the subject rats were evaluated with a test battery consisting of open field, light/dark field and Morris water maze tests. Evaluations were made with Kruskal-Wallis and post hoc Dunn test. (HMKÜ HADYEK, 2022/06-21).

RESULTS: Although aluminum chloride (AlCl₃) treatment weakened the locomotor activity and exploratory behavior measured by the total distance traveled and the number of rearing in the open field test, it was observed that this effect did not reach the level of statistical significance. It was also found that Al toxicity increased anxiety-like behavior, evaluated by the time spent in the bright field in the light/dark field test, compared to subjects treated with PRP, but the treatment effect of PRP did not reach the level of significance. Morris water maze test which is conducted in an aversive environment, it was observed that PRP application was found to be ineffective in mitigating the Al-related spatial memory impairment.

CONCLUSIONS: In conclusion, the potential benefits of PRP application in locomotor and cognitive disorders due to Al toxicity in rats has been demonstrated. It is understood that the protective effect of PRP on cognitive performance in Al toxicity is associated with and limited by anxiety-inducing factors.

Keywords: Aluminium, Toxicity, Platelet Rich Plasma, Learning, Memory

OC-19

Investigating the Effects of Diisobutyl Phthalate Chemical on Feeding Behavior and Obesity

Elif Maide Beyoğlu¹, Tuba Keskin², Kevser Tanbek², Süleyman Sandal²

¹Gaziosmanpaşa University, Faculty of Medicine, Department of Physiology, Tokat, Türkiye

²Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Phthalates are known as a subgroup of endocrine-disrupting chemicals widely used worldwide, implicated in causing obesity. Among these, diisobutyl phthalate (DIBP), primarily used as a plasticizer, lacks clear elucidation regarding its relationship with dietary behaviors and obesity when compared to other phthalate groups. The aim of this study is to investigate the effects of DIBP on obesity and appetite metabolism.

METHODS: In this study, 32 male Sprague Dawley rats were used. The rats were divided into a control group and three different dose groups of diisobutyl phthalate (DIBP) (0.1, 0.5, and 1 g/kg/day) (n=8 per group). DIBP was dissolved in corn oil and administered orally via gavage for eight weeks. The control group received only corn oil. At the end of the experiment, the animals were euthanized, and brain and blood samples were collected. Serum levels of leptin, ghrelin, and irisin were determined using ELISA. AgRP and POMC protein levels in brain tissue were analyzed using Western blot and immunofluorescence. Differences between groups were compared using the Kruskal-Wallis test, with $p < 0.05$ considered statistically significant.

RESULTS: Statistically significant increases were observed in food intake, serum ghrelin, irisin, and AgRP protein levels in the groups treated with DIBP compared to the control group ($p < 0.05$). Additionally, statistically significant decreases were noted in serum leptin and POMC protein levels in the DIBP-treated groups compared to the control group ($p < 0.05$).

CONCLUSIONS: Our study results demonstrated that the environmental pollutant DIBP influenced food intake, exerting these effects by altering the endocrine system and impacting central pathways regulating food intake.

Keywords: AgRP, DIBP, Ghrelin, Leptin, Obesity, POMC

OC-20

The Effect of Cold Exposure and Bee Venom Injection on UCP-1 Gene Expression Levels and Anxiety-Like Behaviors in Rats Fed a High-Fat Diet

Bahar Dalkiran¹, Burcu Acikgoz¹, Ilkay Aksu², Amac Kiray³, Muge Kiray²

¹Dokuz Eylul University, Health Sciences Institute, Department of Physiology, Izmir, Türkiye

²Dokuz Eylul University, Medical Faculty, Department of Physiology, Izmir, Türkiye

³Dokuz Eylul University, Medical Faculty, Department of Anatomy, Izmir, Türkiye

AIM: We investigated the role of increased adipose tissue activity and bee venom (BV) injection on the interaction between UCP-1, metabolic and emotional disorders, as well as its effect on the regression of emotional disorders.

METHODS: In our experiments, three-week-old male Sprague-Dawley rats were used. The rats were divided into the following groups: control, cold exposure (CE), BV 0.5 mg/kg (BV0.5), high-fat diet (HFD, %60 from fat), HFD+BV0.5, HFD+CE, and HFD+CE+BV0.5. The rats were fed a HFD for 8 weeks. During the last 21 days, they were exposed to cold at +4 °C and the last 15 days subcutaneous BV injections were administered. Anxiety and depression-like behaviors were evaluated using the open field (OF), elevated plus maze (EPM) and forced swim test (FST). At the end of the experiment, UCP-1 gene levels were measured by PCR in intrascapular brown adipose tissue (BAT) and subcutaneous white adipose tissue (WAT) from the sacrificed rats. One Way ANOVA test was used to evaluate the data.

RESULTS: In the EPM results, HFD exhibited significantly increased activity with BV injection, spending more time in the open arms and center area, less time in the closed arms ($p < 0.05$). In the FST, HFD+CE+BV0.5 showed significantly less immobility time compared to the control, CE and HFD ($p < 0.05$). When comparing UCP-1 gene expression levels, the HFD+CE+BV0.5 had significantly higher BAT UCP-1 expression levels than the CE, HFD, and HFD+BV0.5 ($p < 0.05$). The HFD+CE+BV0.5 also had significantly higher WAT UCP-1 expression levels than the HFD and HFD+CE ($p < 0.05$).

CONCLUSIONS: Our results show that increased UCP-1 in WAT and BAT through BV injection reduces anxiety and depressive behaviors in rats. UCP-1 may mediate the link between metabolic and emotional disorders, suggesting BV's potential as a thermogenic agent.

This research was supported by Dokuz Eylul University Department of Scientific Research Projects (TDK-2021-2618).

Keywords: High-Fat Diet, Anxiety, Depression, UCP-1, Bee Venom

OC-21

Changes in Nutrition-Related Molecules in Male and Female Rats in an Experimental Model of Autism Spectrum Disorders

Süeda Tunçak, Ayşen Çakır, Bülent Gören, Nevzat Kahveci

Bursa Uludag University, Faculty of Medicine, Department of Physiology, Bursa, Türkiye

AIM: Autism Spectrum Disorders (ASD) are neurodevelopmental pathologies that affect individuals' daily lives and normal brain functions. Similar symptoms are observed between ASD and eating disorders. This study aims to investigate the changes in serum Glucose, Leptin, Orexin-A, and Nesfatin-1 levels in male and female animals in a Valproic Acid (VPA) induced model of ASD.

METHODS: The study was approved by Bursa Uludağ University's ethics committee (numbered:2024-01/08). Pups from pregnant Wistar Albino rats that received either 400mg/kg VPA (n(mother)=4, n(male pup)=8, n(female pup)=8) or Saline (S, 1ml/kg), (n(mother)=4, n(male pup)=8, n(female pup)=8) on embryonic day 12.5 intraperitoneally were included. Pups were decapitated on postnatal day-35 after 16h of fasting. Blood glucose levels were measured and serum Nesfatin-1, Orexin-A, and Leptin levels were analyzed by ELISA kit protocols. Statistical analysis was performed with Two-Way ANOVA on Sigma-Plot, $p<0.05$ was considered significant.

RESULTS: There was a significant interaction between sex and VPA in blood glucose levels ($F(1.31)=20.145$, $p<0.001$). Compared to the S-male group, blood glucose levels significantly increased in VPA-male group ($p<0.001$), while no significant difference was found between the S-female and VPA-female groups. There was no significant interaction between sex and VPA in Leptin levels. A significant difference was found between male and female groups independent of prenatal exposure ($p=0.012$), also S and VPA groups independent of sex ($p<0.001$) in Leptin levels. There was not a significant interaction between sex and VPA in Nesfatin-1 levels. A significant difference was found between S and VPA groups independent of sex ($p=0.004$) in Nesfatin-1 levels. There was no significant difference in Orexin-A for any groups.

CONCLUSIONS: Although metabolic and nutritional disorders are frequently observed in ASD, few studies investigate the relationship between ASD and molecules which are effective in nutrition. Our results suggest changes in nutrition-related molecules in ASD which may differ by sex.

Keywords: ASD, Leptin, Nesfatin-1, Nutrition, Orexin-A, Sex

OC-22

Investigation of the Effect of Apelin on Dopamine Signalling in the Hypothalamic Paraventricular Nucleus of Mice on High Calorie Diet by Fiber Photometry

Yasin Ali Çimen¹, Yavuz Yavuz², Cihan Süleyman Erdogan², Selim Kutlu³, Bayram Yılmaz²

¹Bezmialem Vakif University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye; Necmettin Erbakan University, Institute of Health Sciences, Department of Physiology, Konya, Türkiye

²Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

³Necmettin Erbakan University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: Obesity is mainly caused by an imbalance between food intake and expenditure. Consumption of a high-fat diet is among the main causes of obesity. In addition to the paraventricular nucleus (PVN), apelin and dopamine (DA) are play role processes of food intake and obesity. The aim of this study was to investigate the effect of apelin on PVN DA'ergic activity in normal diet and high fat diet feeding conditions by fiber photometry method.

METHODS: 32 C57bl/6 male mice were divided into 4 groups: normal diet (ND), high fat diet (YYD), apelin+normal diet (A+ND), apelin+high fat diet (A+YYD) group. After injection of the dopaminergic sensor virus, fiber optic ferules were implanted into the PVN. After resting for 15 days, animals were fed with high fat diet and normal diet for 28 days according to characteristics of groups. In addition to dietary administration, 100µg/kg (ip) apelin was injected into apelin groups every other day. Feed intake, blood glucose and body weights were monitored and fiber photometry records were taken at the end of the 28th day. Fiber photometry recordings were filtered by MATLABsoftware and z-score (dF/F) and area under the curve (AUC) values calculated. Results were analysed by one-way analysis of variance.

RESULT: Body weights of ND ($p<0.01$), YYD ($p<0.001$), A+YYD ($p<0.001$) groups on day 28 were higher compared to day 0. On 28th day, body weight of A+ND group was lower than YYD and A+YYD groups ($p<0.001$). AUC values of A+ND group were higher than ND ($p<0.05$) and A+YYD ($p<0.05$) groups. AUC values in A+ND group tended to decrease compared to the ND group ($p>0.05$).

CONCLUSIONS: The results of our study show that apelin suppresses body weight gain in mice, may have a regulatory effect on PVN DA'ergic activity and may play a protective role in reduced DA'ergic tone in obesity.

Keywords: Apelin, Dopamine, Dopamine receptors, High fat diet, GRAB, PVN

OC-23

Investigation of Hypothalamic and Hippocampal Semaphorin 3A and Receptor Gene Expression Levels in an Experimental Morphine Addiction Model

Kaniye Zeynep Çalışkan¹, Aysu Şen², Emine Nedime Korucu⁴, Ayça Yavuz¹, Hacer Çalkap⁴, Yasin Ali Çimen³, Selim Kutlu²

¹KTO Karatay University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

²Necmettin Erbakan University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

³Bezmialem Vakıf University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

⁴Necmettin Erbakan University, Faculty of Science, Department of Molecular Biology and Genetics, Konya, Türkiye

AIM: Morphine, an opioid agonist, has a strong analgesic effect, on the other hand naloxone is widely used as a general opioid receptor antagonist. Semaphorins are neuronal guidance proteins involved in nervous system development and neurodegenerative diseases. The impact of opioid addiction on semaphorin proteins and receptors in the hypothalamus and hippocampus is unknown. This study aims to investigate if the expression levels of semaphorin 3A and its receptors in the rat hypothalamus and hippocampus change with morphine addiction.

METHODS: Adult male Wistar albino rats were used. In the study, 24 young adult male Wistar albino rats were used. Animals were divided into 4 groups as control group administered vehicle for 5 days (s.c.), morphine group administered 10mg/kg/day morphine sulfate (s.c.), naloxone group administered 3mg/kg naloxone hydrochloride (s.c.) for 5 days and morphine + naloxone group injected 3mg/kg naloxone (s.c.) on the last day after 5 days of morphine administration. Hypothalamus and hippocampus tissues were removed, and gene expression levels of semaphorin 3A, plexin, neuropilin-1 were analyzed by RT-PCR. Statistical evaluation was performed using the One-Way ANOVA test.

RESULTS: The expression level of SMF 3A receptors in the hypothalamus is significantly decreased in the MN group compared to the M group ($p<0.05$). The expressions of NRP1 and PLA1 receptors are significantly higher in the M group compared to the MN group ($p<0.05$). In the hippocampal tissue, the gene expression levels of SMF 3A and NRP1 in the M group are significantly increased compared to the MN group ($p<0.05$).

CONCLUSIONS: The higher levels of semaphorins in the brain tissues of rats with morphine addiction suggest that SMF 3A, NRP1, and PLA1 may also play a mediating role in the neuronal damage occurring in the hypothalamus and hippocampus.

Keywords: Hippocampus, Hypothalamus, mu Opioid receptor, Semaphorin 3A

OC-24

Effects of Dexamethasone-induced Insulin Resistance Model on Self-care Behaviors and Brain-derived Neurotrophic Factor

Hasan Çalışkan¹, Gözde Karabulut²

¹Balikesir University Medicine Faculty, Department of Physiology, Balıkesir, Türkiye

²Kütahya Dumlupınar University, Science Faculty, Department of Zoology, Kütahya, Türkiye

AIM: Insulin resistance (IR) is described as an impaired response to insulin stimulation of target cells. IR causes both physical and psychological adverse effects. The present study was designed to investigate the effect of dexamethasone induced insulin resistance model on self-care behaviors and brain-derived neurotrophic factor (BDNF).

METHODS: 16 adult male Wistar albino rats were divided into control and IR groups ($n=8$). To induce the IR model, dexamethasone was administered by intraperitoneally 1 mg/kg/day for 5 days. Open field and splash tests (Splash test procedure: spraying 10% sucrose water solution to arise emotion of contamination and observation of self care behaviors) were performed to evaluate locomotor activity and self-care-depression-like behaviors, respectively. After the subjects were sacrificed, BDNF was analyzed by ELISA in the striatum and prefrontal cortex. Homo-IR, glucose, insulin, ALT, and AST were analyzed in serum. Changes in kidney, liver, and pancreas were examined histologically. Shapiro-Wilk, Student t, and Fisher's exact test were used as statistical tests.

RESULTS: Total distance traveled, grooming frequency, and grooming time decreased in IR group compared to the control group. Serum ALT, AST, glucose, insulin, and HOMA-IR values increased in the dexamethasone-applied group ($p<0.05$). BDNF decreased in the prefrontal cortex in the insulin resistance group ($p<0.05$). Striatum BDNF level decreased slightly but was not significant ($p>0.05$). Degeneration of islets of Langerhans in the pancreas, tubular degeneration in the kidney, degeneration of hepatocytes, and mononuclear cell infiltration in the liver increased in the IR group compared to the control group ($p<0.05$).

CONCLUSIONS: Insulin resistance negatively affected locomotor activity and self-care behaviors. The prefrontal cortex was found to be a more vulnerable to insulin resistance. Our results suggest that IR deteriorates self-care behaviors and BDNF level of the prefrontal cortex, in accordance with serum biomarkers and histological parameters.

Keywords: BDNF, Insulin resistance model, Self-care behavior, Splash test

OC-25

Effects of Apelin-13 on Oxidative Stress and Auditory Brainstem Responses in STZ-Induced Diabetic Rats

Sevtap Kılınç¹, Rukiye Ölçüoğlu¹, Ayşe Arzu Yigit¹, Özgecan Güneşer¹, Berfin Eylül Aydemir²

¹Başkent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Başkent University, Faculty of Health Sciences, Department of Audiology, Ankara, Türkiye

AIM: Diabetes is one of the common endocrinological disorders worldwide and causes various complications. One of the complications caused by diabetes is hearing loss. Research on the relationship between diabetes and hearing loss has been ongoing for a long time. Apelin is typically expressed in vascular endothelium and fatty tissues, and Apelin-13 is the primary active isoform that specifically binds to the apelin receptor. Apelin receptors are also found in the auditory system. The aim of this study is to investigate the effects of apelin-13 on oxidative stress and auditory brainstem responses in STZ-induced diabetic rats.

METHODS: Thirtytwo male Wistar albino rats were divided into four groups: sham, diabetes, Apelin and Diabetes+Apelin. A single dose of 45 mg/kg ip STZ was administered to create a diabetes model. Apelin groups were given 50 µg/kg apelin-13 intraperitoneally for 7 days. The sham group was also administered ip saline for 7 days. Auditory brainstem responses (ABR) were evaluated at the end of apelin and STZ applications. Then, cochlea tissue was removed and biochemical analyzes were performed. JAMOVİ program was used for statistical analysis and p<0.05 was considered significant.

RESULTS: Compared with diabetic groups, Apelin treatment significantly improved the total antioxidant status (TAS) of the cochlea, while reducing the total oxidant status (TOS) and oxidative stress index (OSI). According to measurements of auditory brainstem responses (ABR), Wave V latencies in diabetic groups were much longer than in control groups. Apelin treatment partially reverses this effect, especially at certain frequency and intensity levels.

CONCLUSIONS: It was determined that apelin may have a therapeutic effect against diabetes-related hearing system damage with its antioxidant effect. These findings support the potential protective role of apelin on the auditory system and are thought to be a new therapeutic approach in the treatment and prevention of diabetic auditory neuropathy.

Keywords: Diabetes, Apelin, Auditory brainstem responses, Oxidative Stress

OC-26

The Effect of Intracerebroventricular Meteorin-Like Protein Infusion on the Hypothalamic-pituitary-testicular Axis

Burak Bircan¹, Güldeniz Şekerci², Suat Tekin², Yavuz Erden³, Çiğdem Tekin⁴

¹Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Medical Services and Techniques, Osmaniye, Türkiye

²İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

³Bartın University, Faculty of Science, Department of Molecular Biology and Genetics, Bartın, Türkiye

⁴İnönü University, Vocational School of Health Services, Department of Health Care Services, Malatya, Türkiye

AIM: Reproductive behaviors are regulated by the central effectors of the brain, with the hypothalamus playing a critical role in this process. Gonadotropin-releasing hormone (GnRH) and other peptides produced in the hypothalamus regulate reproductive functions. In males, GnRH signals trigger the release of luteinizing hormone (LH) and follicle-stimulating hormone (FSH); LH stimulates testosterone production, while FSH promotes spermatogenesis. The hypothalamic-pituitary-testicular (HPT) axis can be regulated by adipokines. Meteorin-like protein (METRNL) is a newly discovered adipokine present in components of the HPT axis, but its role in these tissues remains unclear. The aim of this study is to investigate the effects of METRNL on the HPT axis.

METHODS: In this study, 40 male Wistar rats were randomly divided into four groups (control, sham, 10 nM METRNL, 100 nM METRNL). Brain infusion kits were implanted into the rats' right lateral ventricles, and they were allowed to recover for 7 days. On the 8th day, the rats were anesthetized, and an osmotic mini-pump was connected to the brain infusion kit cannula to infuse METRNL (5 µL/hour for 14 days). At the end of the experiment, the rats were decapitated and blood samples were collected. Serum LH, FSH, and testosterone levels were measured using ELISA. Data were analyzed using the Kruskal-Wallis H test and Bonferroni-corrected Mann-Whitney U test, with p<0.05 considered significant.

RESULTS: Serum LH, FSH, and testosterone levels in the groups that received chronic intracerebroventricular METRNL infusion decreased dose-dependently compared to the control group (p<0.05). However, no significant difference was observed between the control and sham groups (p>0.05).

CONCLUSIONS: Central METRNL infusion in male rats may suppress reproductive functions by reducing LH, FSH, and testosterone levels.

This study was supported by TÜBİTAK (Project No: 123Z074).

Keywords: Meteorin-Like Protein, Hypothalamus, LH, FSH, Testosterone

OC-27

Anti-Cancer Effects of Tangeretin and Delphinidin on Pancreatic Cancer Cells

Şeniz Geniş¹, Derviş Birim², Güliz Armagan², Mumin Erdogan¹

¹ İzmir Katip Çelebi University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

²Ege University, Pharmacy Faculty, Department of Biochemistry, Izmir, Türkiye

AIM: Pancreatic cancer is the 13th most common type of cancer worldwide and the 7th leading cause of cancer-related deaths. The aim of this study is to evaluate the potential anti-cancer effects of tangeretin and delphinidin on pancreatic cancer cells. The rapid progression and high fatality rate of pancreatic cancer limit the effectiveness of current treatment methods. Therefore, the development of new treatment approaches for pancreatic cancer is of critical importance. Our study aims to assess the potential anti-cancer effects of tangeretin and delphinidin on pancreatic cancer cells in an in vitro setting.

METHODS: The human pancreatic cancer cell line (PANC-1) was used in this study. Tangeretin and delphinidin were applied as treatments. In vitro experiments included MTS cell proliferation, colony formation, wound healing test, and western blot analysis. Statistical analyses were performed using SPSS v15.0.

RESULTS: In the study, significant reductions in cell proliferation and colony formation were observed at 50 and 100 µM doses of tangeretin and delphinidin ($p < 0.0001$). In the wound healing test, treatment with 50 µM tangeretin and delphinidin resulted in significant reductions in cell motility. Western blot analysis showed that 50 µM and 100 µM tangeretin and 50 µM delphinidin increased Bax expression and decreased Bcl-2 expression in PANC-1 cells, leading to an increase in the Bax/Bcl-2 ratio and inducing cell death ($p < 0.0001$). In combination, 10 µM tangeretin + 10 µM delphinidin and 50 µM tangeretin + 50 µM delphinidin also significantly reduced cell proliferation, colony formation, and motility while increasing the Bax/Bcl-2 ratio ($p < 0.0001$).

CONCLUSIONS: The data revealed that tangeretin and delphinidin have significant effects on cell proliferation, colony formation, and apoptosis in PANC-1 cells. Combined treatment with tangeretin and delphinidin may be a useful and feasible intervention in pancreatic cancer patients pending further studies.

Keywords: Tangeretin, Delphinidin, PANC-1, Anticancer, Proliferation, Apoptosis

OC-28

Examination of Morphological Changes, Murf1 and Atrogin1 Gene Expression Levels, and Redox Status During Hydrogen Peroxide-Induced Atrophy in Melatonin-Treated Mouse Myoblast Cell Line

Nazlı Karimi Ahmadi¹, Berk Adnan Dinçsoy²

¹Hacettepe University, Medical Faculty, Physiology Department, Ankara, Türkiye

²Muğla Sıtkı Koçman University, Medical Faculty, Physiology Department, Ankara, Türkiye

AIM: It is well known that oxidative stress plays a critical role in the development of disuse muscle atrophy. The use of antioxidants, particularly those targeting mitochondria such as melatonin, has emerged as an important therapeutic option. In this study, we aimed to investigate the effects of melatonin on the redox balance and cellular morphology in an oxidative stress-induced muscle atrophy model in C2C12 cells, as well as the expression levels of Atrogin-1 and MuRF1.

METHODS: Therapeutic doses were determined using the MTT method based on the literature. Four different C2C12 cell groups were created: Control (C), Melatonin (M, 100 µM), H₂O₂ (H, 50 µM), and Melatonin + H₂O₂ (MH). To evaluate treatment outcomes, myotube morphology was assessed at three different regions (25%, 50%, and 75% of their length) using ImageJ. RNA isolation and RT-PCR were performed to examine Atrogin-1 and MuRF1 gene expression levels, with 18S rRNA as the reference gene. The redox status was evaluated by assessing total oxidant-antioxidant status in both cell lysates and culture media.

RESULTS: Statistically significant differences were found in the average myotube diameters between groups and protective effect of the M group on atrophy was confirmed ($p \leq 0.00001$). Although atrogin expression levels decreased in the M group, this difference was not statistically significant. A significant increase in total antioxidant status (TAS) levels was observed in the M and MH groups compared to the C group ($p < 0.05$) in the culture media. In the lysates, significant increase in TAS levels was observed in the MH group compared to the C group ($p < 0.05$), while the increase in the M group was not statistically significant.

CONCLUSIONS: Our results suggest that melatonin has positive effects on muscle atrophy. Melatonin may exert these effects by influencing atrogin expression levels. The lack of statistical significance could be due to the early pronounced expression of atrogenes. Melatonin shows potential as a treatment or preventive agent for muscle atrophy by preventing myotube diameter reduction and enhancing antioxidant capacity.

Keywords: Atrogenes, Muscle Atrophy, Melatonin, Oxidative Stress

OC-29

Evaluation of Potential Anticarcinogenic Characteristics of c-Phycocyanin and Flavonoid Combinations on MDA-MB-231 Cells

Rümeysa Fatma Balaban¹, Talat Yasin Acar², Mehmet Fatih Seyhan³, Ümit Yılmaz⁴

¹Bursa Uludağ University, Faculty of Medicine, Department of Medical Biology, Bursa, Türkiye

²Medipol University, Faculty of Medicine, Department of Histology and Embryology, İstanbul, Türkiye

³Istanbul Yeni Yüzyıl University, Faculty of Arts and Sciences, Department of Molecular Biology and Genetics, İstanbul, Türkiye

⁴Karabük University, Faculty of Medicine, Department of Physiology, Karabük, Türkiye

AIM: Triple negative breast cancer (TNBC) is a heterogeneous group of tumors that are negative for estrogen, progesterone and HER2 amplification. Due to the resistance to chemotherapy and side effects seen in TNBC patients, new drug discoveries and alternative effective treatments are needed for the treatment of TNBC. C-phycocyanin; is a pigment-protein complex derived from *Spirulina* sp. and is a promising therapeutic agent that has been shown to have anti-inflammatory, antitumor effects. In this study, we aimed to investigate the anticancer activity of C-phycocyanin on MDA-MB-231 breast cancer cell line. Additionally, we focused on identifying a more effective and safe combination therapy that could be used to treat TNBC by preparing combinations with curcumin and quercetin, which have known synergistic effects, to increase the efficacy of C-phycocyanin.

METHODS: MDA-MB-231 and L929 healthy cell lines were treated with C-phycocyanin, curcumin, quercetin flavonoids separately and in combination. Effects of combinations on cell viability were evaluated by MTT test. Then, treated cells' morphology was determined with AO/EtBr staining, and antioxidant activity was evaluated with DCF-DA test. Effects of flavonoid combinations on cell migration and cell-cell interactions were analyzed by scratch assay method.

RESULTS: MDA-MB-231 cells were treated with five different doses of combination, 5-2.5-20 µg/ml, 10-5-40 µg/ml, 20-10-50 µg/ml, 25-15-75 µg/ml, 30-25-100 µg/ml. The effective dose was determined as 5-2.5-20 µg/ml for 48 hours. The C-phycocyanin/flavonoid combination was found to inhibit MDA-MB-231 cell viability by 90%. Based on AO/EtBr staining results, early and late apoptotic cells were determined in MDA-MB-231 cells. We also determined that C-phycocyanin/flavonoid combination inhibits cell migration by approximately 90% compared to C-phycocyanin alone and triggers oxidative stress-induced cell death ($p < 0.001$).

CONCLUSIONS: The findings showed that the C-phycocyanin/flavonoid combination created synergy between them compared to their use alone and the combined treatment was more effective on the MDA-MB-231 cell line.

Keywords: Triple-negative breast cancer, C-phycocyanin, MTT, DCF-DA, Scratch assay, AO/EtBr

OC-30

Polysaccharide Coated Silver Nanoparticle with Effectiveness in Reducing the Viability of Triple Negative Breast Cancer

Adnan Berk Dinçsoy¹, Ulviye Bunyatova²

¹Mugla Sitki Kocman University, Faculty of Medicine, Department of Physiology, Mugla, Türkiye

²Baskent University, Program of Biomedical Engineering, Ankara, Türkiye

AIM: The side effects and high costs of cancer drugs have increased research on biocompatible, low-cost alternatives. Studies investigating nanoparticles' effects on cancer are growing. Chitosan is a biocompatible, biodegradable material with antibacterial and antitumoral properties. These properties are also preserved in chitosan-based nanocomposites. Using a newly developed method, N-carboxymethyl chitosan polysaccharide-based silver nanoparticles (C@AgNP) were synthesized, and their effects on triple-negative breast cancer (TNBC) cells were investigated. TNBC is a type of cancer with a poor prognosis, characterized by the deficiency of estrogen, progesterone receptors and human epidermal growth factor receptor-2. The aim of this study is to investigate the potential of newly synthesized C@AgNP to reduce the viability of TNBC cells.

METHODS: C@AgNP was synthesized using the new "White-light method" and characterized by SEM and TEM. 4T1 and MDA-MB-231 cells were seeded at 25.103 cells/well in 96-well plates. After 24 hours, C@AgNP was applied at doses of 0.00312, 0.00625, 0.0125, and 0.025 mg/mL in triplicate. The control group received culture medium. MTT lysis buffer was added at the 24th hour, and absorbances were read at 570 nm in a spectrophotometer. The control group was accepted as 100%, and %viabilities were determined. IC50 values were found using GraphPad Prism. 4T1 cells treated at IC50 for 24 hours and apoptosis rates were determined via flow cytometry using Annexin V-FITC/PI kit. One-way ANOVA was used for statistical analysis.

RESULTS: After 24 hours of application, cell viability decreased dose-dependently in both 4T1 and MDA-MB-231 cells ($P < 0.05$), with IC50 values of 0.00571 ± 0.00052 mg/mL and 0.00726 ± 0.0018 mg/mL, respectively. In 4T1 cells, the reduction of viability was supported by approximately 66% apoptosis at 24 hours, consistent with the MTT results.

CONCLUSIONS: C@AgNP, synthesized using the new method at lower cost and time, effectively reduced TNBC cells viability at low doses and showing promise as a potential anticancer agent.

Keywords: Triple negative breast cancer, Chitosan-Coated Silver Nanoparticle, Nanoparticle

OC-31

The Interplay Between Sirtuin 1 (SIRT1) and Autophagy/Mitophagy in Serum-Starved SH-SY5Y Cells

Yasemin Kartal¹, Ünal Metin Tokat², Berkay Bozkurt³, Pelin Kelicen Uğur⁴, Murat Timur Budak⁵

¹Kırklareli University, Faculty of Medicine, Department of Physiology, Kırklareli, Türkiye

²Medicana Health Group, Precision Oncology Center, Istanbul, Türkiye

³Izmir Institute of Technology, Department of Biotechnology and Bioengineering, Izmir, Türkiye

⁴Hacettepe University, Faculty of Pharmacy, Department of Pharmacology, Ankara, Türkiye

⁵Hacettepe University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: This study aimed to evaluate the interaction between SIRT1 and autophagy/mitophagy pathways in SH-SY5Y cells under serum-starvation conditions.

METHODS: In the present study, the gene expression levels of autophagy-related markers including ULK1, and BECN1 as well as mitophagy-related markers, such as PINK1, PARKIN, and MFN2 were evaluated by qRT-PCR in SH-SY5Y cells under serum-depletion condition for 24h. In addition, these marker levels were assessed in the presence of SIRT1 siRNA in media with/without serum for 24h. Furthermore, miRNA target genes were evaluated with multiple miRNA-target prediction tools, such as TargetScan and miRWalk. Gene Ontology (GO) analysis was conducted to assess the molecular functions, biological processes, and cellular components associated with these miRNAs or their targets. Additionally, this study was approved by Kırklareli University, Scientific Research Ethics Committee with approval no: E-37844677-199-85871 on 19 May 2023.

RESULTS: The expression levels of the ULK1 and BECN1 genes significantly increased in response to serum deprivation in the cells (respectively, *** $p \leq 0.001$, **** $p \leq 0.0001$). Furthermore, the expression levels of PINK1, PARKIN, and MFN2 genes also significantly elevated under these starvation conditions (* $p \leq 0.05$). SIRT1 demonstrated a positive regulatory effect on ULK1 in both serum-containing and serum-deprived media (* $p \leq 0.05$) while it negatively regulated PINK1 specifically in serum-containing media (** $p \leq 0.01$). Additionally, PARKIN gene expression tended to decrease in the presence of SIRT1 siRNA, regardless of serum conditions ($p > 0.05$). As a result of bioinformatics analysis, 4 miRNAs that could potentially regulate SIRT1 and ULK1 were determined.

CONCLUSIONS: As a result, prominent shreds of evidence that prove a direct link between SIRT1 and mitophagy/autophagy markers was determined in SH-SY5Y cells. Additionally, the identification of key miRNAs, hsa-miR-128-3p, hsa-miR-216a-3p, hsa-miR-181b-5p, as well as hsa-miR-181a-5p, provides an approach with novel insights, paving the way for the development of targeted therapies for neurodegenerative diseases.

Keywords: Hsa-miR-128-3p, Hsa-miR-181a-5p, Hsa-miR-181b-5p, Hsa-miR-216a-3p, Mitophagy/autophagy, SIRT1

OC-32

Ramelteon Exhibits Anticancer Effects in Different Types of Human Cancer Cells

Senanur Türkol¹, Tuba Keskin¹, Güldeniz Şekerci¹, Çiğdem Tekin², Suat Tekin¹

¹İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

²İnönü University, Vocational School of Health Services, Department of Home Care, Malatya, Türkiye

AIM: Cancer is a disease characterized by the uncontrolled proliferation of body cells and the involvement of apoptotic and inflammatory processes, leading to its spread throughout the body. Among proposed treatments for various cancer types, the administration of anti-inflammatory hormones or drugs plays a significant role. The hormone melatonin, known for its anti-inflammatory properties, has been extensively studied in relation to different cancer types. Ramelteon, an analogue of melatonin, is primarily used for the treatment of insomnia. Literature reviews have shown that Ramelteon suppresses the proliferation of neuroblastoma and endometrial cancer cells; however, its broader relationship with cancer has not yet been fully reported. This study aims to investigate effects of Ramelteon on cell viability and DNA damage in A2780 (ovarian), MCF-7 (breast), Caco-2 (colon), and LNCaP (prostate) cell lines.

METHODS: In this study, A2780, MCF-7, Caco-2, and LNCaP cell lines were used. Ramelteon was applied to these cell lines at concentrations of 5, 10, 25, 50, 100, and 500 μ M, followed by incubation for 24 hours. Changes in cell viability were assessed using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay. After determining dose-dependent efficacy, 50% inhibitory concentration (IC50) values were calculated using GraphPad Prism 8. Based on the identified effective dose, cytotoxic effects were evaluated using the Comet Assay. Comparisons between the groups were made using the Kruskal-Wallis H-Test, with $p < 0.05$ considered statistically significant.

RESULTS: The results showed that Ramelteon reduced cell viability in A2780 cell line at doses of 50, 100, and 500 μ M, MCF-7 cell line at all concentrations, Caco-2 cell line at all doses except 5 μ M, and LNCaP cell line at doses of 100 and 500 μ M ($p < 0.05$). Moreover, Ramelteon exhibited statistically significant cytotoxic effects on the A2780, MCF-7, Caco-2, and LNCaP cell lines ($p < 0.05$).

CONCLUSIONS: The results demonstrate that Ramelteon exhibits anticancer activity in these cell lines and may be a potential candidate for the development of new cancer treatment strategies.

This study was supported by the İnönü University Scientific Research Projects Unit (TSA-2024-3546).

Keywords: Ramelteon, Cancer, Melatonin

OC-33

Effects of Intermittent Fasting on Oxidative Stress, Tissue Histology, and Behavioral Parameters in Acrylamide Exposure.

Aslı Şan Daglı Gül¹, Okan Arıhan¹, Mahire Bayramoğlu Akkoyun², Hurrem Turan Akkoyun³, Tuncer Kutlu⁴, Ahmet Uyar⁴, Ahmet Onur Daştan¹, Sezgi Fırat Özgür¹, Ayşen Erdem¹

¹Hacettepe University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Siirt University, Veterinary Faculty, Department of Biochemistry, Siirt, Türkiye

³Siirt University, Veterinary Faculty, Department of Physiology, Siirt, Türkiye

⁴Mustafa Kemal University, Faculty of Medicine, Department of Histology and Embryology, Hatay, Türkiye

AIM: Acrylamide is a toxic substance found in various foods, cigarettes, and industrial chemicals. Intermittent fasting has been shown to reduce oxidative stress and inflammation and aid in cell renewal and protection. This study aims to investigate the protective effects of intermittent fasting on oxidative stress parameters, tissue histology, and behavioral parameters during acrylamide exposure.

METHODS: Twentyeight adult male Wistar albino rats, weighing 200-250 grams, were divided into four groups (n=7): control (C), acrylamide (AC), intermittent fasting (IF), and acrylamide+ intermittent fasting (ACIF). For 28 days, intermittent fasting was applied every other day, and acrylamide was administered intraperitoneally at a dose of 30 mg/kg three times a week. On the final day, anxiety tests (Elevated Plus Maze, Open Field Test) and a locomotor activity test (rotarod) were performed. Oxidative stress parameters (CAT, GPX, SOD) were measured in liver, kidney, and brain tissues, and histopathological analyses were conducted.

RESULTS: In the rotarod test, the walking duration of the AC group (16.1±14.1s) was observed to be significantly lower compared to the IF group (50.7±14.9s) and the C group (47±16.9s). In liver and kidney histopathology, intermittent fasting was found to reduce the congestion and hydropic degeneration in hepatocellular and tubular epithelium caused by acrylamide. In the elevated plus maze anxiety tests, the percentage of time spent in the closed/open arm was significantly higher in the AC (68.43±41.58) group than in the IF (7.86±11.25) group. It was observed that acrylamide administration had similar effects on brain, kidney and liver tissues and decreased CAT, GPX and SOD values.

CONCLUSIONS: Intermittent fasting reduced oxidative stress and tissue damage caused by acrylamide exposure. These findings suggest that intermittent fasting may have protective effects on acrylamide exposure. This study was supported by Hacettepe University Scientific Research Projects Unit project number THD-2021-19804.

Keywords: Acrylamide, Behaviour, Histopathology, Intermittent fasting, Oxidative stress

OC-34

Regulatory T Cells in Sick Cell Anemia: Prognostic Value and Relationship with Non-Lymphocytic Leukocytes

Rukiye Ölcüoğlu¹, Funda Tanrikulu², Sevtap Kılınç¹, Süheyl Asma³, Can Boğa³, Hakan Özdoğu³, Eda Çakmak⁴, İlknur Kozanoğlu⁵

¹Başkent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Çukurova University, Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Adana, Türkiye

³Başkent University, Faculty of Medicine, Adana Dr. Turgut Noyan Application and Research Hospital, Adana, Türkiye

⁴Başkent University, Faculty of Health Sciences, Department of Audiology, Ankara, Türkiye; ⁵Acıbadem Labmed Clinical Laboratories, Hematology, Istanbul, Türkiye

AIM: Sick cell anemia (SCA) is hereditary disease characterized by vascular occlusions and organ damage caused by sickle-shaped erythrocytes, involving inflammatory disease associated with excessive immune activation. Regulatory T cells (Tregs) play critical role in regulating immune system. Studies examining immunophenotypes of adults with SCA are limited. Our previous study, presented at hematology conference, found Treg levels were higher in acute patients presenting with painful crises. Since Tregs counts are not routinely evaluated in clinical practice, determining their possible relationship with routine complete blood count parameters may provide insight into Treg activation. This study aims to evaluate relationship between Tregs and non-lymphocytic leukocytes assessed by complete blood count.

METHODS: The study included 37 SCA patients and 31 healthy volunteers, all over 18 years old. Exclusion criteria included pregnancy, cancer, autoimmune diseases, acute infections, and medication use for SCA. FoxP3 was used for flow cytometric analysis of Tregs. Multiple linear regression analysis was conducted to determine parameters affecting Tregs count.

RESULTS: Moderate significant correlation was observed between Treg count and monocyte ($r=0.356$, $p=0.003$) and leukocyte counts ($r=0.427$, $p<0.001$) across all subjects. Leukocyte count significantly predicted Treg count (Treg count = $3.437 + 2.841 \cdot \text{leukocyte count}$). In patients experiencing painful crises ($n=15$), neutrophil and monocyte counts significantly predicted Treg count (Treg count = $21.004 + 22.361 \cdot \text{neutrophil} - 69.864 \cdot \text{monocyte}$). In stable SCA patients ($n=22$), leukocyte count was significant (Treg count = $-8.070 + 2.875 \cdot \text{leukocyte count}$). Significant differences in leukocyte ($p=0.001$) and monocyte ($p=0.008$) counts were observed among patient groups with low, medium and high Treg levels.

CONCLUSIONS: Tregs are promising targets for therapies aimed at modulating immune responses in SCA. Our findings suggest that Treg levels correlate with leukocyte and monocyte count variations. Despite small sample size, this study serves as preliminary investigation and is expected to guide larger-scale studies.

Keywords: Flow cytometry, Regulatory T cells, Sick cell anaemia

OC-35

Protective Effects of Asiatic Acid on Organophosphate Poisoning

Hakan Balci¹, Özge Darakci², Figen Güzelgöl³, Nilgun Yersal⁴, Burcu Hatipoğlu⁵, Rûmeysa Abdullahoğlu⁵, Ayhan Bozkurt⁵

¹Bilecik Şeyh Edebali University, Faculty of Medicine, Department of Pharmacology, Bilecik, Türkiye

²Bilecik Şeyh Edebali University, Faculty of Medicine, Department of Physiology, Bilecik, Türkiye

³Tokat Gaziosmanpaşa University, Faculty of Pharmacy, Department of Biochemistry, Tokat, Türkiye

⁴Tokat Gaziosmanpaşa University, Faculty of Medicine, Department of Histology and Embryology, Tokat, Türkiye

⁵Ondokuz Mayıs University, Faculty of Medicine, Department of Physiology, Samsun, Türkiye

AIM: Chlorpyrifos (CPF), an organophosphate pesticide used in agriculture, disrupts the oxidant/antioxidant balance, causing cellular damage. Our study investigates the protective effects of asiatic acid (AA), a triterpenoid from *Centella asiatica*, on CPF-induced changes in oxidant/antioxidant parameters in rat liver, brain, and serum.

METHODS: A total of 30 male Sprague-Dawley rats (200-250 g) were used (n=6). AA (35, 70, or 140 mg/kg/day) was administered orally by gavage for 14 days. On the 15th day, the rats were treated with chlorpyrifos (279 mg/kg; s.c.). Twenty-four hours after chlorpyrifos administration, blood, brain, and liver tissue samples were collected from the decapitated rats. In these tissues, levels of malondialdehyde (MDA) as a marker of lipid peroxidation, advanced oxidation protein products (AOPP) as a marker of protein oxidation, and the antioxidant enzymes superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) were evaluated. Brain and liver tissue damage was examined histopathologically. Data were analyzed with One-Way ANOVA and Tukey's post-hoc test was used for intergroup comparisons.

RESULTS: CPF increased MDA and AOPP levels in the liver, brain, and serum (p<0.05-0.01); decreased SOD and CAT in the liver, GPX-1 in the brain, and SOD, CAT, and GPX-1 in the serum (p<0.05) compared to the control group. At 140 mg/kg, AA prevented the CPF-induced increase in MDA and AOPP levels in the liver, brain, and serum (p<0.05-0.01). Additionally, at this dose, AA prevented the CPF-induced decrease in SOD and CAT in the liver and serum, and SOD in the brain (p<0.05-0.01). The histopathological damage scores caused by CPF in the brain and liver (p<0.05) were prevented by the administration of 140 mg/kg asiatic acid (p<0.05).

CONCLUSIONS: It can be concluded that asiatic acid supplementation may exert a therapeutic effect by reducing CPF-induced oxidative stress and tissue damage in rat liver, brain, and serum through antioxidant mechanisms.

Keywords: Asiatic acid, Chlorpyrifos, Organophosphate, Oxidative stress, Pesticide toxicology

OC-36

Effect of Apelin-13 on Percentage Change in Body Weight, Disease Activity Index, Colon Weight/Length Ratio and Mucus Content in the Colon Wall in an Experimental Colitis Model

Kamil Erdoğan¹, Vecihe Nimet İzgüt-Uysal², Sevil Aksu¹, Özlem Özbey³, İlknur Birsen¹

¹Akdeniz University, Faculty of Science, Department of Chemistry, Antalya, Türkiye

²Akdeniz University, Faculty of Medicine, Department of Physiology, Antalya, Türkiye

³Akdeniz University, Faculty of Medicine, Department of Histology and Embryology, Antalya, Türkiye

AIM: Inflammatory bowel disease (IBD), a disease characterized by recurrent inflammation in the digestive system, is a chronic global health problem that reduces the quality of life of patients. It is very important to elucidate the mechanisms involved in the development and prevention of IBD and to search for new therapeutics. Therefore, this study was planned to investigate the effects of apelin-13, whose effects in IBD are not fully known, on the colon during 2,4,6-trinitrobenzene sulfonic acid (TNBS)-induced colitis.

METHODS: Adult male Wistar rats (200-250 g) were randomly divided into four groups (n=8 in each group): 1) Control; 2) Sham; 3) TNBS; and 4) TNBS+apelin. Colitis was induced through administration of TNBS (100 mg/kg, intra-rectal) mixed with absolute ethanol in 1:1 ratio. In the TNBS+apelin group, apelin-13 (150 µg/kg/day, i.p.), was administered immediately after the TNBS administration for 3 days. Weight change, stool consistency and rectal bleeding were evaluated daily in all animals. At the end of the experiment, macroscopic damage levels and mucus content in the colon were calculated, colon weights and lengths of the subjects were determined, and the disease activity index (DAI) in the subjects was evaluated. 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.

RESULTS: Weight loss (p<0.01) and an increase in DAI (p<0.05) and colon weight/length ratio (p<0.05) were observed in the TNBS group. Also, TNBS application increased macroscopic injury (p<0.001) and decreased mucus content (p<0.05) in colon tissue compared with control and sham group. Apelin-13 significantly reduced the TNBS-mediated damaging effects in colon.

CONCLUSIONS: These findings suggest that apelin-13 has protective effects in TNBS-induced colitis in rats. This work was supported by Akdeniz University Scientific Research Projects Coordination Unit (Project code: TSA-2023-6412).

Keywords: Apelin-13, TNBS, Mucus, Colitis

OC-37

Investigation of The Protective Effects of Zinc Picolinate in An Experimental Ulcerative Colitis Model

Gonca Han, Sevil Arabacı Tamer

Sakarya University, Faculty of Medicine, Department of Physiology, Sakarya, Türkiye

AIM: Zinc deficiency negatively impacts gut health and can exacerbate the symptoms of inflammatory bowel diseases. It has been suggested that zinc absorption in humans can be enhanced by complexing zinc with picolinic acid. However, there is no literature on the effects of zinc picolinate on the treatment or prevention of colitis. The aim of this study is to investigate the protective effect of zinc picolinate supplementation against colitis damage in an experimentally induced ulcerative colitis model in rats.

METHODS: Sprague Dawley male rats (n=35) were randomly divided into five experimental groups: control, colitis, colitis + zinc, colitis + zinc picolinate, and colitis + sulfasalazine. To induce colitis, rats were given an anal injection of acetic acid solution (AA; 1 ml, 5% v/v) following a 24-hour fasting period under ether anesthesia. Control rats received a physiological saline (PS) injection. Treatment or PS was administered daily (10 doses) starting 10 days prior to the AA induction of colitis. Twenty-four hours after PS or AA administration, rats were anesthetized (xylazine: 10 mg/kg; ketamine: 50 mg/kg, i.p.), and intracardiac blood was collected to conclude the experiment. Colon tissues were collected for macroscopic evaluation, and were then analyzed for oxidant parameters using spectrophotometric methods and cytokine determination via ELISA.

RESULTS: The macroscopic damage score, malondialdehyde (MDA) levels, TNF- α , and IL-6 levels in the colitis group were significantly higher compared to the control group ($p<0.001$), while the antioxidant glutathione (GSH) content was decreased ($p<0.001$). Zinc administration suppressed the macroscopic damage score ($p<0.01$), whereas zinc picolinate did not produce a significant difference in the score. Both zinc and zinc picolinate reduced the elevated cytokine and MDA levels in the colitis group ($p<0.05-0.001$) and increased GSH content ($p<0.05$).

CONCLUSIONS: In the acetic acid-induced ulcerative colitis model, pre-treatment with zinc picolinate suppressed oxidative damage and inflammation in the colon tissue.

Keywords: Ulcerative colitis, Zinc picolinate, Oxidative damage, Inflammation

OC-38

Investigation of the Activity of Agomelatine on Some Female Reproductive Hormones in an Experimental Abortion Model

Orhan Sayın¹, Ahmed Sait Bozyıl¹, Mehtap Pervin¹, Zeynep Dila Öz¹, Mehmet Rıdvan Özdede¹, Fatih Tan¹, Abdullah Yaşar², İhsan Serhatlıoğlu³, Emine Kaçar¹

¹Fırat University Faculty of Medicine, Department of Physiology Elazığ, Türkiye

²Fırat University, Vocational School of Health Services, Elazığ, Türkiye

³Fırat University Faculty of Medicine, Department of Biophysics Elazığ, Türkiye

AIM: Agomelatine is an antidepressant with melatonergic agonist and serotonergic receptor antagonist (5HT_{2C}) effects. It is known to have positive effects on the female reproductive system. In this context, the main purpose of our study is to investigate the therapeutic efficacy of agomelatine in abortion, an important early pregnancy complication, in terms of biochemical parameters.

METHODS: Control, sham, abortion, melatonin (M), agomelatine (A), progesterone (P), melatonin+progesterone (MP), agomelatine+progesterone (AP) groups were formed from 80 intact female Sprague-Dawley rats of 8-10 weeks of age with regular cycles (n=10). Agomelatine (10 mg/kg/day), progesterone (3.02 ml/kg/day), melatonin (10 mg/kg/day) were administered by oral gavage. The experimental abortion model was created by administering mifepristone (50 mg/kg) on the 11th day of pregnancy. Indirect micro ELISA method was used in the study, and One-Way ANOVA and post-hoc Tukey test were used in statistical analysis ($p<0.05$).

RESULTS: Serum prolactin levels were lower in group A compared to the control group, serum β -hCG levels were lower in the other 5 groups compared to the control group, and PGF₂ α levels were lower in the AP group compared to the control group ($p<0.05$). It was determined that the PGF₂ α level was lower in the AP group compared to the abortion group and that the PGF₂ α level was lower in the AP group compared to the progesterone group ($p<0.05$). Serum oxytocin levels were found to be lower in the AP group compared to the control group and in the other 4 groups compared to the abortion group ($p<0.05$).

CONCLUSIONS: Agomelatine has been shown to have similar or even more positive effects than progesterone in biochemical parameters. We believe that its use in combination with progesterone, which has been the only treatment option to date, may be a possible therapeutic agent for abortion. This study was supported by TUBITAK (Project No: 123S215).

Keywords: Abortion, Agomelatine, Pregnancy, Rat, ELISA

OC-39

The Effect of Calorie Restriction on Hematological Parameters in the Aging Process

Ayça Coşkun¹, Esra Toker², Arzu Keskin-Aktan³, Kazime Gonca Akbulut²

¹Sakarya University of Applied Sciences, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Sakarya, Türkiye

²Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

³Afyonkarahisar University of Health Sciences, Faculty of Medicine, Department of Physiology, Afyonkarahisar, Türkiye

AIM: Aging is a risk factor for the immune system, diabetes, obesity, atherosclerosis and coronary artery disease. Age-related changes leukocytes decrease, glucose levels increase, kidney and liver function parameters and various lipid profiles change. Calorie restriction (CR) is known to delay aging and prevent chronic diseases, including neurodegenerative disorders. This study aims to investigate CR's effects on age-related parameter changes.

METHODS: In the study, young and old (3 months, 20 months) rats were divided into randomized groups as control (n = 12) and experimental (n = 12) groups. The experimental group received a low-calorie diet comprising 14% fat, 52% protein, and 34% carbohydrates, providing about 1/3 of their daily calorie intake (~1,303 kcal/kg). In blood samples taken at the end of 10 weeks, hemogram values were measured by the impedance method, and blood glucose, HDL, LDL, cholesterol, triglyceride (TG), urea, uric acid (UA), creatine (Cre), blood urea nitrogen (BUN), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were measured by the colorimetric method. Data were analyzed using ANOVA, paired sample t-tests, and Pearson's correlation.

RESULTS: Body weight increased with aging and decreased with CR. CR decreased WBC and mean hemoglobin count (MCH), gamma-glutamyl transferase, Cre, blood glucose in both old and young. Aging decreased leukocyte count (WBC), monocyte percentage [MO (%)] and mean hemoglobin concentration (MCHC) while increasing cholesterol, TG, BUN, Cre, UA, AST and ALT levels. CR increased neutrophil percentage, MO%, MCHC, and HDL, while reducing lymphocyte percentage, UA, and TG in aged rats.

CONCLUSIONS: Our study shows that medium-term CR is protective in healthy aging by reducing the metabolic risks caused by aging and preventing immune system, metabolic, cardiovascular risk factors and hematological disorders.

This project was supported by Gazi University Scientific Research Project Unit (Project No: TCD-2023-8842/Project ID: 8842).

Keywords: Calorie Restriction, Aging, Lipid profile, Biochemical Analysis

OC-40

Investigation of Serum Obestatin and Ghrelin Levels in Girls Diagnosed with Central Precocious Puberty

Fatma Büşra Kara¹, Sevinç Odabaşı Güneş², Hüdaverdi Kara³, Onur Akın², Esin İleri Gürel⁴

¹University of Health Sciences, Gulhane School of Medicine, Department of Physiology, Ankara, Türkiye

²University of Health Sciences, Gulhane Training and Research Hospital, Department of Pediatric Endocrinology, Ankara, Türkiye

³Sincan Training and Research Hospital, Department of Child Health and Diseases, , Ankara, Türkiye

⁴Hacettepe University, School of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Precocious puberty occurs before 8 in girls and 9 in boys. Central PP (CPP) is produced by early hypothalamic-pituitary-gonadal axis activation. The mechanisms that activate this axis remain unknown. Ghrelin and obestatin, which regulate energy metabolism and gonadal activity, may contribute to PP pathogenesis. This study investigated the link between blood obestatin and ghrelin levels and the obestatin/ghrelin ratio in CPP females.

METHODS: The study included 34 girls between the ages of 5-10 who were diagnosed with CPP and had not received treatment and 34 healthy girls within the same age who did not show signs of puberty as a control group. The children's age, bone age, anthropometric measurements (height, weight, BMI), puberty (Tanner) stage, and hormone levels (FSH, LH, and E2) were obtained retrospectively from file records. The CPP and control groups' blood samples were tested for obestatin and ghrelin using ELISA. Student-t tests and Mann-Whitney U tests were used to compare variables with and without normal distributions, respectively. Multiple linear regression was used to assess factors affecting ghrelin and obestatin.

RESULTS: Serum obestatin levels were higher in girls with CPP (P=0.003), while no difference was found in ghrelin levels. Ghrelin/obestatin ratio was lower in girls with CPP (P=0.005). Age (r=0,398, P=0,003) and ghrelin (r=0,323, P=0,008) levels positively affected obestatin levels, while age (r= -0,412, P=0,002) negatively affected ghrelin levels. No relationship was detected between BMI and obestatin or ghrelin levels.

CONCLUSIONS: Our study revealed that girls with CPP had higher obestatin levels, while ghrelin decreased with increased chronological age in both groups, regardless of pubertal age. Our findings also showed that age and ghrelin can modulate obestatin levels during puberty. This suggests that the balance between obestatin and ghrelin may play a role in the timing of pubertal development.

Keywords: Precocious puberty, Ghrelin, Obestatin, Tanner stage, LH, FSH

OC-41

The Effect of Zinc Deficiency and Supplementation on Testis TEX101 and ZnT8 Expression in Maternal Zinc Deficient Rats

Gözde Acar¹, Elif Gülbahçe Mutlu², Saltuk Buğra Baltacı³, Rasim Moğulkoç¹, Abdülkerim Kasım Baltacı¹

¹Selcuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

²KTO University, Faculty of Medicine, Department of Biology, Konya, Türkiye

³Istanbul Medipol University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

AIM: There are reports showing that TEX101, a glycoprotein synthesized mainly from testicular tissue, as well as ZFAND3, a zinc-binding protein, and ZnT8, a family of zinc carrier proteins, play a role in testicular function. There are no publications investigating the possible relationship between both maternal zinc deficiency and dietary zinc status and TEX101, ZFAND3, ZnT8 and the male reproductive system. The aim of this study is to investigate the relationship between zinc, an indispensable element in the male reproductive system, and TEX101, ZFAND3 and ZnT8.

METHODS: The study, conducted on 40 male Wistar rats, was approved by the local animal ethics committee (SUDAM 22.10.2021 date and 2020-20 decision number). The first three groups in the study were obtained from mothers who were fed a zinc-deficient diet during pregnancy and until they were separated from their offspring. Group 1 was fed with a zinc deficient diet (2.8 mcg/kg zinc). Groups 2 and 4 were fed with standard rat chow. Zinc supplementation (5 mg/kg/day intraperitoneal zinc sulfate) was provided to the animals in Group 3. Group 4 was used as the control group. At the end of the treatments, TEX101, ZnT8 and ZFAND3 gene expressions were determined in testicular tissue samples taken from sacrificed animals using real-time PCR technique. ANOVA and Duncan tests were used in the statistical analysis of the study. $P < 0.05$ was considered significant.

RESULTS: The lowest testicular TEX101, ZnT8 and ZFAND3 gene expressions were obtained in the zinc deficient (G1) and normal (G2) diet-fed groups ($p < 0.05$). Zinc supplementation (G3) reversed testicular TEX101, ZnT8 and ZFAND3 gene expressions ($p < 0.05$).

CONCLUSIONS: The current study is the first to demonstrate the existence of a critical relationship between both maternal zinc deficiency and dietary zinc status and testicular TEX101, ZnT8 and ZFAND3 gene expression, which play important roles in the male reproductive system.

Keywords: Dietary zinc status, Maternal zinc deficiency, Testis, TEX101, ZFAND3, ZnT8

OC-42

The Effects of Humanin on Sexual Dysfunction and Sperm Parameters

Rümeysa Esra Köm¹, Mehmet Emre Akipek¹, Eda Çoban Ercan¹, Ebru Gökdere¹, İbrahim Halil Güngör², Ahmet Tuluhan Atmaca¹, Gaffari Türk², Sinan Canpolat¹

¹Fırat University, Faculty of Medicine, Department of Physiology Elazığ, Türkiye

² Fırat University, Faculty of Veterinary, Department of Reproduction and Artificial Insemination Medicine, Elazığ, Türkiye

AIM: Sexual dysfunction is defined as the disruption of normal physiological and psychological processes, adversely affecting quality of life. Paroxetine, one of the antidepressants used in the treatment of psychiatric disorders, is known to cause sexual dysfunctions such as decreased libido and erectile dysfunction, as well as reduced sperm concentration and motility. Although studies have explored the relationship between the mitochondrial-derived peptide humanin and the reproductive system, its effect on antidepressant-induced sexual dysfunction is unknown. This experimental study aims to investigate the effect of humanin on paroxetine-induced sexual dysfunction.

METHODS: Male Sprague-Dawley rats, approximately 3-4 months old and sexually active, were selected and divided into five groups: control, sham, humanin, paroxetine, and paroxetine+humanin ($n=8$). The paroxetine and paroxetine+humanin groups received paroxetine (20 mg/kg/day) via oral gavage for 8 weeks. Sexual behavior tests (SBT) were conducted in the 4th week to confirm paroxetine-induced sexual dysfunction. Subsequently, the humanin and humanin+paroxetine groups received humanin (0.25 mg/6 μ L/day) subcutaneously via a mini-osmotic pump for 4 weeks. All rats underwent a 30-minute SBT. At the end of the experiment, sperm parameters were evaluated. Normality was verified using the Shapiro-Wilk test; one-way ANOVA was used for parametric data, and the Kruskal-Wallis H test was used for non-parametric data.

RESULTS: Humanin administration increased ejaculation frequency, mating ratio, and sexual activity index, which had been reduced by paroxetine ($p < 0.05$); it also decreased mount frequency and ejaculation latency, which had been increased by paroxetine ($p < 0.05$). Humanin increased total motility and spermatozoon density, which had been decreased by paroxetine ($p < 0.05$). Sperm anomalies and total acrosomal damage, increased by paroxetine, were reduced by humanin treatment ($p < 0.05$).

CONCLUSIONS: These results indicate that humanin administration has positive effects on paroxetine-induced sexual dysfunction and sperm parameters in male rats.

This study was supported by TÜBİTAK (Project No: 122S419).

Keywords: Sexual Behavior, Humanin, Paroxetine, Spermatological Parameters

OC-43

Investigation of Effects of Repeated Hyperthermia on Skeletal Muscle and Motor Function in Mice

Cansu Yakin, Cihan Suleyman Erdogan, Yunus Kosif, Bayram Yilmaz

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

AIM: Muscle functionality depend on protein and energy homeostasis, which are disrupted under hyperthermic conditions. Our study aimed to investigate the effects of repeated whole-body hyperthermia on mitochondrial dynamics in muscle and its impact on motor function and anxiety-like behavior in mice.

METHODS: Healthy Swiss albino mice were exposed to either 39°C (39E, n=16) or 41°C (41E, n=16) for 15 minutes daily over a 7-day period, while the control group (n=8) was exposed to normothermic conditions. Following exposures, half of the mice in each group were allowed a 7-day recovery period (control, n=4; 39ER and 41ER, n=8). Behavioral assessments were conducted using the open field, elevated plus maze, grip strength and rotarod tests. Mitochondrial dynamics-related gene expression in the gastrocnemius muscle was analyzed by RT-qPCR.

RESULTS: Muscle strength significantly decreased in the 39ER, 41E, and 41ER groups ($p<0.05$, $p<0.01$ and $p<0.0001$, respectively). Locomotor activity decreased in both 39E and 39ER groups ($p<0.05$, $p<0.01$, respectively). Notably, 39E and 41E groups exhibited increased closed-arm frequencies, with the 41ER group showing decreased open-arm frequency ($p<0.05$). Pgc1 α expression significantly decreased in 39E and 41E groups ($p<0.05$). Levels of Lc3b, and Parkin, significantly decreased in 39E and 41E groups ($p<0.05$). Pgc1 β and Parkin expressions were elevated in the 41ER group ($p<0.01$). Nrf1, Tfam, and Ucp2 expressions increased in the 39ER group ($p<0.05$).

CONCLUSIONS: Our results indicate that repeated exposure to distinct hyperthermic conditions differentially alter the muscle strength by regulating mitochondrial and autophagy-related gene expressions.

Keywords: Hyperthermia, Mitochondria, Strength

OC-44

Investigation of the Analgesic Interaction Between Melatonin and Clonidine on Rats

Gülçin Durdağı¹, Emine Çakıröz², Eser Öz Oyar¹

¹Izmir Katip Çelebi University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

²Manisa Celal Bayar University, Faculty of Medicine, Department of Physiology, Manisa, Türkiye

AIM: The aim of the study was to evaluate the antinociceptive

effects of melatonin (MEL) and clonidine (CLO) administered alone and in combination on acute thermal pain in rats.

METHODS: 32 Wistar albino male rats were randomly divided into 4 groups: Control, MEL, CLO, MEL+CLO. The effect of drug applications on acute thermal nociception was evaluated by tail-flick and hot-plate tests, and the effect on locomotor activity was evaluated by the rotarod test. One Way ANOVA and Bonferroni multiple comparison test were applied for repeated measurements to evaluate the effect of the drug or drugs given to each group and its relationship with the time the measurements were taken. Between-group comparisons of each time point were made by one-way analysis of variance One Way ANOVA and post hoc multiple comparison Tukey test. $P<0.05$ was considered statistically significant.

RESULTS: Doses of 60 mg/kg melatonin and 50 μ g/kg clonidine administered alone showed analgesic effects in both tail-flick and hot-plate tests ($p<0.01$). The combined application of the two drugs strengthened the effect produced by both drugs alone in all time periods after injection and prolonged the duration of effect ($p<0.001$). The findings obtained from the rotarod test we used to evaluate the locomotor function of rats showed that the doses we applied did not cause motor incoordination in the group where both agents were administered alone or in the group where they were administered in combination.

CONCLUSIONS: In light of the data obtained, it is predicted that the combination of MEL+KLO may be an alternative analgesic agent that creates a stronger antinociceptive response than the effect produced by the two drugs alone, without causing any motor disorders, and will help minimize possible side effects.

Keywords: Antinociception, Clonidine, Hot-plate, Melatonin, Rotarod, Tail-flick

OC-45

Differential Effects of Mast Cell Stabilizers on Mechanisms Responsible for Migraine in Experimental Migraine Models

İbrahim Ethem Torun¹, Yasemin Baranoglu Kilinc², Erkan Kilinc¹

¹Bolu Abant İzzet Baysal University, Faculty of Medicine, Department of Physiology, Bolu, Türkiye

²Bolu Abant İzzet Baysal University, Faculty of Medicine, Department of Pediatrics, Bolu, Türkiye

AIM: Meningeal mast cell (MMC) activation plays key role in migraine pathogenesis by inducing neurogenic inflammation via inflammatory mediators in their granules. We explored the effects of mast cell stabilizers cromolyn and quercetin on the mechanisms underlying migraine in in-vivo and ex-vivo migraine models.

METHODS: Wistar male rats (8-12 weeks-old) were divided into 6 groups (n=6/group). Following intraperitoneal administration of vehicle to control and migraine groups, 10 mg/kg cromolyn to Cr+NTG group, 25 mg/kg quercetin to Qu+NTG group, cromolyn

and quercetin together to Cr+Qu+NTG group, and 600 µg/kg migraine-drug sumatriptan to Sum+NTG group for five days, 30 minutes later control received vehicle and the other groups received 10 mg/kg NTG for migraine induction, in-vivo. In ex-vivo experiments, vehicle was treated to control group, and capsaicin(100 nM), cromolyn (100 µM), quercetin (100 µM), sumatriptan (30 µM) or their various combinations to meningeal preparations(n=6/group). Mechanical hyperalgesia was assessed by von-Frey test, calcitonin gene-related peptide(CGRP) in trigeminal ganglia and ex-vivo samples, and brainstem c-Fos and CGRP concentrations by ELISA, and MMCs by toluidine-blue staining. Data were analyzed by one-way ANOVA.

RESULTS: Quercetin or combining quercetin+cromolyn reduced NTG-induced hyperalgesia, trigeminal ganglion CGRP and brainstem CGRP and c-fos expression, and MMC degranulation and number in vivo ($p<0.05$). Cromolyn did not affect NTG-induced hyperalgesia and c-fos expression, but reduced the other parameters. Ex-vivo, cromolyn or combining quercetin+cromolyn, but not quercetin, reduced capsaicin-induced CGRP release. Neither treatment affected basal CGRP release. Sumatriptan inhibited all the induced effects.

CONCLUSIONS: Quercetin, unlike the effects of cromolyn, reduced mechanical hyperalgesia and brainstem c-fos expression in-vivo, whereas cromolyn reduced CGRP release ex-vivo, while quercetin was ineffective, suggesting that the two mast cell stabilizers have different modes of action. The therapeutic effects of the combining quercetin and cromolyn in-vivo and ex-vivo suggest that mast cell stabilization may be an effective approach to prevent neurogenic inflammation underlying migraine.

Keywords: CGRP, Mast cell stabilizers, Meningeal mast cells, Migraine, Neurogenic inflammation

OC-46

Attenuation of Neuropathic Pain by P2X7 Receptor Antagonist Brilliant Blue G

Güner Çalış¹, Ataç Sönmez¹, Erhan Caner Akkaya², Helin Demirtaş³, Bahar Dalkıran³

¹Dokuz Eylül University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

²Uşak University, Faculty of Medicine, Department of Physiology, Uşak, Türkiye

³Dokuz Eylül University, Institute of Health Sciences, Department of Physiology, Izmir, Türkiye

AIM: There is growing evidence in recent years that pro-inflammatory mediators play a key role in the development of neuropathic pain through central and peripheral sensitization mechanisms. Brilliant Blue G (BBG) is a non-competitive antagonist of the P2X7 receptor, which is exclusively activated by high extracellular ATP concentrations, causing the intense release of

pro-inflammatory cytokines. This study aimed to evaluate the effectiveness of BBG following traumatic injury in a peripheral neuropathy model in rat and assess both the sensory and the affective components of neuropathic pain in the chronic process.

METHODS: Male Sprague-Dawley rats were used in the study. The neuropathic pain model was established by partial ligation of the saphenous nerve. BBG was administered intraperitoneally at a daily dose of 50 mg/kg for one week following the ligation. Animals were divided into four experimental groups: Sham, SPL, SPL + Vehicle and SPL + BBG. Mechanical pain thresholds were evaluated with the Dynamic Plantar Aesthesiometer weekly and analgesic effectiveness of BBG was evaluated with the Dynamic Hot Plate on 7th day. On the last day of the experiment, Forced Swim Test was used to assess depression-like behavior.

RESULTS: For the nerve-ligated animals, a significant decrease in mechanical pain threshold was observed compared to baseline values, from the first measurement after the ligation to the last measurement day ($p<0.05$). On the 6th day, it was found that the pain threshold of the BBG group decreased significantly less than the SPL and SPL + Vehicle groups'. Analgesic effectiveness of BBG was detected in the Dynamic Hot Plate test. In the Forced Swim Test, the immobility score of the nerve-ligated animals was significantly higher than the Sham group.

CONCLUSIONS: Treatment options for neuropathic pain are still limited. Designing pre-clinical pain models which includes both sensory and affective components may aid the development of more effective treatment modalities.

Keywords: Neuropathic Pain, P2X7 Receptor, Brilliant Blue G, Affective Component of Pain

OC-47

Differential Physiological and Inflammatory Responses to Trypophobic Stimuli

Elif Barış¹, Hasan Kazdağlı², Arda Kıpçak³, Süleyman Öztürk⁴, Deniz Ceylan⁵, Ayşe Banu Demir⁶, Burak Erdeniz⁷

¹Izmir University of Economics, School of Medicine, Department of Medical Pharmacology, Izmir, Türkiye

²Izmir University of Economics, Vocational School of Health Sciences, Izmir, Türkiye

³University of Virginia, Department of Psychology, Charlottesville, United States

⁴University of Padova, Department of General Psychology, Padova, Italy

⁵Koç University, School of Medicine, Department of Psychiatry, İstanbul, Türkiye

⁶Izmir University of Economics, School of Medicine, Department of Medical Biology, Izmir, Türkiye

⁷Izmir University of Economics, Department of Psychology, Izmir, Türkiye

AIM: The immune system activates an inflammatory response through pro-inflammatory proteins to defend the body against external pathogens. Previous studies have shown that stimuli evoking fear and disgust can trigger an immune response; however, specific immune proteins and physiological changes related to tryphobia remain unclear. Tryphobia is defined as a fear or disgust of irregular clusters of holes or patterns. This study aims to investigate the inflammatory and physiological responses to both skin-related and non-skin-related tryphobic images. **METHODS:** Fifty healthy participants (n=50) were assessed using the Tryphobia Questionnaire (TQ). Participants were randomly divided into two groups: those exposed to skin-related and non-skin-related tryphobic images. Blood samples were collected before and after visual exposure, and IL-6 and TNF- α levels were analyzed using ELISA and RT-qPCR methods. Heart rate variability (HRV) was evaluated using photoplethysmogram (PPG) recordings, and low-frequency (LF) and high-frequency (HF) components were analyzed. LF typically reflects sympathetic nervous system activity, while HF is indicative of parasympathetic activity.

RESULTS: Significant differences were observed in IL-6 and TNF- α levels before and after exposure ($P<0.05$). There was also a significant interaction between the mRNA expression of these cytokines and participants' tryphobia scores ($P<0.05$). HR and HRV parameters, particularly LF and HF components, showed statistically significant changes during and after visual stimulation ($P<0.05$).

CONCLUSIONS: The findings suggest that tryphobic stimuli may be linked to variations in immune responses and activity levels of the sympathetic and parasympathetic nervous systems. The fear associated with tryphobia may be related to sympathetic activation, while parasympathetic activity was associated with changes in HRV.

Keywords: Tryphobia, Immune system, Inflammation, Pro-inflammatory cytokines, Heart Rate Variability (HRV)

OC-48

Investigating the Long-term Effects of UNC2025-mediated Mer Tyrosine Kinase Inhibition After Neonatal Hypoxic Ischaemia

Enes Doğan¹, Buse Balaban², Zeynep Balçıklı³, Mehmet Serif Aydın¹, Nursena Şengün⁴, Zehra Değirmenci¹, Ulkan Kilic², Taha Keleştemur¹, Mustafa Beker⁴, Ertugrul Kilic⁴

¹Istanbul Medipol University, Research Institute for Health Sciences and Technologies (SABITA), Istanbul, Türkiye

²University of Health Sciences, School of Medicine, Department of Biology, Istanbul, Türkiye

³Demiroğlu Bilim University, School of Medicine, Department of Physiology, Istanbul, Türkiye

⁴Istanbul Medeniyet University, School of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Neonatal hypoxic ischemia (NHI) is the major cause of perinatal morbidity and mortality resulting from insufficient supply of oxygen. Although Mer Tyrosine Kinase (MerTK) is involved in

phagocytosis of apoptotic cells, our understanding of post-NHI pathophysiology remained insufficient. High MerTK expression in the chronic period following brain injury suggests that MerTK is a critical in adaptation to post-NHI conditions and degenerative processes. In this study, the long-term effects of UNC2025-mediated MerTK inhibition were investigated by employing NHI model.

METHODS: 7-day-old (P7) C57BL-6 mouse pups were anaesthetized with 1% isoflurane (30% O₂; N₂O) and their carotid arteries were surgically ligated. Mice were kept in units containing 8% O₂ and 92% N₂ for 90 minutes and returned to cages. Mice were randomly assigned as vehicle (0.7% NaCl) or UNC2025 (65 mg/kg in 30 μ L) groups before operation. Behavioral tests were conducted on P30, P42, P55 to assess the locomotor activity, anxiety, and motor coordination. Neuronal nuclei were stained for neuronal survival, biotinylated dextrane amine and Cascade Blue for axonal projection, and 5-bromo-2'-deoxyuridine for neurogenesis. MerTK's effects on gene expression were evaluated with polymerase chain reaction. Independent sample t-test was used to assess significance between groups and $p<0.05$ was considered statistically significant.

RESULTS: MerTK inhibition improved motor activity and coordination, while decreasing anxiety and depression ($p<0.05$). UNC2025 administration increased neuronal survival and axonal projection after NHI ($*p<0.05$). Neurogenesis increased in the dentate gyrus following NHI in the vehicle group. MerTK inhibition increased the expression of several genes involved in the growth, proliferation, and differentiation of nerve cells after injury.

CONCLUSIONS: In neurodegenerative conditions, MerTK inhibition was shown to have neuroprotective effects and modulate the axonal plasticity. UNC2025 administration improved the behavioral patterns after NHI. In accordance with these findings, MerTK inhibitor administration could be an alternative therapeutic approach following NHI.

Keywords: MerTK, Neonatal hypoxic-ischemia, UNC2025

OC-49

Effect of 1-Week 3',4'-Dihydroxyflavonol Administration on Motor Function and Learning in Rats: Role of AQP 4, Caspase 3 and IL-10

Tuğçe Aladağ, Gözde Acar, Rasim Mogulkoc, Abdulkemim Kasim Baltacı

Selcuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: Ischemia is defined as the decrease or loss of blood supply to a region of the body due to various reasons. 3', 4'-dihydroxyflavonol (DiOHF) is a synthetic flavonoid and its protective effect has been determined in different ischemia-reperfusion studies. This study aimed to determine the effect of 3',

4'-dihydroxyflavonol on motor function and learning in rat brain ischemia-reperfusion experimentally and the role of caspase 3, AQP4 and interleukin-10.

METHODS: The study, which was conducted with 28 Wistar-albino male rats at the Experimental Medicine Application and Research Center of Selçuk University, was approved by the same ethics committee (2022-35). Experimental groups were established as 1-Control, 2-Sham, 3-Ischemia-reperfusion, 4-Ischemia-reperfusion + DiOHF (3',4'-dihydroxyflavonol) (10mg/kg). Animals were anesthetized, the carotid artery was ligated for 30 minutes and reperused. Along with reperfusion, the animals were given DiOHF intraperitoneally at a dose of 10 mg/kg for 1 week. In hippocampus tissue samples taken from animals under anaesthesia, caspase 3 and AQP4 levels were determined by PCR and interleukin-10 levels by ELISA. The effect of ischemic injury on motor function and learning was observed behaviorally by neurological scoring and NOR (novel object recognition) test. Results were defined as mean \pm standard deviation. Kruskal-Wallis analysis of variance was used for intergroup comparison and Mann-Whitney U test was applied for $p < 0.05$ level. $P < 0.05$ was considered statistically significant.

RESULTS: With brain ischemia reperfusion, caspase 3 and AQP4 levels in hippocampus tissue significantly increased, while interleukin-10 decreased ($P < 0.001$). However, 1 week of DiOHF supplementation significantly reduced the increased caspase 3 and AQP4 levels and significantly increased interleukin-10 levels ($P < 0.001$). DiOHF treatment positively affected the NOR test and neurological scoring test values.

CONCLUSIONS: Our study shows that cerebral ischemia and subsequent reperfusion in rats causes tissue damage, but DiOHF administration for 1 week has a healing effect.

Keywords: 3' 4'-dihydroxyflavonol, Apoptosis, AQP4, Brain ischemia, IL-10, NOR

OC-50

Central Neuropeptide-S Mitigates Cognitive Impairments by Regulating Hippocampal Synaptic Plasticity in Hemiparkinsonian Rats

Aysegül Gemici Sinen¹, Narin Derin¹, Osman Sinen²

¹Akdeniz University, Faculty of Medicine, Department of Biophysics, Antalya, Türkiye

²Akdeniz University, Faculty of Medicine, Department of Physiology, Antalya, Türkiye

AIM: Neuropeptide-S (NPS) is known to ameliorate learning and memory deficits induced by experimental Parkinson's Disease (PD) models. However, the mechanisms through which NPS influences cognitive functions remain unclear. This study aims to investigate the effects of central NPS administration on learning and memory alterations associated with an experimental hemiparkinsonian model at both electrophysiological and molecular levels.

METHODS: Adult male Sprague Dawley rats ($n=39$) were divided into three groups: sham, 6-OHDA, and 6-OHDA+NPS. To create the hemiparkinsonian model, 6-OHDA was stereotactically injected into the right medial forebrain bundle. Central NPS (1nmol, icv) was administered into the lateral ventricle via a cannula for 7 days following the 6-OHDA surgery. Motor performance was assessed using the open field test while learning and memory were evaluated using the Morris water maze and object recognition tests. Long-term potentiation (LTP) recordings were taken to assess hippocampal synaptic plasticity. The expression levels of tyrosine hydroxylase in the substantia nigra and phosphorylated CaMKII, GluR1, and GluR2 expressions in the hippocampus were determined by immunohistochemistry. Statistical analyses were performed using ANOVA with Tukey's post-hoc test or Kruskal-Wallis test with Dunn's post-hoc test. Our study was approved by the Akdeniz University Local Ethics Committee for Animal Experiments (protocol no:1479/2022.07.006).

RESULTS: NPS administration significantly ($p < 0.05$) reduced 6-OHDA-induced motor and cognitive impairments. In 6-OHDA-lesioned rats, NPS treatment significantly ($p < 0.05$) increased the diminished amplitude of LTP induced at the dentate gyrus/performant path synapses. In the hippocampus, the decreased number of pCaMKII and GluR1 immunoreactive cells due to 6-OHDA was significantly ($p < 0.05$) increased with central NPS administration, except for GluR2 levels, which showed no change. Moreover, centrally administered NPS significantly ($p < 0.05$) reduced nigral dopaminergic neuron loss induced by 6-OHDA.

CONCLUSIONS: These results contribute to elucidating the mechanism by which central NPS enhances cognitive function in an experimental PD model.

Keywords: Hippocampus, Neuropeptide-S, Parkinson's Disease, Synaptic Plasticity

OC-51

Potential Roles of Enriched Environmental Conditions on Motor Behavior in a Cerebellar Infarct Mice Model

Ayten Kardaş¹, Sanem Aslıhan Aykan², Yavuz Yavuz¹, Bayram Yılmaz¹

¹Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

²Harvard Medical School, Department of Radiology, Boston, USA

AIM: Cerebellar infarct (CI) is a rare stroke that causes severe motor deficits like ataxia and gait disturbances, leading to difficulties in daily activities and a serious decline in quality of life. This study aims to evaluate the effects of various enriched environmental conditions on motor performance in a CI mouse model and explore their potential therapeutic impacts.

METHODS: Forty male C57BL/6 mice were divided into 5 groups: physical enrichment, enriched environment, enriched environment +3 healthy mice, standard housing, and sham. The CI

model was induced in mice via stereotaxic injection of N5-(1-iminoethyl)-L-ornithine dihydrochloride. Motor performance was assessed pre-infarct and on specific days post-infarct using the wire walk test and footprint test. The infarct area was identified by Hematoxylin & Eosin staining. Immunohistochemistry was employed to visualize Biorientation Defective 1 (BOD1), a factor associated with motor coordination, utilizing a confocal microscope. Data were analyzed by two-way ANOVA, with $p < 0.05$ considered significant.

RESULTS: CI resulted in decreased motor performance and negatively impacted balance and coordination in mice; these effects were modulated by environmental factors. Statistically significant differences were observed in the overlap distance of right steps among the groups ($p < 0.01$). However, no significant differences were noted in foot faults between the experimental groups.

CONCLUSIONS: This study highlights the beneficial and detrimental effects of various enriched environmental conditions on diminished motor performance following CI. Accordingly, it may offer significant insights for the development of innovative treatment and rehabilitation strategies.

Keywords: Cerebellar Infarct, Enriched Environment, Motor Performance

OC-52

Sleep Disorders with Individuals in Prediction with Cerebral Lateralization Reasoning Ability, Evaluation of Attention

Melike Bastoklu¹, Beste Menteşe¹, Hikmet Yılmaz², Necip Kutlu¹

¹Manisa Celal Bayar University, Faculty of Medicine, Department of Physiology, Manisa, Türkiye

²Manisa Celal Bayar University, Faculty of Medicine, Department of Neurology

AIM: Sleep is characterized as a temporary loss of consciousness. An adult individual needs to sleep at least 6 hours in order to perform the functions in our body. If insomnia lasts for a long time, conditions such as attention deficit, lack of concentration, and inability to flow information occur. OSAS is observed in 1-2% of middle-aged women and 2-4% of men. Studies have found that sleep disorders other than sleep apnea do not cause death. In a study, night and day shifts were compared and it was observed that assistants who were on night duty, that is, people who had insomnia problems, had a close margin of error and suffered more loss of cognitive function. The aim of this study is to examine the relationships between cognitive skills such as attention deficit, selective attention, sustained attention, reasoning ability, and reaction time in patients with OSAS and any sleep disorder (CPAP) before and after treatment.

METHODS: Our study was conducted among 41 healthy and voluntary individuals, without any age limit. Before and after using CPAP, cognitive skill tests applied in the psychotechnical laboratory

were the reasoning ability test (SPMIQ), reaction time test (RTms), response speed-quality test under stress (DT- DTduration), sustained attention and problem solving (COGyes-COGno). Selective attention (SIGNAL) test was also applied. In addition, psychological surveys such as BECK depression scale, STAI1 (state anxiety), STAI2 (trait anxiety) and lateralization questionnaire were applied. Psychological surveys were administered both before and after CPAP, and comparisons were made between tests and surveys.

RESULTS: After the treatment, Dt (reaction under stress), Signal (selective attention), SPM (judgment ability) increased ($p < 0.05$).

CONCLUSIONS: It has been determined that sleep disorder may have an effect on the higher functions of the brain and that there may be an increase in brain cognitive functions after its treatment.

Keywords: CPAP, Cerebral Lateralization, Handedness, OSAS, Sleep Disorder, Attention

OC-53

The Direct Effects of SARS-COV-2 Spike Protein Subunit S1 on Secondary Hemostasis and Fibrinolysis

Evren Kılınç¹, Fatıma Şeyma Elbeyoğlu², Batuhan Görkem İrez³, Neslihan Özyaka², Zeynep Aslıhan Durer⁴, Engin Sağdılek⁵

¹University of Health Sciences, Hamidiye School of Medicine, Department of Biophysics, Istanbul, Türkiye

²Acibadem Mehmet Ali Aydınlar University, Institute of Health Sciences, Department of Biophysics, Istanbul, Türkiye

³Istanbul University Fundamental Sciences Programme (TEBİP), Biology Undergraduate Programme, Istanbul, Türkiye

⁴Acibadem Mehmet Ali Aydınlar University, School of Medicine, Department of Biophysics, Istanbul, Türkiye

⁵Bursa Uludag University, School of Medicine, Department of Biophysics, Bursa, Türkiye

AIM: In patients with severe Covid-19, the clinical presentation is characterized by profound infection and inflammation, contributing to disruptions in hemostatic processes. However, the direct influence of the virus on hemostasis remains uncertain. This study aims to investigate the potential direct effects of the spike protein S1 subunit on secondary hemostasis and fibrinolysis.

METHODS: The recombinant S1 protein was prepared at concentrations of 50, 5, and 1 ng/ml in phosphate-buffered saline (PBS) and incubated at 37°C for 2 hours. The incubation involved citrated whole blood, platelet-rich plasma (PRP), and platelet-poor plasma (PPP) obtained from the same donor ($n=5$). Subsequently, PPP samples were isolated through the centrifugation of blood and PRP samples at 13000 rpm for 5 minutes, while PPP samples were used as it is. Measurements including prothrombin time (PT), international normalized ratio (INR), activated partial thromboplastin time (aPTT), fibrinogen, and D-Dimer were conducted on the obtained PRP samples.

RESULTS: Significantly reduced aPTT values were observed in whole blood, PRP, and PPP samples, exclusively at the 50 ng/ml S1 concentration compared to the buffer control. A decrease in fibrinogen levels was observed solely in whole blood at the 50 ng/ml S1 concentration. Elevated D-Dimer levels were evident in whole blood across all doses and in PRP at the 5 ng/ml S1 concentration.

CONCLUSIONS: The combined interpretation of shortened aPTT, decreased fibrinogen, and increased D-Dimer levels underscores a direct influence of the Spike S1 protein, particularly on the intrinsic pathway. This suggests its direct involvement in the secondary hemostasis process and fibrinolysis.

This research was funded by The Scientific and Technological Research Council of TÜRKİYE (TÜBİTAK; grant number 122Z772).

Keywords: Blood coagulation, Secondary Hemostasis, Fibrinolysis, Spike S1 subunit, SARS COV-2

OC-54

Effects of Taurine Administration on Cognitive Functions, Apoptosis, miR-34a, Inflammation and Oxidative Stress Markers in Alzheimer's-Like Disease Rat Model

Burak Kayabaşı¹, Nida Aslan Karakelle², Çisem Yeşil Kayabaşı³, Zeynep Yığman³, Sibel Dinçer¹

¹Gazi University, Faculty of Medicine, Department of Physiology Ankara, Türkiye

²Lokman Hekim University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

³Gazi University, Faculty of Medicine, Department of Histology and Embryology, Ankara, Türkiye

AIM: Apoptotic, inflammatory, oxidative processes play important role in the pathogenesis of Alzheimer's disease. We aimed to evaluate the effects of taurine, which has antiapoptotic, antioxidant and anti-inflammatory properties, on these processes in Alzheimer's-like disease rat model induced by intracerebroventricular (icv) Amyloid Beta 1-42 (Aβ1-42) injection. **METHODS:** Thirtytwo male Wistar Albino rats were divided into groups as Preliminary study (n:2), Control (n:7), Taurine (n:7), Aβ1-42 (n:8), Aβ1-42+Taurine (n:8). After icv Aβ1-42 (10μg/10μl) administration to the relevant groups, 250 mg/kg/day taurine was given to the taurine groups via oral gavage for 32 days. Morris Water Maze (MWM) test was performed to evaluate learning and memory. On day 33, rats were sacrificed and brain tissues were collected. The presence of Aβ plaques in brain tissue was evaluated by Congo red staining. Bax, bcl-2, cleaved caspase-3 proteins were analyzed by Western Blot to evaluate apoptosis and miR-34a, which is associated with apoptosis, was analyzed by qPCR. Parameters such as TNFα, IL-1β, IL-10, Total Antioxidant Status (TAS), Total Oxidant Status (TOS), Malondialdehyde, Glutathione which related to inflammatory and oxidative processes were evaluated by ELISA and colorimetric tests. Nonparametric tests were used, p<0.05 was considered statistically significant.

Supported by Gazi University-BAP (Project No: TTU-2022-7774). Ethical approval: G.Ü.ET-22.013.

RESULTS: The presence of amyloid plaques with Congo Red staining and cognitive impairment in MWM test indicated the formation of an Alzheimer's-like disease model. Aβ1-42 administration increased bax, cleaved caspase-3 apoptotic proteins (p<0,05) and decreased bcl-2 antiapoptotic protein (p<0,05) which was not observed in Aβ1-42+taurine group. While plasma miR-34a decreased in Aβ1-42 injection groups (p<0,05), brain miR-34a were unchanged. IL-10 levels were higher in Aβ1-42+taurine group compared to Aβ1-42 group (p<0,05). While Aβ1-42 increased serum TOS and brain Malondialdehyde (p<0,05), this changes were not observed in Aβ1-42+taurine group.

CONCLUSIONS: Taurine may be used as a supportive agent in the treatment of neurodegenerative diseases such as Alzheimer's disease, if supported by further studies.

Keywords: Aβ1-42, Alzheimer's disease, Apoptosis, Inflammation, miR-34a, Oxidative stress

OC-55

Conjunctival IgD, LL-37, and Pentraxin Levels and Their Relationship with Visual Electrophysiological Responses in the Development of Diabetic Retinopathy

Aykut Oruç¹, Emre Tekkaya², Kadriye Yağmur Oruç³, Hakkı Oktay Seymen¹

¹Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

²Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Ophthalmology, İstanbul, Türkiye

³İstinye University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

AIM: Diabetic retinopathy (DR) involves interactions of various factors like inflammation and oxidative stress. Studies show increased serum Pentraxin-3 (PTX3) in DR, with IgD triggering PTX3 and LL-37 secretion from basophils. This study investigates conjunctival IgD, LL-37, and PTX3 levels in DR patients and evaluates their correlation with visual electrophysiological responses.

METHODS: Ninety participants: 30 healthy (C), 30 diabetic without DR (D), and 30 with DR (aged 30-69) were examined. Conjunctival samples were collected using Schirmer strips, and IgD, LL-37, PTX3 levels were measured by ELISA and immunohistochemistry. Retinal functions were assessed using 61' scaled multifocal electroretinography (mERG) and long duration ERG (ldERG). Signal intensity-s/sp in first-order kernel (10) and N1P1-P1N2 intensities/amplitudes in second-order kernel (20) were measured. D-wave amplitudes and intensities were measured in ldERG. Correlations with other parameters were evaluated. Normality was assessed by Shapiro-Wilk test, homogeneity by Levene test. One-way ANOVA and post-hoc Tukey test were used

for normally distributed data; Kruskal-Wallis and post-hoc Dunn tests for non-normally distributed data. Pearson correlation was used. Ethical approval was obtained from Istanbul University-Cerrahpasa Clinical Research Ethics Committee (QDj4U8Sy).

RESULTS: No significant increase in IgD, LL-37, PTX3 in D group, but significant increases in DR group ($p<0.05$). No significant difference in mERG-10 responses between C and D, but significant decreases in DR ($p<0.05$). Significant decreases in 2O responses in both D and DR compared to C ($p<0.05$). Significant reductions in IdERG responses in D and DR compared to C ($p<0.05$). Significant correlations between 2O-mERG and IdERG responses and all conjunctival findings across all groups.

CONCLUSIONS: Findings help understand inflammatory mechanisms of DR. Increased IgD and other parameters suggest contribution to retinopathy due to disrupted blood-retina and blood-aqueous barriers. Monitoring 2O-mERG and IdERG in diabetic patients without retinopathy may provide early information for preventive measures.

Keywords: Diabetic retinopathy, IgD, LL-37, PTX3, Electroretinography

OC-56

The Role and Mechanisms of Type-1 Diabetes, Insulin and Insulin Receptor in Migraine Pathophysiology

İbrahim Ethem Torun¹, Hümeysra Çelik², Erkan Kılınç¹, Muhammet Güzel Kurtoglu³

¹Bolu Abant İzzet Baysal University, Faculty of Medicine, Department of Physiology, Bolu, Türkiye

²Alanya Alaaddin Keykubat University, Faculty of Medicine, Department of Physiology, Alanya, Türkiye

³Bolu Abant İzzet Baysal University, Faculty of Medicine, Department of Medical Microbiology, Bolu, Türkiye

AIM: Clinical studies suggest that diabetes may protect against migraine, but the underlying mechanisms are unknown. We investigated the possible roles and mechanisms of type-1 diabetes, insulin and insulin receptor in migraine pathobiology in in-vivo and ex-vivo migraine models.

METHODS: Wistar male rats (8-10 weeks-old) were divided into 9 groups ($n=7/\text{group}$). Control, Migraine, Diabetes+Migraine, Diabetes+Insulin+Migraine, Diabetes, Diabetes+Insulin, Insulin+Migraine, BMS+Insulin+Migraine, BMS+Migraine groups were administered vehicle, insulin (9 IU, s.c.), insulin receptor antagonist BMS (12.5 mg/kg, s.c.) or BMS+insulin 7 days after vehicle or streptozotocin (60 mg/kg, i.p.) injection to induce diabetes; the next day, nitroglycerin (NTG, 10 mg/kg, i.p.) or its vehicle was administered to induce migraine. Ex-vivo meningeal, trigeminal ganglion and brainstem preparations ($n=6/\text{group}$) were topically administered vehicle (control), capsaicin (100 nM), insulin (10 μM), BMS(100 nM), capsaicin+insulin, BMS+insulin or capsaicin+BMS.

Blood glucose was assessed by glucometer, pain threshold by von-Frey, calcitonin gene-related peptide(CGRP) levels in trigeminal ganglia and ex-vivo superfusates, and brainstem c-Fos and CGRP concentrations by ELISA, and meningeal mast cells by toluidine-blue staining. Data were analyzed by one-way ANOVA.

RESULTS: Insulin further increased NTG-induced hyperalgesia, brainstem CGRP and c-fos, trigeminal ganglion CGRP levels, and mast cell activation ($p<0.05$). BMS blocked insulin's effects ($p<0.05$) but was ineffective in the migraine model. Hyperglycemia did not alter triggered parameters in the migraine model. Insulin stimulated CGRP release in ex-vivo meningeal and trigeminal ganglion preparations and further increased capsaicin-stimulated CGRP release ($p<0.05$). BMS blocked insulin's effects ($p<0.05$) but did not alter basal CGRP release. In brainstem preparations, insulin or BMS had no effects.

CONCLUSIONS: Our findings suggest that the lower prevalence of migraine in diabetic patients is not due to hyperglycemia but to a decreased interaction between insulin and its receptor due to insulin deficiency. Modulation of the interaction between insulin and its receptor may be a good target for new therapeutic approaches. This study was supported by TUBITAK[Project-number: 222S289].

Keywords: Diabetes, İnsulin, Insulin receptor, Migraine, Neurogenic inflammation

OC-57

Impact of Metallothioneins on DNA Damage and Apoptosis in Multiple Sclerosis: A Comparative Study Using Comet Assay

Hande Yüce¹, Mehmet Tecelioğlu², Yasemin Berberoğlu³, Kevser Tanbek⁴, Şeyma Yaşar⁵, İlker Ateş⁶, Neşe Başak Türkmen¹, Songül Ünüvar¹, Süleyman Sanda¹

¹İnönü University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Malatya, Türkiye

²İnönü University, Faculty of Medicine, Department of Neurology, Malatya, Türkiye

³Pamukkale University, Faculty of Medicine, Department of Medical Biology, Denizli, Türkiye

⁴İnönü University, Faculty of Medicine, Department of Physiology Malatya, Türkiye

⁵İnönü University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Malatya, Türkiye

⁶Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Türkiye

AIM: Multiple sclerosis (MS) is one of the most common neurological diseases in the young adult population worldwide. Characterized by the presence of numerous focal demyelinating areas in plaques or lesions within the central nervous system, multiple sclerosis involves inflammation and axonal loss. The aim of this study is to determine the levels of Zn and Cu in serum

samples of patients diagnosed with multiple sclerosis, investigate the protective effects of metallothionein subtypes (MT-I, MT-II, MT-III) on neural damage, and compare DNA damage and the metallothionein-Zn/Cu balance, which are effective in the pathogenesis of multiple sclerosis.

METHODS: Seventy individuals diagnosed with MS (study group) and 30 healthy individuals (control group) were included in this study. The demographic characteristics and DNA damage levels in peripheral lymphocytes of the study and control groups were determined. Human neuroblastoma (SH-SY5Y) and mouse fibroblast (L929) cell lines were treated with ZnSO₄·7H₂O and CuSO₄, and cell viability was assessed using the MTS assay. The gene expressions of MT-IIA, MT-III, metal transcription factor-1 (MTF-1), and metal responsive element 11 (MRE11) were analyzed by RT-PCR, while DNA damage was analyzed using the comet assay.

RESULTS: According to the comet analysis results, DNA damage was found to be higher in multiple sclerosis patients compared to healthy individuals. Following a 48-hour exposure of SH-SY5Y cells to zinc and copper salts, a significant increase in MT-IIA and MT-III gene expressions and DNA damage, dependent on MTF-1, was detected.

CONCLUSIONS: In this study, which is the first to evaluate DNA damage in multiple sclerosis patients using the comet assay, it was determined that DNA damage is pronounced and that genes encoding metallothioneins activate apoptotic cell death pathways in neuroblastoma cells. Financial Disclosure: This study was supported by the Scientific Research Projects Unit of İnönü University (Project No: TDK-2022-3012).

Keywords: Multiple sclerosis, Metallothionein, Zinc, Copper, Comet

OC-58

Effects of Circadian Rhythm Disruption on Cellular Survival and Brain Protein Profile in an Experimental Parkinson's Model

Enes Doğan¹, Halil İbrahim Koç¹, Hayriye Ecem Yelkenci¹, Çiğdem Bayraktaroğlu¹, Ayşenur Özpinar¹, Buse Balaban², Serdar Altunay¹, Ertuğrul Kılıç³, Mustafa Çağlar Beker³

¹Istanbul Medipol University, Health Science and Technology Research Institute (SABITA), Istanbul, Türkiye

²University of Health Sciences, Faculty of Medicine, Department of Medical Biology, Istanbul, Türkiye

³Istanbul Medeniyet University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Parkinson's disease (PD) is the second leading neurodegenerative disorder in globally, and its prevalence is steadily increasing. Circadian rhythm is a biological clock that regulates physiological processes and behaviors and is thought to be involved in Parkinson's disease pathophysiology. The purpose of

this study is to investigate into the effects of circadian rhythm disruption on Parkinson's disease in the brain.

METHODS: Experimental PD model was induced in 8-12 week male C57BL/6J mice by intracerebral injection of 7.5 µg 6-OHDA. The mice were randomly assigned as normal and circadian rhythm disrupted groups. Motor activity and anxiety were evaluated by rotation test and open field test on days 7, 14, 21 and 28 after PD model. Mice were sacrificed on day 28 and neuronal survival and dopaminergic cell density were analyzed by neuronal nuclei and tyrosine hydroxylase immunofluorescence staining of coronal brain slices from the striatum and substantia nigra (SN) regions. Proteomic analysis of tissue samples from the striatum and SN revealed the protein profile related to these processes. Independent samples t-test was used for statistical significance between groups and p<0.05 was considered statistically significant.

RESULTS: The circadian disrupted group showed increased anxiety (p<0.05) and decreased locomotor activity. Additionally, the circadian disturbed group had greater dopaminergic neuronal death (p<0.001) and reduced neuronal survival rates (p<0.001). Proteomic studies showed significant (p<0.05) changes in 115 proteins in the striatum and 427 proteins in the SN. Bioinformatic analyses uncovered that the PD and Neurodegeneration Pathways - Multiple Diseases pathways are the most effective.

CONCLUSIONS: Circadian rhythm disruption is thought to have behavioral and neuronal effects on PD. In Additionally, the identified pathways are thought to be protein biomarkers that may explain the interplay between PD and circadian rhythm.

Keywords: Circadian rhythm, Parkinson disease, Proteomics.

OC-59

The Role of Astrocytes After Ischemic Stroke

Sevban Bayırlı¹, Halil İbrahim Koc¹, Buse Balaban², Saltuk Bugra Baltacı³, Serdar Altunay³, Nursena Şengün⁴, Zehra Değirmenci², Çiğdem Bayraktaroğlu¹, Mustafa Çağlar Beker⁵, Ertuğrul Kılıç⁵

¹Istanbul Medipol University, Research Institute for Health Sciences and Technologies, Istanbul, Türkiye

²Istanbul University of Health Sciences, Institute of Health Sciences, Istanbul, Türkiye

³Istanbul Medipol University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

⁴Istanbul Medeniyet University, Institute of Health Sciences, Istanbul, Türkiye

⁵Istanbul Medeniyet University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Stroke is one of the leading causes of mortality and morbidity worldwide. In recent years, it has become clear that glial cells play an important role in the pathophysiology of stroke as well as neurons. Astrocytes are known to play an active role in this process through G protein-coupled receptors, but how different G protein-

coupled receptors shape ischemic insult has not been elucidated. This study aims to determine the contribution of astrocytic Gq and Gi pathways to the development of ischemic brain injury pathophysiology using chemogenetic methods.

METHODS: To determine the contribution of astrocytic Gq and Gi pathways to ischemic injury, 8-12 week old GFAP-Cre (Jax: 24098) mice were divided into three groups: hM4Di, hM3Dq and GFP. The expression of hM4Di and hM3Dq receptors was induced by injecting Cre-dependent viruses into the left striatum of the animals, which allowed us to activate Gq and Gi pathways. Control animals expressed GFP in a Cre-dependent manner. Then, stroke was induced in mice by middle cerebral artery occlusion model for 30 minutes. From the onset of ischemic injury, hM4Di and hM3Dq receptors were activated until 72 hours when the injury development was complete and animals were sacrificed. Subsequently, mice were sacrificed and brains were collected. NeuN staining was performed to analyze ischemic injury and TUNEL staining was performed to identify apoptotic cells.

RESULTS: Activation of astrocytic Gq and Gi pathways exacerbated ischemic injury and reduced neuronal survival ($p<0.01$). Similarly, apoptotic cell death was increased by astrocyte-specific activation of Gq and Gi pathways ($p<0.05$).

CONCLUSIONS: Data demonstrate that activation of Gq and Gi subtypes of astrocytic G protein-coupled receptors exacerbates ischemic injury and ischemia-induced apoptotic cell death. Our results suggest that different types of G protein-coupled receptors expressed in astrocytes determine the severity of ischemic injury and may be important therapeutic targets for stroke.

Keywords: Astrocytes, Chemogenetics, G protein-coupled receptors, Ischemic stroke

OC-60

Investigation of the Effect of Systemic Irisin Administration on Locomotor Activity and Learning-Memory Function in Cerebral Ischemia Model in Rats

Aslı Karakılıç¹, Özgür Bulmuş¹, Emrah Özcan², Elif Aksöz³, Burak Şafak¹, Yunus Emre Özer¹

¹Balıkesir University, School of Medicine, Department of Physiology, Balıkesir, Türkiye

²Balıkesir University, School of Medicine, Department of Anatomy, Balıkesir, Türkiye

³Balıkesir University, School of Medicine, Department of Pharmacology, Balıkesir, Türkiye

AIM: Myokines produced in skeletal muscle can affect tissues/organs through autocrine, paracrine and endocrine pathways. Irisin, a myokine discovered in recent years that can cross the blood-brain barrier, can directly affect neuronal activity and synaptic plasticity. The aim of this study is to investigate the effectiveness of irisin on learning-memory in systemic administration in rats with a cerebral ischemia model.

METHODS: Thirtyeight adult male Wistar albino rats were randomly divided into 5 groups (group1=control, group2=sham, group3=irisin, group4=ischemia, group5=ischemia+irisin). Bilateral occlusion of common carotid artery was applied to the ischemia groups as a model of chronic cerebral hypoperfusion. The day after the operation, 100ng/kg irisin was administered intraperitoneally to the irisin groups, 3days/week for 4 weeks. Then, locomotor activity was tested with an open field (OF) test device, and learning-memory function was tested with a Morris water maze (MWM). All statistical analyzes were performed with SPSS, version 22. Significance between groups was analyzed by one-way ANOVA and post-hoc Bonferroni test.

RESULTS: There was no significant difference between the groups in terms of total distance moved and mean velocity in the OF device. While the time to find the platform decreased day by day in the control, sham and irisin groups during the 4-day learning process in MWM ($p<0.05$), no significant difference was detected in the ischemia groups. On the 5th day of the test, the time spent in the target quadrant by the ischemia group was significantly lower than the control group ($p<0.05$). However, it was observed that there was no significant difference in the ischemia+irisin group. While the frequency of entry into the target quadrant in the ischemia group was lower compared to the control and sham groups ($p<0.05$ and $p<0.01$, respectively), this significance was observed to disappear in the ischemia+irisin group. The time the irisin group spent in the opposite quadrant was shorter compared to the control, ischemia and ischemia+irisin groups ($p<0.05$).

CONCLUSIONS: This study reveals that the cerebral ischemia model negatively affects learning-memory, but systemic irisin administration may have curative effects on the impairment in learning-memory functions. In this respect, our study may form the basis of studies on the systemic use of irisin in ischemic brain diseases such as stroke and vascular dementia, where exercise is not possible.

Keywords: Cerebral ischemia, Irisin, Learning, Memory

OC-61

A New Model of Depression: Earthquake-induced Stress, Anxiety and Depression

Okan Tutuk

Hatay Mustafa Kemal University, Faculty of Medicine Department of Physiology, Hatay, Türkiye

AIM: The incidence of post-earthquake anxiety-depression and post-traumatic-stress disorder is quite-high. People exposed to earthquakes have psychological-symptoms and comorbidities that are common even 1-year after the event. It is seen that the limited number of studies examining post-earthquake depression and accompanying diseases are clinically weighted and preclinical-studies are almost non-existent. We aimed to develop a new-

method of depression as a result of the creation of conditions that can be exposed to post-earthquake with earthquake-simulation. With this new-model, it is aimed to examine the relationship between earthquake-stress and disease in many preclinical-studies
METHODS: It was performed in 2 groups as control (n=12) earthquake group (n=12). Depression by Earthquake (DD): In the automatic-shaking-cage, which we created the prototype model for earthquake-simulation, 3-major shocks (each 5 minutes) and 15-50 aftershocks (with durations ranging from approximately 30 seconds to 1-2 minutes) were applied to the experimental animals at different times a day with earthquake sound. In addition, conditions that may develop after the earthquake; 6-10 hours of food/water and movement-restriction, cold-hot exposure, light-dark cycle changes were applied. Behavioral and biochemical analyzes were performed.

RESULTS: In the DD-group compared to the control-group: Decreased locomotor-activity ($p<0.0001$), in terms of anxiogenic-effect; increased time in closed/arms ($p<0.001$) dark/box ($p<0.0001$), decreased depression-related sucrose-preference ($p<0.0001$)-increased sedentary time ($p<0.0001$), slow learning ($p<0.001$) affected memory function ($p<0.0001$). 21 In the DD-group: decreased locomotor-activity ($p<0.001$), stay time in closed arms ($p<0.05$) dark box ($p<0.05$), decreased sucrose preference ($p<0.05$) increased sedentary time ($p<0.001$) indicating the continuation of depression-like behavior ($p<0.05$) increased sedentary time ($p<0.001$), slow learning in terms of learning-memory ($p<0.001$). Similarly in the biochemical-analyses, Cortisol ($p<0.0001$), ACTH ($p<0.0001$), TOS ($p<0.0001$), OSI ($p<0.0001$) indices were statistically significantly increased.

CONCLUSIONS: As a result of major earthquakes, it is seen that post-traumatic stress disorder, depression-anxiety and accompanying diseases that can affect the quality of life, including occupational performance, may occur, which is supported preclinically by our study. The behavioral-biochemical results of our DD group, which we established with earthquake-simulation, support the validity of the method in terms of further preclinical investigation of such a subject that can have such widespread effects. It is also an important result that long-term anxiety, depressive-cognitive impairment persists after earthquake-simulation. With this methodology, both post-earthquake studies and some pathological relationships can be successfully examined.

Keywords: Earthquake, Depression by earthquake, Anxiety, Stress, Behavioral tests, Methodology

OC-62

Investigation of the Effects of Nicotinamide Riboside in a Ketamine-Induced Rat Model of Schizophrenia

İlkay Yılmaz¹, Esin Yakıt², Fulya Tuzcu², Ersin O. Koylu²

¹Ege University, Institute of Health Sciences, Department of Neuroscience, Izmir, Türkiye

²Ege University, Faculty of Medicine, Department of Physiology Izmir, Türkiye

AIM: Schizophrenia is a major health concern that impairs social and cognitive abilities. Brain energy metabolism and mitochondrial dysfunction are thought to be involved in the pathology of the disease. On the other hand, there are also reports that antipsychotics used in treatment have disruptive effects on mitochondrial function. This study aimed to evaluate the effects of nicotinamide riboside, a natural precursor of nicotinamide adenine dinucleotide, which is a raw material for mitochondrial function, in a rat model of schizophrenia.

METHODS: Sixty adult male Sprague-Dawley rats were included in the study. Groups were formed as follows: Control (C), Schizophrenia model-ketamine (KET), nicotinamide riboside (NR), ketamine+nicotinamide riboside (KETNR), ketamine+antipsychotic (KETAP), and ketamine+antipsychotic+nicotinamide riboside (KETAPNR). Ketamine was administered 25 mg/kg for 10 days, followed by AP (risperidone) and NR 10 mg/kg and 300 mg/kg respectively for 15 days. Following the last injection day, locomotor activity test, sucrose preference test and novel object recognition tests were performed. Statistical analyses were conducted using Kruskal-Wallis ANOVA and Games-Howell post-hoc tests.

RESULTS: The novel object recognition test revealed a significant difference between the KETAP and KETAPNR groups ($p<0.05$). A significant difference was also observed between these groups in the locomotor activity test ($p<0.05$). In the sucrose preference test, significant differences were found between the KETAPNR and C groups ($p<0.05$).

CONCLUSIONS: Our results suggest that the combined use of antipsychotics and nicotinamide riboside in a ketamine-induced schizophrenia model improves cognitive functions and reduces positive symptoms, but also negatively affects mood-related behaviors. Our findings indicate that nicotinamide riboside which is a precursor of adenine dinucleotide, is a potential candidate for improving mitochondrial dysfunctions and related symptoms in schizophrenia pathogenesis. Our study was supported by the Ege University Scientific Research Projects Coordination with project number 32205.

Keywords: Cognitive functions, Ketamine, Mitochondrial dysfunction, Schizophrenia

OC-63

Differences in the Expression of Dopamine Receptor and Dopamine Transporter mRNAs in the Brains of Nicotine-Preferring Rats

Merve Pozlu Çifçi, Ramazan Can Gökmen, Esin Yakıt, Doğan Çetin, Ayşegül Keser, Lütfiye Kanit, Ersin O. Koylu, Oğuz Gözen, Burcu Balkan

Ege University Faculty of Medicine, Department of Physiology, Izmir, Türkiye

AIM: The key brain circuit involved in the development of addiction is known as mesocorticolimbic system (MCLS). This circuit involves the mesolimbic pathway from ventral tegmental area (VTA) to the nucleus accumbens (NAc) and the mesocortical pathway from VTA to the prefrontal cortex (PFC). Dopamine is the primary neurotransmitter in MCLS. To investigate nicotine addiction, we have been breeding a nicotine-preffering rat line (N) in our laboratory. Our study aimed to investigate differences in the regulation of dopamine receptor 1 (D1R), 2 (D2R), 3 (D3R) and dopamine transporter (DAT) mRNAs in MCLS during nicotine reward in N and control (C) animals.

METHODS: Oral nicotine was administered for five weeks, 10 mg/L for the first 2 weeks and 20 mg/L for the next 3 weeks. Study groups: C receiving water (WC), C receiving nicotine (NC), N receiving water (WN), N receiving nicotine (NN). Animals were decapitated. D1R, D2R, D3R and DAT mRNA expressions were determined in PFC, NAc, VTA by RT-PCR. Data were analyzed by ANOVA, post-hoc Tukey and T-Tests.

RESULTS: N rats consumed ($p<0.001$) and preferred ($p<0.05$) more nicotine than C throughout the 5 weeks. Weeks 4 and 5, N consumed more nicotine than C ($p<0.001$) and preferred nicotine more ($p<0.001$). D1R ($p<0.02$), D2R ($p<0.01$) mRNA expression in NAc and D3R ($p<0.001$), DAT ($p<0.01$) mRNA expression in VTA decreased in nicotine-receiving animals compared to water-receiving animals. In the VTA of N rats, D3R ($p=0.008$) and DAT ($p<0.005$) mRNA decreased compared to the C. In the NAc of the NN, D1R ($p<0.05$) and D2R ($p<0.05$) mRNA was decreased compared to the WN. In the VTA of WN and NC, D3R ($p<0.05$, $p<0.005$, respectively) and DAT ($p<0.01$, $p<0.05$, respectively) mRNA decreased compared to WC.

CONCLUSIONS: D1R, D2R, D3R and DAT regulate reward process in MCLS. These findings may underlie high nicotine-preference in N animals.

(Project number: BAP TS-TUT-2023-29642– HADYEK-2024-051)

Keywords: Nicotine, Dopamine, DAT, D1R, D2R, D3R

OC-64

Investigation of the Effects of Agomelatine Administration on Apoptosis and Autophagy in Experimental Cerebral Ischemia/Reperfusion Modeled Rats

Semiha Nur Özkaya¹, Kevser Tanbek², Furkan Yüksel³, Suat Tekin²

¹Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Physiology, Kahramanmaraş, Türkiye

²İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

³Necmettin Erbakan University, Faculty of Veterinary Medicine, Department of Physiology, Konya, Türkiye

AIM: According to World Health Organization, stroke is second leading cause of global death and is mostly characterized by

blockages in cerebral vessels. This condition includes Cerebral Ischemia (CI) and Reperfusion (R) injury, leading to neuronal pathophysiological processes involving apoptotic and autophagic pathways. Current literature has limited studies on effectiveness of Agomelatine, noted for its role in melatonergic and serotonergic system activity and neurogenesis, on CI/R damage. This study aims to analyze effect of Agomelatine on proteins involved in apoptotic and autophagic pathways in CI/R damage.

METHODS: Male Sprague Dawley rats were divided into four groups ($n=10$): Control, CI/R and CI/R+Agomelatine (20 and 40 mg/kg). Except for control group, rats underwent Middle Cerebral Artery Occlusion (MCAO) model for 60 minutes to induce CI/R. One hour post-MCAO, hydroxyethyl cellulose was administered to CI/R group, and Agomelatine at 20 and 40 mg/kg was administered to CI/R+Agomelatine groups intraperitoneally. At end of experiment, animals were decapitated and brain tissues were collected. Western Blot analysis was used to assess levels of apoptosis (BCL-2 and BAX) and autophagy (Beclin-1, ATG5, ATG7, and p62) proteins in the infarct area of brain tissues. Statistical comparisons among groups were conducted using Kruskal-Wallis-H test in IBM-SPSS-24.0 for Windows program; $p<0.05$ considered statistically significant.

RESULTS: The analyses showed that the apoptosis protein BCL-2 was higher and BAX was lower in the CI/R+Agomelatine groups compared to the CI/R group ($p<0.05$). In addition, the autophagy protein Beclin-1, ATG5 and ATG7 levels were higher and the p62 level was lower in the agomelatine-treated groups compared to the CI/R group ($p<0.05$).

CONCLUSIONS: It was concluded that in the CI/R model agomelatine application affected levels of apoptosis and autophagy proteins in a way that would inhibit apoptosis and induce autophagy.

This study was supported by İnönü University Scientific Research Projects unit with project number TYL-2022-3072.

Keywords: Cerebral Ischemia, Reperfusion, Apoptosis, Autophagy, Agomelatine

OC-65

Rosmarinic Acid Exerts Neuroprotective Effects in an in Vitro Alzheimer's Disease Model

Aysu Şen¹, Canan Eroğlu Güneş², Ebru Nur Dursun², Ercan Kurar², Selim Kutlu¹

¹Necmettin Erbakan University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

²Necmettin Erbakan University, Faculty of Medicine, Department of Medical Biology, Konya, Türkiye

AIM: Alzheimer's Disease (AD) is the most common neurodegenerative disorder, characterized by increased neurotoxicity and apoptosis. Rosmarinic acid (RA) is known to have

anticancer, antioxidant and anti-inflammatory effects. This study aims to investigate the effects of RA on amyloid-beta (A β), tau protein, α -synuclein, abelson tyrosine kinase (ABL) levels and apoptosis in an in vitro AD model.

METHODS: SH-SY5Y cells were differentiated into cholinergic neurons using retinoic acid. The cells were then divided into the following groups: control, A β (Alzheimer's model), A β +RA and RA. To determine the appropriate doses of RA, A β , and A β +RA, CCK-8 assays were performed on the differentiated cells. The expression of apoptosis-related genes was analyzed using qRT-PCR, while the levels of tau, α -synuclein, abelson tyrosine kinase (ABL) and A β proteins were determined by using ELISA.

RESULTS: CCK-8 analysis revealed that the 0.5, 1.5, and 5 μ M doses of RA were non-toxic on the differentiated cells. A β IC40 dose was determined as 20 μ M. After RA pretreatment, 20 μ M A β treatment was performed and it was found that RA (1.5mM) showed neuroprotective effect. The expression levels of BAX, CASP3, CASP7, CYCS, FADD, and FAS genes in A β group were significantly increased compared to the control group, while a significant decrease in these gene expressions was observed in A β +RA group compared to the A β group. ELISA analyses indicated that tau, α -synuclein and A β protein levels were increased in A β group compared to control, while they were decreased in A β +RA group ($p<0.05$). ABL level was found to be significantly higher only in A β +RA group ($p<0.05$).

CONCLUSIONS: The findings of this study reveal that RA has neuroprotective and antiapoptotic effect in AD, in vitro.

Keywords: Alzheimer's Disease, Apoptosis, Abelson Tyrosine Kinase, Neuroprotection, Rosmarinic Acid, SH-SY5Y cells

OC-66

Investigation of Cytomorphological Changes of Astrocytes in the Amygdala in Alzheimer's Disease

Sevim Kandis¹, David Vega-Avelaira², Miguel Ángel García Cabezas²

¹Dokuz Eylul University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

²Autónoma University of Madrid, School of Medicine, Department of Anatomy, Histology, and Neuroscience, Madrid, Spain

AIM: Alzheimer's Disease (AD) is a progressive neurodegenerative disorder marked by the loss of neurons and synapses leading to cognitive decline. AD progression is associated with the spread of hyperphosphorylated tau proteins across the cerebral cortex and the spread of tau is used to stage AD in postmortem brains. Braak and Braak identified six stages of AD, beginning in the transentorhinal region and eventually affecting the neocortex. The amygdala was shown to have significant quantity of neurofibrillary tangles and neurotic plaques in AD. Astrocytes, crucial for neuronal support and metabolism, play a significant role in AD progression, particularly through their involvement in amyloid-beta (A β)

clearance and their pathological changes, which may worsen cognitive and behavioral symptoms.

METHODS: In the present work we measured astrocytes area of amygdala in postmortem human brains with AD and neurotypical subjects. We carry the measurements in one pallial (Lateral) and one subpallial (Central) amygdalar nuclei. We used Nissl-stained brain sections from 4 human neurotypical, 8 AD (2 Braak I-II, 1 Braak III-IV, and 5 Braak V-VI) postmortem brains.

RESULTS: in the central and lateral nucleus, we demonstrated a statistically significant increase in astrocyte area at Braak I-II, Braak III-IV, and Braak V-VI stages compared to neurotypical subjects. In the lateral nucleus, there is no significant difference between Braak stages, suggesting that the damage in the lateral nucleus begins at the early stages of AD.

CONCLUSIONS: Our study shows that the pallial and subpallial amygdala astocytes is affected at the early, intermediate and advanced Braak AD stages. Astroglial cells play a key role in neurological diseases, influencing their pathogenesis and outcome. Astrocytes are involved in all neurodegenerative processes and show significant changes in AD. It is believed that early changes in astrocytes may influence the development of AD. Targeting astroglia could offer new treatment options for early-stage AD.

Keywords: Alzheimer's Disease, Amygdala, Astocytes

OC-67

Effect of Piriformis, Hamstring, Gastrocnemius-Soleus Muscle Statistic Stretch Exercises on Pain, Life and Sleep Quality in Women doing Instrumental Pilates

Rahime Aslankoç, Özlem Cartilli, Oğuzhan Kavruk

Süleyman Demirel University, Faculty of Medicine, Department of Physiology, Isparta, Türkiye

AIM: The most common type of equipped pilates is instrumented pilates. In patients who have not been able to complete joint movement in recent years, static stretching exercises are more often preferred. The study investigated the effect of static stretch exercises on the piriformis, hamstring, and gastrocnemius-soleus muscles on pain, quality of life, and sleep in women doing instrumental pilates.

METHODS: Thirty women aged 20 to 45 who applied to do instrumental pilates at a health center in Isparta participated in the study. The study studied the effect of static stretching exercises on pain, quality of life, and sleep quality with pre-test-end test applications, using two days a week for eight weeks.

RESULTS: The participants' age, height, body weight and body mass index (BMI) were evaluated with an average age of 3 ± 5.2 , an average height of 165.83 ± 3.92 , a body weight of 62.46 ± 8.47 and an average BMI of 22.79 ± 3.46 . 63.3% of the participants were smokers, 43.3% were married, 66.7% were working in the public

sector, and 40% came on the suggestion of their pilates friends. Pain measurements revealed statistically significant differences between pre-test and final test data in the back, waist and lower limbs. SF-36 pre-test final test analysis revealed significant differences in physical functions, vitality, mental health, social functioning, pain, and general health variables. A significant difference was found between the pre-test and final test data of the PUKI score. According to the analysis of pre-test-final test data of PUKI components, the difference between subjective sleep quality, latency, duration, usual sleep yield and daytime dysfunction has been statistically significant.

CONCLUSIONS: The study found that static stretching exercises on piriformis, hamstring, and gastrocnemius-soleus muscles, in addition to instrumental pilates, can have a positive effect on pain, quality of life and sleep.

Keywords: Instrumental Pilates, Piriformis, Hamstring, Static Stretching, Gastrocnemius-Soleus

OC-68

Effects of Chemotherapy and Chronic Aerobic Exercise on Cognitive Functions in Glioblastoma Model Rats

Aslı Nur Bahar¹, Leman Arslan Arıtürk¹, İkbâl Tan², Nisanur Duman², Nurhan Beyza Düzgün², Sakine Beyza Üstün², Zülal Sorkun², Banu Taktak Karaca³, Dila Şener Akçora⁴, Özgür Kasımay¹

¹Marmara University, School of Medicine, Department of Physiology, İstanbul, Türkiye

²Marmara University, School of Medicine, 3rd Year Medical Students, İstanbul, Türkiye

³Marmara University, School of Medicine, Department of Immunology, İstanbul, Türkiye

⁴Marmara University, School of Medicine, Department of Histology and Embryology, İstanbul, Türkiye

AIM: Glioblastoma (GBM) is a common, aggressive brain tumors in adults. Treatments like temozolomide (TMZ) and the tumor can reduce patients' quality of life. This study evaluates the effects of moderate aerobic exercise on oxidative stress and cognitive functions in glioblastoma-bearing rats, with and without chemotherapy.

METHODS: Male Sprague Dawley rats (n=50) were divided into five groups: sham-operated (S), glioblastoma (GBM), glioblastoma + temozolomide (GBM+T), glioblastoma+exercise (GBM+E), and glioblastoma+temozolomide+exercise (GBM+T+E). Exercise groups did moderate-intensity exercise for 8 weeks. Five weeks later, 1x10⁶ glioma cells were injected to create the tumor model. Temozolomide (10 mg/kg) or saline was administered for five days. Spatial memory was assessed with the Y-maze test; anxiety with the hole board test; and depressive symptoms with sucrose preference and Porsolt tests. Brain tissue weight index, malondialdehyde (MDA) levels, myeloperoxidase (MPO) activity,

glutathione (GSH) levels, and superoxide dismutase (SOD) activities were measured. ANOVA and Student's t-test were used.

RESULTS: Spatial memory assessed by the Y-maze test decreased in the GBM group but improvement with exercise and TMZ (p<0.05-0.01). In the hole board test, anxiety was lower in the GBM group but higher in the exercise groups (p<0.05-0.001). The sucrose preference index was higher in the TMZ and TMZ+exercise groups compared to the GBM and control groups (p<0.05-0.01). In the Porsolt test, immobility time increased in the GBM group and was suppressed with TMZ (p<0.05). The brain weight index decreased in the GBM group but increased in the exercise groups (p<0.05-0.001). MDA levels and MPO activity increased in the GBM group and decreased with exercise and/or TMZ (p<0.05-0.01). SOD activity was higher in the exercise and/or TMZ groups compared to the GBM group (p<0.05-0.01).

CONCLUSIONS: GBM formation increases anxiety-like behavior, decreases spatial memory, reduces brain weight index, and elevates oxidative stress. Moderate exercise improved these parameters. This study was supported by the TÜBİTAK 2209 Project.

Keywords: Glioblastoma, temozolomide, exercise, cognitive function

OC-69

Protective Effects Of Vitamin D On Pancreas Damage Induced by High-Fructose Corn Syrup Consumption

Cahide Aslan¹, Rahime Aslankoç¹, Özlem Özmen², Buse Nur Sülük¹, Oğuzhan Kavrak¹

¹Süleyman Demirel University, Faculty of Medicine, Department of Physiology, Isparta, Türkiye

²Mehmet Akif Ersoy University, Faculty of Medicine, Department of Veterinary Pathology, Burdur, Türkiye

AIM: High Fructose Corn Syrup (HFCS); It is a widely used additive for various reasons such as being very sweet, extending the shelf life of foods and being cheap. Diet rich in fructose: It causes various metabolic disorders characterized by diabetes and insulin resistance, hyperglycemia, hypertriglyceridemia and fatty liver. It is stated that vitamin D affects glucose tolerance by affecting β -cell function in HFCS-fed rats with its anti-inflammatory and antioxidant effects. It is thought that vitamin D may improve insulin secretion and insulin resistance associated with T2DM. In our study, we aimed to investigate pancreatic damage caused by chronic consumption of HFCS and protective effects of vitamin D on pancreas.

METHODS: Wistar albino male rats (6-8 week old) were divided into 3 groups; control (tap water/saline), HFCS (11% HFCS-55/saline) and HFCS+D Vit (11% HFCS-55/42 μ g vitamin D). At the end of one month, rats were sacrificed and blood and pancreas tissues were collected. Biochemical, immunohistochemical and histopathological analyzes were performed.

RESULTS: Biochemically, the MDA level in pancreas was increased in HFCS group compared to control; SOD, CAT enzyme activity and serum insulin levels were found to decrease ($p=0.001$, $p=0.009$, $p=0.008$ $p=0.036$, respectively). It was observed that MDA level decreased in Vit D group compared to HFCS group; SOD, CAT enzyme activity and serum insulin levels were found to increase ($p=0.027$, $p=0.045$, $p=0.048$, $p=0.013$, respectively). In histopathological examination, hyperemia, atrophy and degeneration of some Langerhans cells were observed in the pancreatic tissue of HFCS group rats. Significant decreases in insulin, amylin and glucagon expressions compared to control; Significant improvements were seen in these parameters in Vit D group.

CONCLUSIONS: In conclusion, vitamin D reduces lipid peroxidation and free radicals in HFCS-induced pancreatic damage; It was effective in increasing antioxidant activity. Therefore, it may affect glucose tolerance by affecting β -cell function in HFCS-fed rats.

Keywords: Vitamin D, HFCS, Pancreas, Insulin, Oxidative stress

OC-70

The Effect of Caffeine Intake on Respiratory Functions, Cardiopulmonary Exercise Test Parameters, and Post-Exercise Heart Rate Variability

Mert Ali Aydın¹, Göktuğ Ömercioğlu², Ayşe Demirci Şahin², Zeynep Eda Erden², Yeşim Özçatal³, Yaren Düşünceli¹, Serdal Kenan Köse⁴, Metin Bastug²

¹Ankara University, School of Medicine, Student of Term III, Ankara, Türkiye

²Ankara University, School of Medicine, Department of Physiology, Ankara, Türkiye

³Ankara University, Graduate School of Health Sciences, Department of Physiology (Medicine), Ankara, Türkiye

⁴Ankara University, School of Medicine, Department of Biostatistics, Ankara, Türkiye

AIM: Caffeine has effects on numerous bodily systems, including the neurological system, through adenosine receptors. The aim of the study was to investigate the effects of caffeine on pulmonary function tests (PFT), cardiopulmonary exercise test (CPET), and heart rate variability (HRV) after exercise.

METHODS: The study included 16 male participants aged between 18-25, who did not have high physical activity, with the approval of the Ethics Committee for Human Research at Ankara University School of Medicine. Participants were invited twice: once for caffeine (4 mg/kg) and placebo. PFT and CPET parameters were determined 45 minutes after ingestion, and HRV analysis were performed following rapid recovery phase of HR. PFT data were recorded as percentages of the predicted values. HRV data were recorded before exercise (B), after exercise following the rapid recovery phase of HR (R1), and when HR dropped below 100 bpm

(R2). The data were evaluated using SPSS-22 with significance level of $p<0.05$.

RESULTS: Caffeine increased peak expiratory flow rate (PEF), whereas placebo increased end-expiratory flow rate (MEF75) ($p=0.004$; 0.019). CPET demonstrated that maximal oxygen capacity, power, ventilation, and HR were higher than the placebo ($p=0.002$; 0.002; 0.004; 0.02). Except for three, there were substantial differences between successive HRV measurements. There were no differences in RMSSD (root mean squared differences between consecutive heartbeats) of those who received only a placebo and LF/HF (low and high frequency ratio) of individuals who received both caffeine and placebo between R2 and R1.

CONCLUSIONS: Increased PEF and decreased MEF75 in PFT suggests that more forceful contraction of expiratory muscles caused by caffeine leads to dynamic airway compression. CPET data demonstrate that caffeine improves exercise performance. The difference in RMSSD between R2-R1 in caffeine and placebo indicates that sympathetic activity is prevailing in caffeine consumption, and the recovery after exercise is accelerated with caffeine.

Keywords: Caffeine, Cardiopulmonary Exercise Testing, Heart Rate Variability, Pulmonary Function Tests

OC-71

Effects of Classical Massage on Some Myokines, Angiogenic and Antiangiogenic Factors in Male Individuals

Kamil Duran¹, Mustafa Aktar¹, Durmuş Ayan², Durmuş Deveci¹

¹Nigde Omer Halisdemir University, Department of Physiology, Nigde, Türkiye

²Nigde Omer Halisdemir University, Department of Biochemistry, Nigde, Türkiye

AIM: Angiogenesis, the formation of new capillaries, increases with higher angiogenic factors and decreases with higher antiangiogenic factors. Few studies have examined massage's impact on these factors, but we hypothesize that massage may influence their release through mechanotransduction. Thus, massage could benefit with conditions like cancer, stroke, paralysis, and wound healing. Our aims to investigate the effects of massage on these factors and whether applying it to different muscle areas matters. **METHODS:** The study included twenty-two sedentary males aged 18-30, divided into two groups: Back Massage (SM, $n=11$) and Lower Extremity Massage (AEM, $n=11$). Venous blood samples were collected at three points: before massage (control), 2 hours after first session (acute), and 2 hours after last session (chronic). Serum levels of Vascular Endothelial Growth Factor(VEGF), Angiopoietin-1(ANG-1), Thrombospondin-1 (TSP-1), Endostatin (ES), Interleukin-6 (IL-6), and Interleukin-8 (IL-8) were measured

using the ELISA method. Repeated Measures ANOVA was used to compare changes in both groups over time.

RESULTS: In SM, angiogenic factors VEGF and ANG-1 levels showed a nonsignificant increase, while they nonsignificantly decreased in AEM. IL-8, a myokine that promotes angiogenesis, increased significantly in both groups ($p<0.05$), with a greater increase in the SM group. Among antiangiogenic factors, TSP-1 showed no significant changes in either group, while Endostatin (ES) increased significantly (25%) in AEM compared to control in chronic ($p<0.05$). No significant changes occurred in IL-6 levels in either group, but increase was greater in SM group.

CONCLUSIONS: The back region has more red (oxidative) muscle fibers, suggesting that back massage may stimulate angiogenic factors more effectively. Therefore, back massage could be more beneficial than lower extremity massage for conditions like stroke and paralysis. Conversely, Endostatin increased only in AEM, lower extremity massage may be more effective than upper extremity massage in preventing unwanted angiogenesis (cancer). Further studies with larger sample sizes are needed to understand these changes better.

Keywords: Massage, Angiogenesis, Angiogenic Factor, Antiangiogenic Factor, Myokine

Poster Communications (PC 01 - PC97)

PC-01

Protective Effect of Aerobic Exercise Against Temozolomide-induced Hepatotoxicity in Rats with an Experimental Glioblastoma Model

Aslı Nur Bahar¹, Leman Arslan Arıtürk¹, İkbâl Tan², Nisanur Duman², Nurhan Beyza Düzgün², Sakine Beyza Üstün², Zülal Sorkun², Banu Taktak Karaca³, Dila Şener Akçora⁴, Özgür Kasımay¹

¹Marmara University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

²Marmara University, School of Medicine, 3rd Year Medical Students, İstanbul, Türkiye

³Marmara University School of Medicine, Department of Immunology, İstanbul, Türkiye

⁴Marmara University, School of Medicine, Department of Histology and Embryology, İstanbul, Türkiye

AIM: Glioblastoma (GBM) is a common and aggressive brain tumour with a median survival of 12-15 months. Temozolomide (TMZ) is the main chemotherapeutic agent used in the treatment of GBM. Liver injury has been reported in patients treated with TMZ. In this study, we aimed to investigate the protective role of moderate aerobic exercise against TMZ-induced hepatotoxicity in rats with glioblastoma.

METHODS: A total of 50 three-month-old Sprague-Dawley rats were used to form 5 groups; sham-operated (S), glioblastoma

(GBM), glioblastoma+temozolamide (GBM+T), glioblastoma+exercise (GBM+E) and glioblastoma+temozolamide+exercise (GBM+T+E). A moderate-intensity exercise protocol at 50-60% of the rats' VO₂max was applied to the exercise groups for 30 min/day for a total of 8 weeks. The tumour model was established by intracerebroventricular injection of 1x10⁶ glioma cells into the rats by the stereotaxic method. Subsequently, the chemotherapy groups were given 10 mg/kg TMZ by oral gavage. After sacrifice, liver tissues were isolated and the levels of MDA, GSH and catalase, SOD and MPO in tissue; ALT and AST in serum were measured by spectrophotometer. Histopathological scoring was performed. Statistical evaluation was performed by one-way ANOVA and post hoc LSD.

RESULTS: GBM administration increased MDA levels in liver tissue. However, MDA levels decreased in the exercise groups (GBM+E and GBM+TMZ+E) ($p<0.05$). There was no significant difference in MDA levels between the GBM and GBM+T groups. The antioxidant catalase activity increased with exercise and/or TMZ administration compared to the control group ($p<0.01$). GSH levels increased in the GBM, GBM+E and GBM+TMZ+E groups compared to the control group ($p<0.05$). TMZ treatment increased plasma ALT and AST, whereas exercise decreased them ($p<0.05$). The histopathological score increased in G and GT groups and decreased in GE and GTE groups ($p<0.05$).

CONCLUSIONS: The results of the study showed that moderate aerobic exercise was beneficial in reducing the detrimental effects of temozolamide on the liver. (supported by TUBITAK-2209-A).

Keywords: Glioblastoma, Temozolomide, Exercise, Hepatotoxicity

PC-02

A Preliminary Study About Possible Effects of High Intensity Interval Training on Adipokine and Myokine Levels in Young Female Basketball Players

Rıza Altınel, Emine Kılıç Toprak, Özgen Kılıç Erkek, Hasan Akça, Tunahan Anber, Dilek Sayın, Gizem Akan, Melek Bor Küçükataç

Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

AIM: Basketball challenges athletes' speed, balance, strength, and aerobic/anaerobic capacities. To improve in basketball, athletes must train frequently over long periods. High-Intensity Interval Training (HIIT) is popular for its short duration and positive impact on performance. This study aimed to investigate the effects of both acute and chronic (6 weeks) HIIT on adipokines like leptin, visfatin, obestatin and myokines like FGF-21 and BDNF in young female basketball beginners and elite players and whether these effects vary based on training status.

METHODS: With ethical approval from Pamukkale University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (16.08.2022, 12), 20 elite female basketball players (E group, training for 3 years \pm 1 month, 14 \pm 0,8 years old) and 19

using the ELISA method. Repeated Measures ANOVA was used to compare changes in both groups over time.

RESULTS: In SM, angiogenic factors VEGF and ANG-1 levels showed a nonsignificant increase, while they nonsignificantly decreased in AEM. IL-8, a myokine that promotes angiogenesis, increased significantly in both groups ($p<0.05$), with a greater increase in the SM group. Among antiangiogenic factors, TSP-1 showed no significant changes in either group, while Endostatin (ES) increased significantly (25%) in AEM compared to control in chronic ($p<0.05$). No significant changes occurred in IL-6 levels in either group, but increase was greater in SM group.

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Poster Communications (PC 01 - PC97)

PC-01

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¹Marmara University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

²Marmara University, School of Medicine, 3rd Year Medical Students, İstanbul, Türkiye

³Marmara University School of Medicine, Department of Immunology, İstanbul, Türkiye

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PC-02

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Rıza Altınel, Emine Kılıç Toprak, Özgen Kılıç Erkek, Hasan Akça, Tunahan Anber, Dilek Sayın, Gizem Akan, Melek Bor Küçükataç

Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

AIM: Basketball challenges athletes' speed, balance, strength, and aerobic/anaerobic capacities. To improve in basketball, athletes must train frequently over long periods. High-Intensity Interval Training (HIIT) is popular for its short duration and positive impact on performance. This study aimed to investigate the effects of both acute and chronic (6 weeks) HIIT on adipokines like leptin, visfatin, obestatin and myokines like FGF-21 and BDNF in young female basketball beginners and elite players and whether these effects vary based on training status.

METHODS: With ethical approval from Pamukkale University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (16.08.2022, 12), 20 elite female basketball players (E group, training for 3 years \pm 1 month, 14 \pm 0,8 years old) and 19

beginners (B group, $16 \pm 0,9$ years old) were included. Participants were divided into HIIT and control groups, balanced by age and body weight. While the control group maintained routine training, the HIIT group followed a Tabata protocol (3 days/week, 20 seconds exercise/10 seconds rest, 8 sets) for 6 weeks. Venous blood samples were collected before exercise in first week and after the final session in sixth week. Serum levels of obestatin, visfatin, leptin, FGF-21 and BDNF were measured using ELISA method. Data were analyzed with t-test, Mann-Whitney U or Wilcoxon paired test, with significance set at $p < 0.05$.

RESULTS: Pre-exercise obestatin levels at 6th week of the E-HIIT group were significantly decreased compared to the E-control group and pre-exercise leptin levels at 6th week of the YB-HIIT group were significantly decreased compared to 1th week. The difference in the other parameters analysed did not reach statistically significant level.

CONCLUSIONS: These findings suggest that in elite athletes, the effects of HIIT on obestatin are predominant, whereas the effects on leptin are more predominant in beginners. Further studies are needed on the effects of HIIT on adipokines and myokines.

Keywords: HIIT, Adipokine, Obestatin, Leptin, Elite

PC-03

Effect of Concentric and Eccentric Exercises on Some Myokines, Angiogenic and Antiangiogenic Factors in Male Individuals

Mustafa Aktar¹, Kamil Duran¹, durmuş Ayan², Durmuş Deveci¹

¹Omer Halisdemir University, Department of Physiology, Niğde, Türkiye

²Omer Halisdemir University, Department of Biochemistry, Niğde, Türkiye

AIM: Angiogenesis is the formation of new capillaries from existing ones. Angiogenesis is regulated by the balance of pro-angiogenic and anti-angiogenic factors in the blood. When pro-angiogenic factors dominate, angiogenesis increases and results in conditions such as cancer formation or progression, when anti-angiogenic factors dominate, angiogenesis is prevented. Exercise has been shown to suppress some cancers. This study aims to examine the effects of concentric (CE) and eccentric (EE) exercise on angiogenic and antiangiogenic factors.

METHODS: Twenty-four healthy sedentary males (ages 18-30) participated in a 2-week (6 sessions) CE or EE protocol. Venous blood samples were collected before exercise (control), 1 hour after the first session (acute) and 1 hour after the last session (chronic), and serum was obtained. These serum samples were used for analysis of Vascular Endothelial Growth Factor (VEGF), Angiopoietin-1 (ANG-1), Endostatin (ES), Thrombospondin-1 (TSP-1), Interleukin-6 (IL-6), Interleukin-8 (IL-8) and Creatine Kinase (CK). Repeated Measures ANOVA method was applied to examine whether the changes in the 2 groups and dependent variables over time were significant.

RESULTS: VEGF increased significantly in both groups (CE $p < 0,05$; EE $p < 0,005$). ANG-1 remained unchanged in either group. Endostatin increased significantly in the EE group ($p < 0.05$) but remained unchanged in the CE group. TSP-1 decreased significantly in both groups ($p < 0,05$). IL-6 and IL-8 increased significantly in both groups ($p < 0,001$). CK increased significantly in the EE group ($p < 0,05$), but remained unchanged in the CE group. Angiogenic index increased more in CE group than in EE group.

CONCLUSIONS: Studies show exercise benefits cancer patients. Additionally, our study indicates the type of exercise is also matters. Our results suggest that eccentric exercise may be more effective than concentric exercise in tumoral conditions such as cancer, and concentric exercise may be more effective than eccentric exercise in conditions such as myocardial infarction and peripheral artery diseases where angiogenesis is desired.

Keywords: Angiogenic, Antiangiogenic, Concentric, Eccentric, Exercise

PC-04

Investigation of the Effects of 24-Hour REM Sleep Deprivation on Memory and Hippocampus in Adult Rats Subjected to Treadmill Exercise

Ümmühan Adam Utli, Ahmet Can Türkoğlu, Leyla Şahin

Mersin University, Faculty of Medicine, Department of Physiology, Mersin, Türkiye

AIM: Sleep is an important biological need for living things and has a cyclical process. Disruption of this cycle causes various behavioral and neurological damages. In this study, the effects of exercise on learning-memory performance and hippocampal NGF and BDNF in REM sleep deprived rats were investigated.

METHODS: M.Ü. after receiving the approval of the ethics committee (2023/37), 32 samples were collected for the study. A 3-month-old Wistar albino male rat was used. Rats were divided into 4 groups ($n=8$): control (1st), REM sleep deprivation (2nd), Exercise (3rd) and REM sleep deprivation+exercise group (4th). In the exercise protocol applied without determining the maximum performance of the rats, the first week was 15 minutes, and the exercise duration was increased by 15 minutes every week for the following 3 weeks. The moderate exercise protocol was performed on a treadmill device at a speed of 10m/min at a 0° incline, with a 5-minute break every 15 minutes during the exercise. After completion of the exercises, 24-hour REM sleep deprivation was performed and then MWM was used for learning and memory assessment. BDNF and NGF levels were determined by ELISA on hippocampus tissue taken after decapitation.

RESULTS: In the first four days of MWM, where learning evaluation is carried out. The total distance covered, swimming speed and time to find the platform decreased significantly in the inter-day evaluations ($p < 0.05$). On the last day when memory was evaluated, the performances of the 2nd group and the 4th group decreased

significantly compared to the 1st group ($p < 0.05$). According to ELISA results, no significant difference was observed in hippocampal BDNF levels; NGF levels increased significantly in the 2nd group compared to the 1st and 3rd groups ($p < 0.05$).

CONCLUSIONS: In our results, REM sleep deprivation showed negative effects for memory, and the positive effect of exercise was not significant. NGF level increased in REM sleep deprivation.

Keywords: REM deprivation, Exercise, Learning and memory

PC-05

Acoustic Rhinometry in the Assessment of Sympathetic Activation After Exercise

İşinsu Karaoğlu¹, Mehmet Düzlülü²

¹Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Gazi University, Faculty of Medicine, Department of Otorhinolaryngology, Ankara, Türkiye

AIM: The respiratory system is one of the systems where changes that occur due to the sympathetic system activated by exercise are most clearly observed. In our study, the effect of acutely induced sympathetic activity on nasal passage volumes in sedentary young people was evaluated by acoustic rhinometry measurements.

METHODS: Thirty healthy volunteer students participated in this study, which received ethics committee approval. Participants' blood pressure and heart rate were measured before and after exercise, and a treadmill exercise was applied in which participant's resting heart rate was doubled and exercise was continued for 5 minutes. Nasal measurements were evaluated separately for both nostrils with acoustic rhinometry measurements applied before exercise, after exercise, and 20 minutes after exercise.

RESULTS: Total nasal volume values of the right and left nasal passages before exercise were not statistically significant. There was a significant increase in both nasal passage volumes after exercise compared to before exercise. It was determined that the increase in the right nasal passage was higher than the left ($p < 0.05$). In measurements repeated 20 minutes after exercise, the right nasal passage volume was higher than the left, and the difference between them was significant.

CONCLUSIONS: The main mechanism responsible for the nasal response that occurs during exercise is sympathetic system discharge. Expected volume increase as a result of decongestion in the nasal mucosa due to adrenergic discharge was significant for both nostrils after exercise compared to before exercise in our study, and the right nasal passage volume was found to be higher than the left. In the nasal cycle-cerebral dominance relationship, right nostril dominance indicates that the left hemisphere is stimulated and therefore an increase in sympathetic activity. In addition, the higher right nasal passage volume compared to the left in the measurements made 20 minutes after exercise ($p < 0.05$) suggested that sympathetic activity continued.

Keywords: Exercise, Sympathetic activation, Acoustic rhinometry, Nasal volume, Nasal cycle

PC-06

Effects of Exercise and Linagliptin on Body Weight, Blood Glucose and Serum Total Oxidant/Antioxidant Capacity in Rats with Type 2 Diabetes

Melis Cayır, Ayşe Arzu Yigit

Baskent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: The aim of the study was to investigate the effects of aerobic exercise training and linagliptin treatment separately and in combination on body weight, blood glucose, serum total oxidant capacity and total antioxidant capacity in rats with type 2 diabetes induced by streptozotocin.

METHODS: The study was approved by Başkent University Animal Experiments Local Ethics Committee (DA24/15). The 45 rats used in the study were equally divided into 5 groups as sham control, diabetes, diabetes+exercise, diabetes+linagliptin and diabetes+exercise+linagliptin. In the diabetes groups, type 2 diabetes was induced with streptozotocin after 2 weeks of high-fat diet and swimming exercise 30 min/day 5 days a week for 6 weeks and linagliptin 3 mg/kg/day was administered by oral gavage. Body weight and blood glucose levels of rats were measured at the beginning and end of exercise training and linagliptin treatment. At the end of the experiment, total oxidant and total antioxidant capacity levels were evaluated in the serum of the rats. Statistical analysis was performed using GraphPad Prism 10 software, dependent t test, one-way ANOVA and Tukey's multiple comparison test, $p < 0.05$ was considered significant.

RESULTS: As a result of the study, when aerobic exercise training and linagliptin treatment were applied separately or in combination, blood glucose levels decreased compared to the beginning of the experiment ($p < 0.0001$, $p = 0.031$, $p = 0.0016$, respectively). Body weight at the end of the experiment decreased in the diabetes group ($p < 0.0001$) and increased in the linagliptin treatment group ($p < 0.0001$) compared to the beginning. Both treatment modalities, separately or in combination, had no effect on serum total oxidant capacity and total antioxidant capacity.

CONCLUSIONS: Aerobic exercise training and 3 mg/kg linagliptin administered independently or in combination to diabetic rats for 6 weeks had positive effects on reducing blood glucose, but had no effect on serum total oxidant and total antioxidant capacity.

Keywords: Type 2 diabetes, Aerobic exercise, Linagliptin, Rat

PC-07

Effect of Curcumin on Locomotor Activity and Exercise Capacity in Exercised Aged Rats.

Serap Keskin^{1*}, Basar Koc^{1*}, Burcu Acikgoz¹, Bahar Dalkiran¹, Ilkay Aksu¹, Amaç Kiray², Muge Kiray¹

¹Dokuz Eylul University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

²Dokuz Eylul University, Faculty of Medicine, Department of Anatomy, Izmir, Türkiye

*First and second authors contributed equally.

AIM: Physical activity/exercise training may influence the aging process by modulating key signaling pathways. Exercise has been shown that Curcumin, a polyphenolic compound isolated from *Curcuma longa*, exhibits anti-aging properties shown. The aim of this study: To investigate the effects of curcumin on exercise capacity and locomotor activities in exercised aged rats and to compare the effects of curcumin with exercise.

METHODS: In this study in which 32 20-month-old female Sprague Dawley rats were used, rats were given curcumin (50mg/kg/day) by oral gavage for 3 weeks. I. group: Control n=8 (no treatment); II. group: curcumin group n=8 (5 days a week for 3 weeks by oral gavage); III. group: n=8 exercise group (treadmill exercise), IV. group: n=8 exercise + curcumin. Treadmill exercise application: Rats in groups 3 and 4 underwent adaptation training for 20 min/day in the first week. The exercise capacity of all rats was determined indirectly before training. Starting at a speed of 5 m/min, the rats were made to run until exhaustion by increasing the speed by 5 m/min every 3 min. Fatigue time (min) and workload (m/min) were determined as exercise capacity indices. Adaptation exercise was performed at 4.2 m/min for the first 2 minutes, 6.3 m/min for the next 4 minutes and 4.2 m/min for the last 2 minutes for a total of 20 min/day. Treadmill exercise was performed for 14 days, running at a speed of 4.2 m/min for the first 4 minutes, 9.5 m/min for 12 minutes and 4.2 m/min for the last 4 minutes for a total of 20 min/day (moderate exercise). Rotarod test was performed at the beginning and end of the experiment. Results were evaluated by two-way anova, post hoc tukey's tests.

RESULTS: Exercise capacity measurements on day 0 group averages Group III (exercise group) 36.25 m/min Group IV (curcumin + exercise group) 38.125 m/min. 3 weeks later exercise capacity measurements results Group III 45 m/min, Group IV 52.5 m/min Rotarod: Curcumin + exercise group had more time to fall from the platform (p<0.05).

CONCLUSIONS: This findings suggest that curcumin increases exercise capacity when administered with exercise.

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Keywords: Curcumin, Exercise, Exercise capacity

PC-08

Does Ibrutinib Affect the Heart's Contractility?

Raviye Özen Koca¹, Behiye Nur Karakuş¹, Atakan Tekinalp², Hatice Solak³, Faik Özdemir¹, Z. Işık Solak Görmüş¹

¹Necmettin Erbakan University Faculty of Medicine, Department of Physiology, Konya, Türkiye

²Necmettin Erbakan University Faculty of Medicine, Department of Hematology, Konya, Türkiye

³Kutahya Health Sciences University Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: Ibrutinib is the first Bruton tyrosine kinase (BTK) inhibitor approved for the treatment of patients with chronic lymphocytic leukemia (CLL). Approximately 20-25% of patients experience dose-limiting side effects, mostly consisting of cardiovascular toxicities such as severe hypertension and atrial fibrillation. The aim of the study was to investigate the effect of ibrutinib on rat atrioventricular tissue contraction.

METHODS: Atrioventricular tissues of Wistar albino rats (n=8) were isolated after cervical dislocation. All tissues were placed in organ baths containing Krebs solution, thermoregulated at 37°C and ventilated (95% O₂ and 5% CO₂). Changes in isometric tensions were recorded using a transducer. Adrenaline (10-1M) was applied to the tissues to induce isometric contractions. When the atrioventricular tissues reached maximum contraction, ibrutinib (10-3M) was added to the chambers and contractions were recorded. Friedman Kruskal Wallis tests were used for statistical evaluation.

RESULTS: When spontaneous contractions in rat atrioventricular tissues and changes in tension values with adrenaline and ibrutinib (10-3M) application were examined, it was observed that adrenaline-induced contractions were inhibited by ibrutinib application (p<0.05). In the evaluation of contraction patterns, adrenaline-induced contractions were inhibited after ibrutinib application and the peak-peak (p-p) value decreased statistically significantly (p<0.05).

CONCLUSIONS: The study results showed that ibrutinib caused negative inotropic effects on the atrial muscle at a single dose. Further studies with different doses are needed to clarify the mechanism of action of ibrutinib more clearly.

Keywords: Ibrutinib, Atrium, Contraction, Isolated organ bath

PC-09

Effects of Ellagic Acid and Berberine on Skeletal Muscle in Hind Limb Ischemia Reperfusion Injury

Esra Tekin¹, Ali Koray Kaya¹, Ayşegül Küçük¹, Mustafa Arslan², Abdullah Özer³, Hüseyin Demirtaş³, Şaban Sezen⁴, Gülay Kip²

¹Kutahya Health Sciences University, Faculty of Medicine, Department of Physiology, Kutahya, Türkiye

²Gazi University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Ankara, Türkiye

³Gazi University, Faculty of Medicine, Department of Cardiovascular Surgery, Ankara, Türkiye

⁴Kırıkkale University, Faculty of Medicine, Department of Histology and Embryology, Kırıkkale, Türkiye

AIM: Hind limb ischemia/reperfusion (I/R) injury is a serious clinical condition. The aim of this study is to compare the effects of ellagic acid and berberine on oxidative stress and cell death pathways in hind limb I/R injury model.

METHODS: Thirty-five male Sprague-Dawley rats were randomly divided into five groups (n=7 each): Sham, I/R, Ellagic Acid+I/R, Berberine+I/R, and Ellagic Acid+Berberine+I/R. The infrarenal abdominal aorta was clamped and reperfused during 2 hours respectively. At the 75th minute of ischemia, ellagic acid (100 mg/kg, ip) and berberine (200 mg/kg, ip) were administered. Oxidative stress markers (MDA, GSH, SOD, CAT), apoptosis (Cleaved caspase-3, Bax, Bcl-2) and pyroptosis (NLRP3, NRF2, Gasdermin D) pathways were evaluated. Muscle tissue was histopathologically assessed with hematoxylin-eosin staining.

RESULTS: Histopathological assessment showed significant increases in muscle atrophy/hypertrophy, degeneration/congestion, nuclear internalization/oval-central nucleus, fragmentation/hyalinization, and leukocyte infiltration in the I/R group. Ellagic acid and berberine reduced them, yielding results close to the sham group. Bax levels increased in I/R group, while ellagic acid and berberine reduced Bax levels. Bcl-2 levels decreased in I/R group but reached normal levels with ellagic acid and berberine. The Bax/Bcl-2 ratio was highest in the I/R group, but ellagic acid and berberine normalized it. NRF2 levels decreased, while NLRP3 and Gasdermin D levels increased in I/R group; ellagic acid and berberine normalized these levels. MDA levels were reduced, while GSH, SOD, and CAT levels were increased with ellagic acid and berberine compared to I/R group.

CONCLUSIONS: Ellagic acid and berberine showed beneficial effects on apoptosis, pyroptosis, and oxidative processes in hind limb I/R injury. The combined use of these antioxidants resulted in more effective outcomes in Bax/Bcl-2 ratio and some histological damage parameters. Ellagic acid and berberine, either separately or in combination, can be considered potential therapeutic agents for hind limb I/R injury.

Keywords: Hind limb, I/R injury, Apoptosis, Berberine, Ellagic acid, Pyroptosis, Rat

PC-10

Comparison of the Effectiveness of Dimethyl Sulfoxide and Trehalose/ Sodium Hyaluronate in Doxorubicin Induced Extravasation Injury

Alper Geyik¹, Basar Koc², Serap Cilaker Micili³, Muge Kiray²

¹Dokuz Eylul University, Faculty of Medicine, Department of Plastic Reconstructive and Aesthetic Surgery, Izmir, Türkiye

²Dokuz Eylul University, Faculty of Medicine, Department of Physiology, Izmir, Türkiye

³Dokuz Eylul University, Faculty of Medicine, Department of Histology and Embryology, Izmir, Türkiye

AIM: Extravasation injury occurs when anticancer agents etc. unintentionally infiltrate into the extracellular space during infusion. Doxorubicin (DOX) is a chemotherapy drug classified as an anthracycline (vesicant substance; causing severe soft tissue damage with formation of blisters that can lead to skin necrosis). The literature emphasizes various treatment options for managing extravasation injury. The first-line treatment for extravasation involves immediately stopping the injection or infusion and then aspirating as much of the extravasated fluid as possible. Some other examples include applying cold packs for anthracyclines, administering antidotes like dexrazoxane and dimethyl sulfoxide (DMSO), micronutrient injection or saline flush out with stab incisions. Trehalose (THA) is a disaccharide formed by two glucose units and produced by some bacteria, fungi, and other invertebrate animals as a result of stress. The human body does not synthesize trehalose. However, it is commonly used in medicine for various purposes, including wound healing, stabilizing cell membranes and proteins, promoting autophagy, and enhancing flap viability. The combination of DMSO and trehalose has displayed promising results as a cryoprotectant.

METHODS: Twenty-eight adult male Sprague-Dawley rats were divided into four groups. All subjects were weighed weekly. DOX injection was performed intradermally. First group received doxorubisin injection (control group). In the second group three drops of topical DMSO were dripped on to the extravasation area. The third group received an intradermal injection of three drops (0.1 mL) of a 3% trehalose and 0.15% sodium hyaluronate solution. Finally, the last group received both topical DMSO and intradermal THA application. All groups were administered their treatments in every eight hours for one week.

RESULTS: The mean surface area of tissue necrosis in control group was 81.2 ± 14.77 mm². All treatment groups had significantly lower necrosis area than control group.

CONCLUSIONS: Our study demonstrates the effectiveness of THA injection in reducing tissue necrosis in a rat model.

Keywords: Skin necrosis, Trehalose, Extravasation

PC-11

Investigation of the Effects of Magnesium Citrate and Melatonin Combination as a Pre-treatment on Hypoxia

Busenur Bolat, Uğur Faruk Kalkan, Cansu Yakın, Ceyda Nur Uçar, Cihan Suleyman Erdogan, Bayram Yilmaz

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

AIM: Excitotoxicity has a key role in many degenerative diseases, including hypoxia-induced diseases. Magnesium can reduce excitotoxicity by blocking N-methyl-D-aspartate (NMDA) receptors. Magnesium citrate (MgC) is known as a form of magnesium that is easy to absorb by cells, but its effect in hypoxia models has not yet been investigated. Melatonin (MLT) is a hormone with neuroprotective effects in the brain and other organs, attributed to its antioxidant properties. Our aim was to investigate both the molecular effects of MgC treatment in the hypoxia model and its potential use as an adjuvant agent in MLT treatment.

METHODS: A total of 350,000 Neuroblastoma-2A (N2A) cells were seeded in petri dishes for each group and treated with MgC (50 mM), MLT (50 μ M), or a combination (MgC+MLT) for 24 hours. Hypoxia was induced using oxygen glucose deprivation (OGD) for 8 hours, followed by 16 hours of reperfusion. Subsequently, cell survival was measured and protein expressions were analyzed via western blot. Statistical analysis was performed using one-way ANOVA, $p < 0.05$ was considered statistically significant.

RESULTS: It was observed that MgC+MLT treatment applied before OGD increased cellular survival under OGD conditions ($p < 0.05$). Expression of phosphorylated mTOR protein was significantly decreased in the MgC+MLT group compared to the control group under OGD conditions ($p < 0.01$). Expression of NMDA ϵ 2 protein was significantly increased in MgC and MLT groups compared to the control group ($p < 0.05$), while a decreasing trend was observed in MgC+MLT group.

CONCLUSIONS: When survival and protein expression analyses were evaluated together, it was observed that combination of MgC+MLT had a protective effect on N2A cells under OGD conditions. It was also observed that MgC+MLT has the potential to reduce excitotoxicity through NMDA receptors. Based on these findings, MgC+MLT combination can be evaluated as a novel therapeutic approach for neurological diseases.

Keywords: Excitotoxicity, Magnesium citrate, Melatonin, Hypoxia

PC-12

Effect of Chronic Exercise on ZFAND3 Gene Expression and Lipid Peroxidation in Liver Tissue in a Diabetic Old Female Rat Model

Ersan Kara¹, Sümeyye Parlattan¹, Saltuk Buğra Baltacı², Ayşenur Feyza Bayıroğlu³, Ebru Kübra Uzdil³

¹Kırşehir Ahi Evran University, Faculty of Sports Science, Department of Coaching Training, Kırşehir, Türkiye

²Istanbul Medipol University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

³Selcuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: Due to its critical importance in glucose metabolism, the liver has been chosen as the therapeutic organ in the treatment of diabetes. However, the relationship of ZFAND3 (Zinc finger AN1-type domain 3), a zinc finger protein, with the liver of diabetic rats has been investigated in only one study. The aim of this study is to investigate how moderate chronic exercise affects ZFAND3 gene expression and lipid peroxidation in liver tissue in an elderly diabetic female rat model.

METHODS: The protocol of the study conducted on old female Wistar rats (16 months old) was approved by the local ethics committee. A total of 40 old female rats were divided into 4 equal groups. Group 1, Control. Group 2, Exercise Control. Group 3, Diabetes. Group 4, Diabetes+Exercise. Diabetes was induced in the animals of groups 3 and 4 by intraperitoneal administration of 40 mg/kg streptozotocin. Animals in groups 2 and 4 were subjected to chronic running exercise for 45 minutes daily on a rat treadmill for 4 weeks. ZFAND3 gene expression was determined by PCR method and MDA and GSH levels were determined by ELISA method in liver tissue samples taken from animals sacrificed 24 hours after the last running exercise.

RESULTS: In the current study, increased MDA and suppressed GSH levels in liver tissues of diabetic aged female rats were reversed by 4 weeks of chronic exercise ($p < 0.05$). We observed increased liver ZFAND3 gene expression values with chronic exercise in exercise groups (G2 and G4) ($p < 0.05$).

CONCLUSIONS: The result of the current study shows that the pathological processes that occur in diabetes can be partially prevented by increasing the liver ZFAND3 gene expression, which is suppressed in the diabetic old female rat model, with chronic exercise. Chronic exercise may be an activator that increases liver ZFAND3 gene expression level.

Keywords: Aged female rat, Chronic exercise, Diabetes, Lipid peroxidation, Liver, ZFAND3

PC-13

Chronic Exercise Prevents Muscle Tissue Damage and Increase in IL-6 Gene Expression in a Diabetic Old Rat Model

Ersan Kara¹, Emine Aydın¹, Ayyüce Kumaş², Nazlı Hilal Eke³

¹Kırşehir Ahi Evran University, Faculty of Sports Science, Department of Coaching Training, Kırşehir, Türkiye

²Selcuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

³Gaziantep Islam Science and Technology University, Faculty of Medicine, Department of Physiology, Gaziantep, Türkiye

AIM: The improving effect of chronic exercise on antioxidant parameters in diabetic elderly rats has not been extensively investigated. The aim of this study is to investigate how moderate chronic exercise affects IL-6 gene expression and lipid peroxidation in muscle tissue in an elderly diabetic rat model.

METHODS: The study was conducted on aged female Wistar rats (16 months old) and was approved by the local experimental animal ethics committee. A total of 40 old female rats were divided into 4 equal groups. Group 1, Control, Group 2, Exercise Control, Group 3, Diabetes, Group 4, Diabetes+Exercise. Diabetes was induced in the animals of groups 3 and 4 by intraperitoneal administration of 40 mg/kg streptozotocin. Animals in groups 2 and 4 were subjected to chronic running exercise for 45 minutes daily on a rat treadmill for 4 weeks. IL-6 gene expression was determined by RT-PCR method and MDA and GSH levels were determined by ELISA method in muscle tissue samples taken from animals sacrificed 24 hours after the last running exercise.

RESULTS: The highest IL-6 gene expression and muscle MDA levels in muscle tissue, as well as the lowest muscle GSH levels, were obtained in the diabetes group (Group 3) ($p<0.05$). While chronic exercise significantly suppressed IL-6 gene expression and muscle MDA levels in diabetic rats (Group 4) compared to Group 3 ($p<0.05$), it also increased muscle GSH levels ($p<0.05$).

CONCLUSIONS: The findings of our study show that 4 weeks of moderate chronic exercise suppresses IL-6 gene expression, an inflammatory parameter, and MDA levels, an indicator of muscle tissue damage, and increases GSH levels, an indicator of muscle antioxidant activity, in diabetic rats. Moderate chronic exercise improves the quality of life both in aging and in diabetes, which is known to increase with age.

Keywords: Diabetic Old Rat, Exercise, GSH, IL-6, MDA, Muscle Tissue

PC-14

Loratadine Reduces Cell Viability in Different Types of Human Cancer Cell Lines

Tuba Keskin, Guldeniz Sekerci, Suat Tekin

İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Due to its high prevalence and mortality rates, cancer remains a prevalent topic in scientific research. Various studies have suggested that anti-inflammatory and antioxidant therapies might prevent or delay the onset and progression of cancer. Recent research has also highlighted the potential effectiveness of antihistamines in cancer treatment. Some investigators have observed that antihistamines could inhibit the proliferation of various cancer cells. Research indicates that these drugs may impart anticancer properties through their effects on cellular growth, apoptosis, and angiogenesis. There is a growing body of evidence that H1 antihistamines may inhibit tumor growth and promote cell death in a range of tumors, including melanoma. Loratadine, an H1 receptor antagonist, is classified as a second-generation antihistamine. Considering all these findings, it is suggested that Loratadine may have a potential impact on cancer. Therefore, our study aims to investigate the effects of Loratadine on human ovarian (A2780), colon (Caco-2), and prostate (LNCaP) cancer cell lines.

METHODS: The cell viability (%) of A2780, Caco-2, and LNCaP cell lines incubated with Loratadine at concentrations of 1, 5, 25, 50, and 100 μ M for 24 hours was determined using the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) Assay method. The statistical significance of the data was evaluated using the non-parametric Kruskal-Wallis variance analysis in IBM SPSS 24 software, with a p-value of <0.05 considered statistically significant.

RESULTS: Loratadine was found to reduce cell viability at concentrations of 25, 50, and 100 μ M in the A2780 cell line; 5, 25, 50, and 100 μ M in the Caco-2 cell line; and at all concentrations in the LNCaP cell line ($p<0.05$).

CONCLUSIONS: The results of this study suggest that Loratadine may exhibit anticancer activity on A2780, Caco-2, and LNCaP cells. Additionally, Loratadine demonstrates that H1 receptor antagonists could be potential candidates in cancer treatment.

Keywords: Cancer, Histamine, Loratadine, A2780, Caco-2, LNCaP

PC-15

Investigation of the Effects of Vildagliptin on Cancer Cell Lines: An In Vitro Study

Guldeniz Sekerci¹, Tuba Keskin¹, Suat Tekin¹

¹Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Cancer is one of the biggest health problems that pose a global threat and the fight against cancer continues with different methods around the world. Despite the advances in the prevention and treatment of cancer, success, considering the high mortality rates in cancer, the inadequacy of currently known treatment methods and the low rate and tumor recurrence make the discovery of new alternative agents or drugs important. A limited number of studies have shown that drugs used in the treatment of diabetes, another global health problem that has increased in recent years, may have anticancer activity. In this regard, it is thought that the antidiabetic drug Vildagliptin, which provides glycemic control, may have anticancer properties. This study was conducted to examine the effect of Vildagliptin on human ovary (A2780), prostate (LNCaP) and colon (Caco-2) cancer cell lines.

METHODS: In the study, A2780, LNCaP and Caco-2 cell lines were incubated with 1, 5, 25, 50 and 100 µM Vildagliptin for 24 hours. The effect of Vildagliptin on cell viability was determined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) Assay method. Cell viability (%) was calculated with IBM SPSS software program for Windows. Statistical significance of the data was evaluated by non-parametric Kruskal Wallis variance analysis and $p < 0.05$ was considered statistically significant.

RESULTS: Vildagliptin significantly decreased cell viability at concentrations of 1, 5, 25, 50 and 100 µM in A2780 and Caco-2 cell lines ($p < 0.05$) and at concentrations of 25, 50 and 100 µM in LNCaP cell line ($p < 0.05$).

CONCLUSIONS: The results of this study suggest that Vildagliptin may have antitumor effects on A2780, LNCaP and Caco-2 cells. Vildagliptin may play a beneficial and protective role in diabetic patients with cancer due to its glycemic control and potential anticancer effects. Therefore, Vildagliptin may be a therapeutic candidate in the development of cancer treatment strategies.

Keywords: Cancer, Diabetes, Vildagliptin, Cell Viability

PC-16

Investigation of In Vitro Cytotoxic and Genotoxic Properties of New Dioxybiphenyl-bridged Spiro Cyclotriphosphazene with Dihydroxycoumarin Groups Synthesized by the Click Method

Tuba Keskin¹, Zeynep Savaşçı², Ferhan Sultan Şeker², Rümeyza Çetiner², Fatih Biryan², Kenan Koran², Suat Tekin¹, Süleyman Sandal¹

¹Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

²Firat University, Faculty of Science, Department of Chemistry, Elazığ, Türkiye

AIM: In this study, we aimed to determine the in vitro cytotoxic and genotoxic effects of new dioxybiphenyl-bridged spirocyclotriphosphazene compound bearing coumarin groups synthesized using the click method against human breast (MCF-7) and human ovarian (A2780) cancer cell lines.

METHODS: Coumarin-substituted cyclotriphosphazene compound (CRG-PA-Click-CH₂-Cum-DiOH) was obtained from the interaction of cyclotriphosphazene compound with alkyne end group (CRG-PA) and 7,8-dihydroxy-4-(azidomethyl)coumarin (DiOH-Cum-CH₂-N₃) with azide end group using the click method. The cell viabilities of the starting and final product phosphazene compounds at concentrations of 1, 5, 25, 50 and 100 µM on MCF-7 and A2780 cell lines were determined by MTT Assay method. The effective dose that decreases cell viability by 50% (LogIC₅₀/IC₅₀) was calculated by Graphpad-6 program. DNA damage (genotoxicity) studies were performed by comet assay method depending on the effect of the compounds at the highest dose. The tail intensity (TI), tail length (TL) and tail moment (TM) parameters induced by the compounds on cancer cells were determined and the presence and rate of DNA damage were determined by the changes in these parameters. The Tamhane's T2 test was used to compare the multiple comparisons since variances were not homogeneous. The value $p < 0.05$ was accepted as statistically significant.

RESULTS: From the results obtained, it was determined that the compounds caused significant decreases in cell viability, especially at high doses ($p < 0.05$). It was determined that the substances had genotoxic effects on both cancer cell lines by affecting the TI, TL and TM parameters at the same doses ($p < 0.05$).

CONCLUSIONS: It was revealed that the substances added to the culture medium caused serious decreases in cell viability rates after 24 hours and that these decreases occurred due to damage in the DNA of the cells.

This study was supported by Inonu University Scientific Research Projects Unit (Project no: TCD-2024-3683) and TUBITAK BİDEB (Project no: 1919B012326997).

Keywords: Dyspirocyclotriphosphazene, A2780, MCF-7, MTT Assay, Comet Assay

PC-17

Evaluation of the Cytotoxic Activity of Citrinin on Human Prostate Cancer Cell Lines

Hande Yüce¹, Dilan Aşkın Özek², Songül Ünüvar¹

¹Inonu University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Malatya, Türkiye

²Firat University, Kovancılar Vocational School, Department of Pharmacy Services, Elazığ, Türkiye

AIM: Citrinin is a mycotoxin produced as a secondary metabolite by species of *Aspergillus*, *Penicillium*, *Monascus*, and other strains. Citrinin causes toxicity in humans and animals. Due to this potential for toxicity, it plays an effective role in cancer progression by exhibiting cytotoxic effects on cancer cells at appropriate doses. Citrinin inhibits cancer progression by inducing apoptosis in cancer cell lines. The aim of this study is to evaluate the cytotoxic activity of citrinin on human prostate cancer (PC-3) and healthy fibroblast (L929) cell lines, which have not been previously investigated.

METHODS: Citrinin was applied to PC-3 and L929 cell lines at increasing concentrations (10, 20, 50, 100, 150, 300 µM), and its cytotoxic activity was evaluated using the MTS (3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium) assay. Cell viability was measured 24 and 48 hours after citrinin application using the ELISA method.

RESULTS: Citrinin exhibited cytotoxic effects on prostate cancer cells without affecting the viability of healthy cells. After 24 hours of application, the IC₅₀ values were found to be 360.4 µM for the L929 cell line and 285.4 µM for the PC-3 cell line. After 48 hours of application, the IC₅₀ values were 229.6 µM for the L929 cell line and 222.3 µM for the PC-3 cell line.

CONCLUSIONS: Citrinin exhibited cytotoxic activity by reducing cell viability in prostate cancer cells compared to healthy cells. Financial Support: This study was supported by the Scientific Research Projects Unit of İnönü University (Project No: TOA-2024-3718).

Keywords: Citrinin, Cytotoxic activity, L929, PC-3

PC-18

In Vitro Investigation of the Anticancer Activity of H1 Antagonist Meclizine in Various Cancer Cell Lines

Semiha Nur Özkaya¹, Suat Tekin²

¹Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Physiology, Kahramanmaraş, Türkiye

²İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: According to the World Health Organization, cancer is one of the leading causes of death. Available treatment methods for cancer are inadequate. This situation requires the discovery of new anticancer agents and therapeutic methods. Current literature focuses on the anticancer activities of H1 receptor antagonist antihistamines. In our study, we aimed to investigate anticancer activity of Meclizine, which is from this drug group, in breast (MCF-7), colon (Caco2) and prostate (LNCaP) cancer cell lines using in vitro methods.

METHODS: In study, MCF-7, Caco2 and LNCaP cells were incubated with Meclizine for 24 hours. Incubation performed with concentrations of 1, 5, 10, 20, 25, 50, 100, 200, 500 and 1000 µM of Meclizine. The effect of this exposure on viability of relevant cells was examined by the 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium-bromide (MTT) Assay method. According to the MTT Assay results, inhibitory concentration 50 (IC₅₀) value was determined with Graphpad Prism-8 program. The IC₅₀ value is a reference for the subsequent Comet Assay. Comparisons between groups were made using Kruskal-Wallis-H test in IBM-SPSS 24.0 Windows package program; value of p<0.05 was considered statistically significant.

RESULTS: After 24 hours of incubation of cells with Meclizine, MCF-7 and LNCaP cell viability levels were determined to decrease significantly at all concentrations except 1 µM dose (p<0.05). Caco2 cell viability was observed to decrease at all concentrations of Meclizine (p<0.05).

CONCLUSIONS: The results obtained show cytotoxic activity of Meclizine on MCF-7, Caco2 and LNCaP cell lines. These findings suggest that Meclizine, an H1 antagonist, may have anticancer activity. This study was supported by İnönü University Scientific Research Projects unit with project number TCD-2024-3615.

Keywords: Cancer, Cell Viability, Meclizine

PC-19

In Vitro Investigation of the Anticancer Activity of H1 Antagonist Cetirizine in Various Cancer Cell Lines

Suat Tekin¹, Semiha Nur Özkaya²

¹İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

²Kahramanmaraş Sütçü İmam University, Faculty of Medicine, Department of Physiology, Kahramanmaraş, Türkiye

AIM: Cancer is one of the public health problems with high incidence and mortality. Available treatment methods for cancer are inadequate. For this reason, studies have focused on discovery of new anticancer agents and therapeutic methods. In current literature, anticancer activities of H1 receptor antagonist antihistamines are remarkable. In our study, we aimed to investigate anticancer activity of Cetirizine, which is from this drug group, in breast (MCF-7), colon (Caco2) and prostate (LNCaP) cancer cell lines in vitro methods.

METHODS: In the study, MCF-7, Caco2 and LNCaP cells were incubated with their own medium (control), dimethyl sulfoxide (solvent) and various concentrations of Cetirizine (1, 5, 10, 20, 25, 50, 100, 200, 500 and 1000 µM) for 24 hours. Effect of exposure to Cetirizine on viability of cells was examined by 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium-bromide (MTT) Assay method. According to the MTT Assay results, inhibitory concentration 50 (IC50) value were determined using the Graphpad Prism-8 program. Comparisons between groups were made using Kruskal-Wallis-H test in IBM-SPSS 24.0 for Windows package program; value of p<0.05 was considered statistically significant.

RESULTS: As a result of the analyses, we determined that cetirizine significantly reduced cell viability in MCF-7 and Caco2 cells at all concentrations, and in the LNCaP cell line at all concentrations except 1 µM (p<0.05).

CONCLUSIONS: The findings show that Cetirizine administration has cytotoxic effects on MCF-7, Caco2 and LNCaP cells. This result suggests that the H1 antagonist Cetirizine may play an anticancer role.

This study was supported by İnönü University Scientific Research Projects unit with project number TCD-2024-3615.

Keywords: Cancer, Cell Viability, Cetirizine

PC-20

Anticancer effects of cannabinoid type 2 receptor agonist JWH-133 on Prostate Cancer cell lines

Seda Sabah Özcan¹, Rehime Yapar¹, İsmail Değerli¹, Levent Elmas², Mehmet Korkmaz¹, Murat Çakır³

¹Manisa Celal Bayar University, Faculty of Medicine, Department of Medical Biology, Manisa, Türkiye

²İzmir Bakırçay University, Faculty of Medicine, Department of Medical Biology, İzmir, Türkiye

³Yozgat Bozok University, Faculty of Medicine, Department of Physiology, Yozgat, Türkiye

AIM: Pharmacological activation of the cannabinoid type 2 receptor (CB2) has been shown to stimulate anti-tumoral mechanisms in different types of cancer. CB2 receptor agonists have been found to have inhibitory effects on tumor cell growth. The aim of this study was to investigate the anti-cancer effects of JWH-133, a CB2 receptor agonist, in LNCaP, Du-145 and PC3 cancer cells.

METHODS: Cytotoxic effects of JWH-133 were determined by MTT assay. Apoptosis of LNCaP, Du-145 and PC3 cancer cells was detected by annexin V-FITC/PI staining using a flow cytometer. Apoptotic gene expressions were analyzed by real-time PCR. Effects of JWH-133 on colony formation, and cell migration were detected by colony formation assay, and wound-healing assay, respectively.

RESULTS: IC50 dose of JWH-133 was found to be 66.68 µM in the 48th hour in the LNCaP cell line, 36.62 µM in the 48th hour in the Du145 cell line and 24.87 µM in the 24th hour in the PC3 cell line. It was found that JWH-133 in LNCaP, Du-145 and PC3 cells suppressed, migration, and colony formation by using wound-healing assay and colony formation assay, respectively. JWH-133 increased bax, P53, P21 and NOXA gene expressions which are associated with apoptosis (p<0,05).

CONCLUSIONS: In conclusion, JWH-133 is thought to exhibit anti-tumor activity on cancer cells by affecting apoptosis, migration and colony formation.

Keywords: Cannabinoid type 2 receptor, JWH-133, Prostate Cancer

PC-21

Investigation of Mitochondrial Oxidative Stress on GnRH mRNA Expression in vitro

Ceyda Nur Ucar, Cihan Suleyman Erdogan, Cansu Yakın, Busenur Bolat, Ugur Faruk Kalkan, Bayram Yilmaz

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

AIM: Mitochondrial function is crucial in regulating cellular processes, including the expression of gonadotropin-releasing hormone (GnRH) by GnRH neurons. This study aimed to investigate the in vitro effects of mitochondrial oxidative stress induced by rotenone-a mitochondrial complex I inhibitor-on GnRH mRNA levels.

METHODS: GT1-7 cells, a GnRH-secreting cell line, were treated with various concentrations of rotenone (0.5–50 μ M) for 24 and 48 hours. Cell viability was assessed using the trypan blue exclusion method to calculate IC50 values. To synchronize the cells, they were either deprived of fetal bovine serum (FBS) for 24 hours before rotenone treatment or directly treated with 0.5 μ M and IC50 doses of rotenone for 24 and 48 hours. RNA samples were collected, and GnRH mRNA levels were measured using quantitative real-time PCR. Data were analyzed using one-way ANOVA followed by Dunnett's multiple comparison test. P-values less than 0.05 considered statistically significant.

RESULTS: Rotenone significantly reduced cell viability at all doses except 0.5 μ M compared to the control group at both time points ($p < 0.0001$). The IC50 values were 2.66 μ M at 24 hours and 1.92 μ M at 48 hours. In FBS-deprived cells, GnRH mRNA levels was not significantly altered at 24 and 48 hours, but a decreasing trend was observed at 48 hours with increasing rotenone concentrations. Conversely, in the presence of FBS, 24-hour treatment with rotenone at the IC50 dose showed a tendency to increase GnRH levels; by 48 hours, GnRH levels were similar across all experimental groups.

CONCLUSIONS: The findings suggest that GnRH mRNA expression responds differently to mitochondrial oxidative stress depending on the cell cycle phase. The observed increase in GnRH levels at 24 hours with rotenone treatment in the presence of FBS may result from the modulation of transcription factors or signaling pathways involved in GnRH synthesis by rotenone-induced reactive oxygen species in the short term.

Keywords: GnRH, GT1-7, qRT-PCR, Rotenone

PC-22

Investigation of the Anticancer Mechanism of N-(p-amylicinnamoyl) Anthranilic acid (ACA) in Prostate Cancer Cell Lines

Murat Çakır¹, Rehime Yapar², İsmail Değerli², Mehmet Korkmaz², Seda Sabah Özcan²

¹Yozgat Bozok University, Faculty of Medicine, Department of Physiology, Yozgat, Türkiye

²Manisa Celal Bayar University, Faculty of Medicine, Department of Medical Biology, Manisa, Türkiye

AIM: N-(p-amylicinnamoyl) anthranilic acid (ACA) is an inhibitor of transient receptor potential melastatin 2 channel (TRPM2) and phospholipase A2. Studies have shown that phospholipase A2 and TRPM2 are associated with cell proliferation, cell death and cancer. The aim of the study is to investigate anti-cancer mechanism of ACA in LNCAP, Du-145 and PC3 cancer cells.

METHODS: Cytotoxic effects of ACA were determined by MTT assay. Apoptosis of LNCAP, Du-145 and PC3 cancer cells was detected by annexin V-FITC/PI staining using a flow cytometer. Effects of ACA on colony formation, and cell migration were detected by colony formation assay, and wound-healing assay, respectively.

RESULTS: IC50 dose of ACA was found to be 78.59 μ M in the 48th hour in the LNCAP cell line, 75.51 μ M in the 48th hour in the Du145 cell line and 49.15 μ M in the 48th hour in the PC3 cell line. It was found that ACA in LNCAP, Du-145 and PC3 cells suppressed, migration, and colony formation by using wound-healing assay and colony formation assay, respectively. ACA significantly induced apoptosis in LNCAP cells (apoptosis rate in control group 6%, in ACA group 84%).

CONCLUSIONS: ACA showed anticancer activity by inhibiting cell proliferation, migration and colony formation and inducing apoptosis.

Keywords: N-(p-amylicinnamoyl) anthranilic acid (ACA), Transient receptor potential melastatin 2 channel, Phospholipase A2, Prostate cancer

PC-23

Investigation of the Effect of Quercetin on the Accumulation of Lipids and the Level of Adiponectin in 3T3-L1 Adipocytes

Gizem Akan, Melek Tunc Tunç Ata, Emine Kilic Kılıç Toprak

Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

AIM: Obesity disrupts the homeostasis of adipose tissue, resulting in increase in the number and size of adipose cells. Quercetin is

known to have beneficial physiological effects through various mechanisms. This study aimed to investigate effects of quercetin on lipid accumulation and adiponectin (ADP) levels in adipocytes.

METHODS: After differentiating, 3T3-L1 adipocytes were treated with high glucose medium to become mature (8 days) and hypertrophic (18 days). The cells were subsequently incubated with 40-80 μ M quercetin for 24 and 48 hours. Lipid accumulation and adiponectin level were measured by ELISA. For statistical analysis; one-way analysis of variance (post hoc: Tukey test) was used to compare independent group differences, and Wilcoxon paired-two-sample test was used to compare dependent groups. $p < 0.05$ was considered statistically significant.

RESULTS: Results of the study, a significant increase in lipid accumulation was detected in hypertrophic adipocytes in all groups compared to mature adipocytes ($p < 0.05$). Quercetin administration to mature adipocytes significantly reduced lipid accumulation ($p < 0.05$). At the same time, 80 μ M quercetin dose in mature adipocytes led to a significant increase in ADP levels compared to all groups ($p < 0.05$). Quercetin administration resulted in an important decrease in ADP levels in hypertrophic adipocytes, as compared to the other groups ($p < 0.05$).

CONCLUSIONS: Our research showed that quercetin dramatically lowers lipid accumulation and raises ADP levels in mature adipocytes. However, although quercetin showed a tendency to reduce lipid accumulation in hypertrophic adipocytes, this decrement was not statistically significant, and it was observed that quercetin significantly reduced ADP levels in these cells. These findings demonstrate the protective effects of quercetin on health in the early obesity period, but its effectiveness in the later stages of obesity remains limited. It can be speculated that this may be due to the long duration of treatment in hypertrophic adipocytes. This study was supported by Pamukkale University Scientific Research Projects Coordination Unit through Project number (2023SABE009).

Keywords: 3T3-L1 adipocyte, Adiponectin, Lipid accumulation, Obesity, Quercetin

PC-24

The First Animal Model of Non-Alcoholic Fatty Pancreas Disease Regarding Exocrine Function: A Methodologic Study

Pelin Şahin¹, Sevtap Kılınç², Müşerref Şeyma Ceyhan³, Zeynep Yiğman⁴, Ayse Meltem Sevgili¹

¹Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Başkent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

³Gazi University, Faculty of Medicine, Department of Histology and Embryology, Ankara, Türkiye

⁴Gazi University Faculty of Medicine, Department of Histology and Embryology, Ankara, Türkiye; Gazi University, Neuroscience and Neurotechnology Center of Excellence (NÖROM), Ankara, Türkiye

AIM: Non-alcoholic fatty pancreas disease (NAFPD); causes significant changes in both endocrine and exocrine functions. Besides the pathophysiology of fatty pancreas not being fully understood, its effects on pancreatic functions have not been entirely elucidated. To explain the pathophysiology, the first step should be to create a reliable animal model of NAFPD. However, there is no animal model for NAFPD in the literature yet. Our aim was to create an animal model for examining exocrine functions in NAFPD.

METHODS: Seventy-two male C57BL/6 mice were first divided into 2 groups for standard or high-fat high-sucrose diet (HFHSD) then into 6 time points (2, 4, 6, 8, 10, 12 weeks), therefore we had 12 groups. Steatosis was evaluated. Serum lipid profile, and amylase were measured. Histopathologically fat score, inflammation and fibrosis in pancreas were evaluated. Statistical analyses were performed via Jamovi program and $p < 0.05$ was considered significant.

RESULTS: While feeding with HFHSD increased body weight, it generally did not alter glucose concentrations. LDL and periepididymal fat weight increased significantly in all groups fed with HFHSD compared to controls of same week. Amylase, cholesterol and HDL levels increased with 6-week diet application. Significant increase was observed in steatosis within diet groups first at 6th week ($p = 0.008$). There was significant increase in fat score in diet groups starting from 6th week ($p = 0.03$) and no significance difference in inflammation and fibrosis within all groups.

CONCLUSIONS: Our results suggest that while HFHSD immediately affects the body fat metabolism, significant increase in pancreatic fat accumulation and amylase levels first detected at 6th week. These results coincide with an increase in steatosis which is the main determinant of the exocrine pancreas dysfunction. We conclude that feeding C57BL/6 mice for 6 weeks with HFHSD is adequate to induce fatty pancreas and subsequent exocrine pancreas dysfunction.

Keywords: Non-alcoholic fatty pancreas, Animal model, Exocrine pancreas

PC-25

The Relationship Between Glycoprotein Non-Metastatic Melanoma Protein B (GPNMB), Blood Glucose Levels and Hepatic Steatosis in Healthy Subjects

Emine İnce¹, Süleyman Nahit Şendur², İlkay S. İdilman³, Adnan Berk Dinçsoy⁴, Muşturay Karcaaltınçaba³, Esin İleri Gürel⁵

¹Van Yüzüncü Yıl University, School of Medicine, Department of Physiology, Van, Türkiye

²Hacettepe University, School of Medicine, Department of Internal Medicine, Division of Endocrinology and Metabolism, Ankara, Türkiye

³Hacettepe University, School of Medicine, Department of Radiology, Ankara, Türkiye

⁴Muğla Sıtkı Koçman University, School of Medicine, Department of Physiology, Muğla, Türkiye

⁵Hacettepe University, School of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Glycoprotein Non-Metastatic Melanoma Protein B (GPNMB) is a hepatokine secreted from the liver and increased in diseases such as diabetes, fatty-liver disease, and obesity. The functions of GPNMB, its role in energy metabolism, and the factors affecting blood GPNMB levels in healthy individuals are not fully known. The aim of this study was to investigate the relationship between blood GPNMB levels and glucose metabolism, lipid profile, liver size, steatosis, and stiffness in healthy individuals.

METHODS: There were 61 participants (30–55 years old, 32 female). Blood samples were taken after 12 hours of fasting for glucose, insulin, GPNMB, lipid profile, ALT, AST, and CRP measurements. After oral glucose tolerance test (OGTT), blood samples were taken again at 30, 60, 90, 120 minutes to measure blood glucose, insulin, and GPNMB levels. The liver size, steatosis and stiffness were evaluated with magnetic resonance imaging after anthropometric measurements and detailed body analysis.

RESULTS: 47.5% of the subjects were normal-weight and 52.5% were overweight/obese. The mean blood GPNMB level of the subjects was 2.91 ± 1 pg/ml. OGTT did not affect GPNMB levels due to blood glucose and insulin changes. GPNMB levels were positively correlated with age ($\beta=0.172$, $P<0.01$), body-weight ($\beta=0.191$, $P<0.0001$), AST/ALT ($\beta=1.244$, $P<0.001$), LDL ($\beta=0.150$, $P<0.05$) and CRP ($\beta=1.244$, $P<0.001$). Liver size ($\beta=0.190$, $P<0.01$) and stiffness ($\beta=0.722$, $P<0.05$) were found to have positive effects on GPNMB levels, while liver steatosis had a negative effect ($\beta=-0.205$, $P<0.001$).

CONCLUSIONS: Serum GPNMB levels are not affected by acute changes in blood glucose levels in healthy individuals. However, serum GPNMB levels are influenced by parameters that reflect long-term changes in energy metabolism, including increased body-weight, LDL, and fatty-liver. Additional research is required to better understand the physiological functions of GPNMB and its link to disorders related to energy metabolism. This thesis study was supported by Hacettepe University Scientific Research Projects Coordination Unit (THD-2022-19610).

Keywords: GPNMB, Hepatokine, OGTT, Fatty liver, Glucose metabolism

PC-26

Effects of High-Molecular-Weight Polyvinyl Chloride on Wistar Rat Gut Microbiota Diversity

Ayper Boğa Pekmezekmek¹, Mustafa Emre¹, Erdal Tunç³, Betül Kalay⁴, Sayad Kocahan⁵, Nesrin Emre⁶, Toygar Emre⁷

¹Çukurova University, School of Medicine, Department of Physiology, Adana, Türkiye

²Çukurova University, School of Medicine, Department of Biophysics, Adana, Türkiye

³Mardin Artuklu University, School of Medicine Department of Medical Biology and Genetics, Mardin, Türkiye

⁴Cukurova University, School of Medicine, Department of Pharmacology, Adana, Türkiye

⁵University of Health Sciences, Gülhane Faculty of Medicine, Department of Physiology, Ankara, Türkiye

⁶Akdeniz University, Faculty of Science, Department of Biology, Antalya, Türkiye

⁷Boğaziçi University, Faculty of Engineering, Department of Industry, İstanbul, Türkiye

AIM: There are more than 100 trillion microorganisms in the healthy human body, 85% of which are beneficial and 15% are opportunistic bacteria called pathobionts. Microbiota, which is a community of microorganisms consisting of bacteria, viruses and archaea, causes changes in the physiological balance of the body in case of dysbiosis.

METHODS: In this study, metagenome analysis was used to determine the effect of chronic administration of High Molecular Weight Polyvinyl Chloride (HMW-PVC) microplastics to young Wistar rats on the intestinal microbiota. A total of 40 young rats were used in the study: 15 in Group1, 15 in Group2 and 10 in Control. HMW-PVC (Group1; 1% of their weight, Group2; 2% of their weight) microplastic was added into the pellets specially produced for feeding. At the end of the experiments, the rats were dissected under ketamine and xylasin anesthesia and the intestines were examined metagenomically. Differential abundance analysis (Deseq2 R package) was performed to identify specific changes between groups and a linear discriminant analysis effect size (LEFSe) search was performed between groups to demonstrate statistically significant taxonomies.

RESULTS: Due to the small number of samples, alpha diversity in the intestinal metagenome study did not show statistically significant differences, but there were differences in bacterial diversity and density across experimental groups. The predominance of *Escherichia coli* and *Shigella* in the experimental groups, compared to the control groups, was evaluated as an increase in metabolic pathways associated with pathogenicity as a result of microplastic exposure.

CONCLUSIONS: The findings reveal that extreme caution should be exercised in the production and use of nano/microplastics that pose a risk to the health of living things.

Keywords: HMW-PVC, Intestine, Krona, Metagenom, Microbiota

PC-27

The investigations of Effects of Citicoline on Experimental Intestinal Ischemia Reperfusion Injury

İnci Turan¹, Hale Sayan Özaçmak¹, Veysel Haktan Özaçmak¹, Mete Keçeci²

¹Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Physiology, Zonguldak, Türkiye

²Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Histology and Embryology, Zonguldak, Türkiye

AIM: Intestinal ischemia/reperfusion (I/R) injury leads to motility dysfunction in the intestines, local and systemic inflammation response, and damage to the intestinal mucosa. Citicoline, also known as cytidine 5'-diphosphocholine, is reported to have neuroprotective effects. The aim of the this study was to investigate the effects of citicoline on the intestinal I/R injury.

METHODS: Thirty two rats were randomized into four groups (n=8). The sham-control, intestinal I/R, and I/R + citicoline 100 mg/kg treated group and I/R + citicoline 250 mg/kg treated group. The induction of ischemia was achieved by clamping the superior mesenteric artery for 45 minutes, followed by a 2-hour period of reperfusion. Citicoline was administered intraperitoneally just before the onset of reperfusion. Ileum contractil activity was investigated using an isolated organ bath. Tissue levels of toll-like receptor 4 (TLR4), Nuclear factor kappa B (NF-κB) was evaluated using ELISA. Histopathological analysis were also evaluated. A one-way analysis of variance (ANOVA) was conducted for statistical comparison of the groups, followed by the Bonferroni test to identify differences between the groups.

RESULTS: Histopathological analysis revealed that intestinal I/R caused intense injury to intestinal tissues. In the I/R group TLR4, NF-κB levels and histopathological scores were increased (p<0.001, p<0.001, p<0.001, respectively). Citicoline treatment decreased TLR4 and NF-κB levels (p=0.020, p=0.012, respectively) in 250 mg/kg dose. Citicoline treatment improved histopathological scores (p=0.033, p=0.033) and reduced contractil activity in 100 and 250 mg/kg doses (p=0.034, p=0.014).

CONCLUSIONS: These findings indicate that citicoline may exerts protective effects against intestinal injury caused by I/R in rats. This study was supported by Zonguldak Bülent Ecevit University Scientific Research Projects Coordination Unit. Project Number: '2021-64154304-01'

Keywords: Citicoline, Intestinal ischemia, Reperfusion injury

PC-28

Dapagliflozin Exhibits a Protective Effect Against Hepatic Ischemia-Reperfusion Injury in Rats

Engin Korkmaz, Asiye Beytur, Suat Tekin, Çiğdem Tekin

Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Hepatic ischemia-reperfusion injury (IRI) is a pathological condition commonly encountered during liver transplantation and certain surgical procedures. Oxidative stress and inflammation play a significant role in the pathogenesis of hepatic IRI. This study aims to investigate the effects of the antioxidant dapagliflozin (Dapa) on hepatic IRI.

METHODS: Adult male *Sprague Dawley* rats (300-350 grams) were randomly divided into four groups (n=10, each): Sham, IRI, Dapa1+IRI and Dapa10+IRI. For 5 days prior to the surgical procedures, Sham and IRI groups were administered saline, while Dapa1+IRI and Dapa10+IRI groups received two different doses of Dapa (1 and 10 mg/kg, respectively) by oral gavage. Subsequently, sham group underwent laparotomy, while the IRI, Dapa1+IRI and Dapa10+IRI groups were subjected to 30 minutes of total hepatic ischemia followed by 2 hours of reperfusion. Plasma ALT and AST levels as well as hepatic TNF-α, IL-1β and NF-κB levels were measured using the ELISA method. Levels of SOD, GSH, CAT, MDA and GSH-Px in liver tissue were determined using spectrophotometric methods. Data were evaluated using the Kruskal Wallis H test. Multiple comparisons were evaluated using the Mann Whitney U test with Bonferroni correction.

RESULTS: Hepatic IRI significantly reduced the levels of antioxidants such as SOD, GSH, CAT and GSH-Px, while significantly increasing the plasma ALT and AST levels and hepatic MDA, TNF-α, IL-1β and NF-κB levels (p<0.05). Pre-treatment with Dapa led to a significant reduction in plasma levels of AST and ALT as well as hepatic MDA, TNF-α, IL-1β and NF-κB levels, in addition to a significant increase in hepatic antioxidant markers (SOD, GSH, CAT, GSH-Px) (p<0.05).

CONCLUSIONS: Dapa exhibited a protective effect against hepatic damage induced by IRI in rats by reducing oxidative stress and inflammatory response.

Acknowledgments: This research was supported by Inonu University Scientific Research Projects Unit (project no: TSG-2024-3564).

Keywords: Dapagliflozin, Hepatic ischaemia, Inflammation, Oxidative stress

PC-29

Role of Glucagon-Like Peptide-1 Receptors and Nitric Oxide in the Effect of Oxytocin on Small Intestinal Fasting Myoelectric Activity of Rats

Özge Darakçı Saltık¹, Hakan Balcı², Burcu Hatipoğlu³, Rümeyza Abdullahoğlu³, Ayhan Bozkurt³

¹Bilecik Seyh Edebali University, Faculty of Medicine, Department of Physiology, Bilecik, Türkiye

²Bilecik Seyh Edebali University, Faculty of Medicine, Department of Pharmacology, Bilecik, Türkiye

³Ondokuz Mayıs University, Faculty of Medicine, Department of Physiology, Samsun, Türkiye

AIM: Migrating myoelectric complex (MMC) is a motility pattern that occurs in the stomach and small intestine during fasting and forms the origin of fasting peristalsis. It is claimed that activation of glucagon-like peptide-1 receptors (GLP-1Rs) and nitric oxide (NO) release have an inhibitory role in the tonic control of MMC. In our previous study, we demonstrated the inhibitory effect of oxytocin administration on MMC activity in fasted rats. Aim of our study was to investigate the possible role of GLP-1Rs and NO in the effect of peripherally administered oxytocin on MMC activity in fasted rats.

METHODS: The experiments were started after the approval of the OMÜ Animal Experiments Local Ethics Committee (HADYEK, 2022/25) was received. For MMC recording, bipolar electrodes were placed at three different sites, 10 cm apart, in the jejunum of 42 male Sprague-Dawley rats (275-325 g) under ketamine+chlorpromazine anesthesia. Animals were randomly divided into 6 groups with 7 rats in each group. Following the 7-day recovery period, experiments were performed after an 18-hour fasting period. Oxytocin (16 µg/kg), nitric oxide synthase inhibitor Nomega-Nitro-L arginine [L-NNA (5 mg/kg)], GLP-1R antagonist exendin 9-39 (200 µg/kg) or physiological saline [FTS (2 ml/kg)] which is the solvent of all these substances, was administered intraperitoneally (i.p.) to each group following the recording of one-hour of basal myoelectric activity. In the combination groups, L-NNA (5 mg/kg) or exendin 9-39 (200 µg/kg) was administered i.p. 5 minutes before oxytocin 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: The inhibitory effect of oxytocin on MMC activity did not change with L-NNA pre-application but decreased with exendin 9-39 pre-application ($p < 0.01$). Exendin 9-39 and L-NNA alone did not cause a significant change in MMC activity.

CONCLUSIONS: Our findings suggest that GLP-1Rs play a role in the inhibitory effect of exogenously administered oxytocin on MMC activity in fasted male rats.

Keywords: Glucagon-like peptide-1, Migrating myoelectric complex, Small intestinal motility, Nitric oxide, Oxytocin, Rat

PC-30

Anti-Inflammatory, Antioxidant and Anti-Apoptotic Effects of GnRH Antagonist Cetrorelix in Rat Ulcerative Colitis Model

Hülya Buzcu¹, Meral Yüksel², Seda Kırmızıkan³, Esra Çikler⁴, Berna Karakoyun¹

¹University of Health Sciences, Hamidiye Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

²Marmara University, Vocational School of Health-Related Professions, Department of Medical Laboratory, Istanbul, Türkiye

³Bezmialem Vakıf University, Faculty of Medicine, Department of Histology and Embryology, Istanbul, Türkiye

⁴University of Health Sciences, Hamidiye Faculty of Medicine, Department of Histology and Embryology, Istanbul, Türkiye

AIM: Cetrorelix (CTX), which is a synthetic decapeptide used to prevent early luteinizing hormone surges in assisted reproduction, has shown anti-inflammatory and antioxidant effects in different disease models. This study aimed to investigate the effects of CTX, a gonadotropin-releasing hormone (GnRH) antagonist, in acetic acid (AA)-induced ulcerative colitis model in rats.

METHODS: Four groups were formed randomly with 8 rats in each group. Control group was administered saline (1ml), whereas colitis groups were administered 5% (pH:2.3) acetic acid (AA) intrarectally. Control group was treated with saline (0.1ml/100g; intraperitoneally); AA colitis groups were treated either with saline or CTX (100µg/kg/day) or sulfasalazine (100mg/kg/day; positive control) used in the treatment of ulcerative colitis, intraperitoneally once a day for 3 days following colitis induction. On the 3rd day, tissue wet weight and macroscopic score measurements were performed on 8-cm colonic tissues. Histological and biochemical parameters [myeloperoxidase (MPO), malondialdehyde (MDA), glutathione (GSH), chemiluminescence, 8-hydroxy-2'-deoxyguanosine (8-OHdG), caspase-3 and pro-inflammatory cytokines (tumor necrosis factor- α , interferon- γ , interleukin (IL)-1 β , IL-6 and IL-8)] were evaluated in tissue samples. Data were analyzed with ANOVA followed by Tukey's multiple-comparison test. This study was approved by the University of Health Sciences Animal Ethics Committee.

RESULTS: When compared with the control group, a decrease in antioxidant GSH levels and an increase in all other parameters were observed in the saline-treated colitis group ($p < 0.05$). CTX treatment significantly decreased macroscopic and microscopic damage scores, tissue wet weight, chemiluminescence, 8-OHdG, caspase-3 and cytokine levels ($p < 0.05$), but had no effect on MPO, MDA and GSH levels. In the sulfasalazine-treated group, improvement was detected in damage parameters except MDA and GSH levels ($p < 0.05$).

CONCLUSIONS: Cetrorelix, which shows anti-inflammatory, antioxidant and anti-apoptotic effects in the experimental AA-colitis model, can be considered as a therapeutic agent in ulcerative colitis. Our study was supported by University of Health Sciences Research Fund (2022/201) and TUBITAK (122S979).

Keywords: Apoptosis, Acetic acid, Cetrorelix, Oxidative stress, Ulcerative colitis

PC-31

Investigation of The Effects of Sinapic Acid on Ethanol-Induced Gastric Injuries

Fazile Nur Ekinci Akdemir¹, Mustafa Can Güler², Ersen Eraslan³, Ayhan Tanyeli², Serkan Yıldırım⁴

¹Ağrı İbrahim Çeçen University, Faculty of Health Science, Department of Nutrition and Dietetics, Ağrı, Türkiye

²Atatürk University, Faculty of Medicine, Department of Physiology, Erzurum, Türkiye

³Bandırma Onyedi Eylül University, Faculty of Medicine, Department of Physiology, Balıkesir, Türkiye

⁴Atatürk University, Faculty of Veterinary, Department of Pathology, Erzurum, Türkiye

AIM: This study aims to investigate the protective effects of sinapic acid (SA) against ethanol (ETH)-induced gastric mucosal damage. The study evaluates whether the antioxidant, anti-inflammatory, and anti-apoptotic properties of sinapic acid can reduce damage to the gastric mucosa.

METHODS: In the experiments, 48 Wistar albino rats were used and divided into 6 different groups: Control, ETH, ETH+OMEPR (omeprazole), ETH + SA 20 mg/kg, and ETH + SA 40 mg/kg. Gastric mucosal damage was induced in the rats using ETH. Biochemical and histopathological analyses were performed on the stomach tissues obtained at the end of the experiment. The measured parameters included Total Antioxidant Status (TAS), Total Oxidant Status (TOS), Glutathione (GSH), Superoxide Dismutase (SOD) levels, Malondialdehyde (MDA) levels, Myeloperoxidase (MPO), Tumor Necrosis Factor-alpha (TNF- α), Interleukin-1 beta (IL-1 β), IL-6, and Bax protein expression. For the biochemical analysis of group differences, one-way ANOVA and Tukey HSD tests were used as multiple comparison tests. A p-value of 0.05 was considered statistically significant. For histopathological results, Kruskal-Wallis and Mann-Whitney U tests were preferred.

RESULTS: ETH application caused significant damage to the gastric mucosa in the rats, resulting in indicators of oxidative stress and inflammation such as increased levels of MDA (p<0.05), MPO (p<0.05), TOS (p<0.05), TNF- α (p<0.05), IL-1 β (p<0.05), and elevated expression of IL-6 and Bax. However, SA treatment reduced these adverse effects, increasing GSH (p<0.05) and SOD (p<0.05) levels, decreasing MDA (p<0.05) levels, and suppressing IL-6 and Bax expression. Additionally, SA also reduced mucosal bleeding and edema.

CONCLUSIONS: Our study demonstrated that SA has a protective effect against ethanol-induced gastric mucosal damage. SA protects the gastric mucosa and reduces damage through its antioxidant, anti-inflammatory, and anti-apoptotic properties. These findings suggest that sinapic acid could be a potential agent for the treatment of gastric ulcers.

Keywords: Ulcer, Sinapic acid, Inflammation, Oxidative stress

PC-32

The Effect of *Myrtus communis* Extract on High Fat Diet Induced Liver Damage in Rats

Gizem Sucu¹, Gul Sinemcan Kabatas¹, Busra Ertas², Ali Sen³, Goksel Sener⁴, Feriha Ercan¹, Dilek Akakin¹

¹Marmara University, School of Medicine, Department of Histology and Embryology, Istanbul, Türkiye

²Marmara University, School of Pharmacy, Department of Pharmacology, Istanbul, Türkiye

³Marmara University, School of Pharmacy, Department of Pharmacognosy, Istanbul, Türkiye

⁴Fenerbahçe University, School of Pharmacy, Department of Pharmacology, Istanbul, Türkiye

AIM: It is known that high-fat diet (HFD) causes liver damage. This study aimed to reveal the possible protective effects of *Myrtus communis* (MC) extract on the liver tissue of HFD-fed rats.

METHODS: Wistar albino male rats (2 months old, 200-250 g) were divided into 3 groups (control, HFD, HFD+MC). Animals in the control group were fed with standard chow, and animals in the HFD and HFD+MC groups were fed with HFD (4 months). MC extract (100 mg/kg) was administered in the HFD+MC group by orogastric gavage for 1 month, starting from the 3rd month. 8-hydroxy-2-deoxyguanosine (8-OHdG), glutathione (GSH) and myeloperoxidase (MPO) activities were examined by biochemical methods in liver samples obtained from rats at the end of the experiment. Hematoxylin&Eosin, Sirius Red, Periodic Acid Schiff staining, as well as Nuclear Factor-kappa B (NF- κ B), Glial Fibrillary Acidic Protein (GFAP) and smooth muscle alpha-actin (α -SMA) immunohistochemistry were performed. Sections were evaluated by light microscope and statistically analyzed with one-way ANOVA and Tukey's multiple comparison tests.

RESULTS: Liver tissue 8-OHdG and MPO levels increased in HFD group compared to controls (P<0.01) and decreased with MC extract application (P<0,01). It was observed that the decrease in tissue GSH levels in the HFD group (P<0.001) increased in the HFD-MC group (P<0.01). In addition, hepatocyte damage, decrease in glycogen distribution, and increased collagen distribution and GFAP, α -SMA and NF- κ B immunoreactivities were observed in the HFD group compared to the control group (P<0.01). It was observed that histological damage decreased with MC application (P<0.05).

CONCLUSIONS: Our results reveal that MC extract has healing effects on liver damage caused by HFD in rats through antioxidant and anti-inflammatory mechanisms. These effects should be supported by further experimental and clinical studies. This study was supported by the Scientific Research Projects Unit of Marmara University (TTU-2020-10030).

Keywords: High Fat Diet, *Myrtus communis* Extract, Liver

PC-33

Investigation of the Relationship Between Gastric Myoelectric Activity Measurements and Gastric Emptying Rate in Healthy and Diabetic Gastroparetic Individuals

Hüda Oflazoğlu Diken¹, Hamza Kaya², Hacer Kayhan Kaya¹, Cemre Uçar Ekin Uçar Ekin¹, Emrah Öz³, Rukan Matsar Öz³

¹Dicle University, Faculty of Medicine, Department of Physiology, Diyarbakır, Türkiye

²Dicle University, Health Sciences Institute, Physiology Department PhD Student, Diyarbakır, Türkiye

³Dicle University, Faculty of Medicine, Department of Radiology, Diyarbakır, Türkiye

AIM: The study aimed to investigate the relationship between gastric myoelectric activity and gastric emptying rate in healthy and diabetic gastroparesis (D-GP) patients, and to evaluate the clinical use of electrogastrography (EGG) techniques.

METHODS: The study was conducted on 40 male subjects, including 20 healthy individuals and 20 with symptomatic D-GP. Gastric myoelectric activity was recorded using cutaneous EGG. After fasting blood samples were collected, preprandial (30 min) and postprandial (60 min) EGG recordings were obtained after consuming a standard test meal (450 kcal). The next day, gastric emptying rate (GER) was assessed using ultrasound-based antral area measurements at 15 and 90 minutes post-meal.

RESULTS: Fasting glucose and HbA1c levels were significantly higher in the D-GP group ($p<0.001$). In both pre- and postprandial periods, dominant frequency (DF) and normogastria percentages were lower in the D-GP group ($p<0.001$), while bradygastria was higher ($p<0.001$). No significant differences were found for tachygastria. Postprandial power change (PPC) was not significantly different between groups. The D-GP group showed significant antral dilation and a decrease in GER ($p<0.001$). A positive correlation was found between GER and PPC in the D-GP group.

CONCLUSIONS: Reduced postprandial power and rhythm disturbances in D-GP patients were associated with slower gastric emptying. These findings suggest that EGG combined with antral area measurements could help differentiate diabetic gastroparesis.

This study was supported by Dicle University Scientific Research Projects Coordination (DUBAP) with project number TIP.20.012.

Keywords: Gastric myoelectric activity, Diabetes, Gastric emptying rate

PC-34

JAK inhibitor Baricitinib Attenuates Kidney Injury in Sepsis Model Induced by Cecal Ligation and Puncture

Betül Tarakçı¹, Semanur Fırat¹, Murat Çakır¹, Burak Bircan², Güldeniz Şekerci³, Ali Aydın⁴

¹Yozgat Bozok University, Faculty of Medicine, Department of Physiology, Yozgat, Türkiye

²Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Medical Services and Techniques, Osmaniye, Türkiye

³İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

⁴Yozgat Bozok University, Faculty of Medicine, Department of Medical Biology, Yozgat, Türkiye

AIM: The Janus kinase-signal transducer and activator of transcription (JAK/STAT) pathway is an essential signaling pathway for the signaling of many important cytokines involved in sepsis. Baricitinib is one of the JAK inhibitors used in the treatment of inflammatory disorders. In this study, we investigated the effects of baricitinib on kidney injury in a sepsis model induced by cecal ligation and puncture (CLP).

METHODS: Forty male Sprague-Dawley rats were divided into 4 groups of 10 animals per group. The cecum of the groups that underwent CLP was ligated with a surgical thread in the distal region so as not to disrupt intestinal transit, and then punctured with a needle and the fecal contents were allowed to spread into the abdominal cavity. Among the three CLP groups, the first group received solvent, the second group received baricitinib at a dose of 3 mg/kg and the third group received baricitinib at a dose of 10 mg/kg. After 24 hours, the kidneys of the sacrificed animals were examined histopathologically. Blood urea nitrogen (BUN), creatinine, tumor necrosis factor alpha (TNF- α), interleukin beta (IL-1 β), interleukin 18 (IL-18) levels were determined in serum.

RESULTS: Serum BUN, creatine, TNF- α , IL-1 β , IL-18 levels increased in the CLP group compared to the control group ($p<0,05$). Increased serum BUN, creatinine, TNF- α , IL-1 β , IL-18 levels in CLP group decreased in both 3 mg/kg and 10 mg/kg baricitinib treated groups ($p<0,05$). Histopathologic examination of the kidney tissue revealed damage in the CLP group compared to the control group ($p<0,05$). Kidney damage in the CLP group decreased in both baricitinib 3 mg/kg and 10 mg/kg groups.

CONCLUSIONS: In this study, we found that 2 different doses of baricitinib (3 mg/kg and 10 mg/kg) showed protective properties by reducing inflammation and kidney damage in CLP-induced experimental sepsis model.

Keywords: Sepsis, Cecal ligation and puncture, Baricitinib, JAK inhibition

PC-35

Capsaicin Reduces Kidney Injury in a Sepsis Model Induced by Cecal Ligation and Puncture

Burak Bircan¹, Semanur Fırat², Murat Çakır², Güldeniz Şekerci³, Samet Öz⁴, Ali Aydın⁵

¹Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Medical Services and Techniques, Osmaniye, Türkiye

²Yozgat Bozok University, Faculty of Medicine, Department of Physiology, Yozgat, Türkiye

³İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

⁴Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Veterinary Services, Osmaniye, Türkiye

⁵Yozgat Bozok University, Faculty of Medicine, Department of Medical Biology, Yozgat, Türkiye

AIM: Sepsis is a serious health problem closely associated with multiple organ failure, with the kidneys being among the most affected organs. Transient Receptor Potential Vanilloid 1 (TRPV1) channels are related to inflammation, and capsaicin, a TRPV1 agonist, possesses antimicrobial, anti-inflammatory, and antioxidant properties. This study aims to investigate the effects of capsaicin on kidney damage in a cecal ligation and puncture (CLP)-induced sepsis model.

METHODS: Male Sprague-Dawley rats weighing 250-320 grams (n=50) were divided into five groups: Control, CLP, Cap2, Cap6, and Cap30. In the CLP procedure, the distal part of the cecum was ligated and punctured to allow the spread of fecal content into the peritoneum. The treatment groups received intraperitoneal capsaicin at doses of 2, 6, or 30 mg/kg, respectively. Rats were sacrificed 24 hours after CLP, and blood and kidney tissue samples were collected. Serum BUN and creatinine levels were measured, and histopathological and immunohistochemical analyses were performed. This study was approved by the Inonu University Animal Research Ethics Committee (protocol no: 2023/5-8).

RESULTS: A significant increase in BUN and creatinine levels was observed in the sepsis group compared to the control group (p<0.05). BUN levels decreased in the groups treated with 6 and 30 mg/kg capsaicin, while creatinine levels decreased in all treatment groups in a dose-dependent manner (p<0.05). Histopathological examination revealed glomerular degeneration, tubular damage, and inflammation in the CLP group, which were reduced by capsaicin treatment. Immunohistochemical analysis showed a decrease in TNF- α , IL-1 β , IL-6, CASP3, TLR4, p-NF- κ B, and p-I κ B- α levels in the treatment groups (p<0.05).

CONCLUSIONS: Capsaicin reduced kidney damage and exhibited anti-inflammatory effects in the CLP-induced sepsis model. This study was supported by Yozgat Bozok University Scientific Research Projects Unit (project no: THD-2023-1192).

Keywords: Sepsis, Cecal Ligation and Puncture, Capsaicin, Kidney

PC-36

Caftaric Acid Reduces Ischemia-Reperfusion Mediated Kidney and Lung Injury

Fazile Nur Ekinçi Akdemir¹, Mustafa Can Güler², Ersen Eraslan³, Ayhan Tanyeli², Serkan Yıldırım⁴

¹Ağrı İbrahim Çeçen University, Faculty of Health Science, Department of Nutrition and Dietetics, Ağrı, Türkiye

²Atatürk University, Faculty of Medicine, Department of Physiology, Erzurum, Türkiye

³Bandırma Onyedi Eylül University, Faculty of Medicine, Department of Physiology, Balıkesir, Türkiye

⁴Atatürk University, Faculty of Veterinary, Department of Pathology, Erzurum, Türkiye

AIM: Caftaric acid (CA) is a phenolic compound present in various plants, known for its pharmacological properties, including antioxidant and anti-inflammatory effects. Oxidative stress and inflammation are key contributors to ischemia-reperfusion (IR) injury. This study aimed to evaluate the effects of different doses of CA on mitigating kidney and lung damage induced by oxidative stress in an IR model.

METHODS: Thirty-two Wistar Albino rats were used and divided into 4 groups (n=8). Sham, IR, and CA treatment groups receiving 40 mg/kg and 80 mg/kg doses. In IR Bilateral kidney arteria and veins were held with atraumatic microvascular clamp for 1 h. Later, allowing blood circulation for 24 h by opening the clamps in reperfusion period. Incision was closed with silk 3/0 suture. After the experimental period, kidney and lung tissues were collected for biochemical, histopathological, and immunohistochemical analyses. Statistical analysis was performed using one-way analysis of variance (ANOVA), followed by post-hoc Tukey tests for inter-group comparisons, with a significance level set at p<0.05.

RESULTS: In the IR group, oxidant parameters (myeloperoxidase (MPO), malondialdehyde (MDA), total oxidant status (TOS), and oxidative stress index (OSI)) were elevated, while antioxidant activity (total antioxidant status (TAS) and superoxide dismutase (SOD)) decreased. Additionally, immunopositivity for microtubule-associated protein light chain 3 (LC3), Cyclooxygenase-2 (COX-2), and Caspase-3 was markedly increased in the IR group, with a concurrent reduction in antioxidant levels. However, CA treatment improved LC3, COX-2, and Caspase-3 immunopositivity, reduced oxidant levels, and enhanced antioxidant capacity. These findings were corroborated by histopathological observations.

CONCLUSIONS: Based on our results, CA appears to be highly effective in protecting the kidneys and lungs from oxidative damage in a renal IR model.

Keywords: Ischemia-reperfusion, Caftaric acid, Kidney, Lung

PC-37

Protective Effects of Apelin-13 on the Hearing System: Normative Data in a Diabetic Rat Model

Berfin Eylül Aydemir¹, Özgecan Güneşer², Sevtap Kılınc², Rukiye Ölçüoğlu², Ayşe Arzu Yiğit²

¹Başkent University, Faculty of Health Sciences, Department of Audiology, Ankara, Türkiye

²Başkent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Diabetes can damage the hearing system by affecting glucose metabolism and cochlear circulation. Auditory brainstem response (ABR) recording can be used diagnostically at 80 dB nHL and to determine hearing thresholds by reducing sound intensity and for screening the presence of wave V at 35 dB nHL. This study aims to examine the effects of apelin-13 on the hearing system in STZ-induced diabetic rats and create normative data for ABR.

METHODS: In the study, 32 male Wistar albino rats were randomly divided into sham, diabetes, apelin, and diabetes+apelin groups. Diabetes and diabetes+apelin groups received a single intraperitoneal dose of 45 mg/kg STZ. The apelin and diabetes+apelin groups received 50 µg/kg apelin-13 intraperitoneally for seven days. ABRs were recorded for all animals under anesthesia. Wave latencies I, II, III, IV, and V were recorded bilaterally at 16, 24, and 32 kHz at 80 dB nHL. Descriptive statistical analyses and Mann-Whitney U tests were used to compare wave latencies between ears and groups, with significance set at $p < 0.05$.

RESULTS: The mean and standard deviation values for wave latencies I, II, III, IV, and V at 16, 24, and 32 kHz at 80 dB nHL were calculated for both ears. No significant differences were observed between groups at any frequency ($p > 0.05$). Within-group ear comparisons showed no significant differences in wave latencies at 16 and 32 kHz, but significant differences at 24 kHz for wave latencies II, III, IV, and V ($p = 0.002$, $p = 0.001$, $p = 0.008$, $p = 0.047$).

CONCLUSIONS: The study concluded that diabetes and apelin do not cause changes in high-intensity ABRs, and normative data were obtained for auditory system evaluation using diagnostic ABRs at 80 dB nHL. It is recommended that studies evaluating the effects of diabetes on the auditory system should not use diagnostic ABR recordings at 80 dB nHL but rather evaluate the effects at hearing threshold levels.

Keywords: Auditory brainstem responses, Diabetes, Animal model

PC-38

Ramelteon Reduces Oxidative Damage in Diabetic Mice

Tuba Keskin & Suat Tekin

İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Diabetes is characterized in literature as a disease that arises from insufficient insulin secretion, deficiency, or disruptions in its metabolism. Research indicates inadequate sleep can hinder insulin secretion and elevate glucose levels, leading to oxidative damage in body. Ramelteon used to treat insomnia, is known to enhance neuronal activity. While various studies suggest that Ramelteon possesses anti-inflammatory properties, its impact on diabetes and oxidative-damage associated with it remains unexplored. This study aims to clarify the effect of Ramelteon administration on oxidative-damage induced by diabetes.

METHODS: In the study, male Balb-C mice (ethical approval 2024/8-1) were randomly divided into four groups ($n = 10$): control, diabetes, diabetes+Ramelteon (3-6 mg/kg). Streptozotocin (150 mg/kg) was administered intraperitoneally (ip) to all groups except the control group, which remained normoglycemic. Mice with blood glucose levels exceeding 250mg/dL after 72-hours were considered diabetic. No injections were given to control group. Twenty-one days after the onset of diabetes, respectively, saline, 3 and 6mg/kg/day of ip Ramelteon were administered to the diabetic groups for 15-days. Finish of the experiment, animals were decapitated, and their pancreatic tissues were harvested. Levels of MDA and GSH, SOD and CAT enzymes, were measured in the pancreatic tissues. Data were analyzed using Kruskal-Wallis H test, with multiple comparisons performed using Mann-Whitney U test with Bonferroni correction; $p < 0.05$ was considered statistically significant.

RESULTS: In diabetic mice, prolonged hyperglycemia led to a significant increase in MDA levels in pancreatic tissues, which was notably reduced by Ramelteon administration ($p < 0.05$). The activities of SOD and CAT enzymes, along with GSH levels, were significantly decreased in the diabetic groups ($p < 0.05$). However, in the Ramelteon-treated groups, the diminished GSH levels and the activities of SOD and CAT enzymes were significantly elevated ($p < 0.05$).

CONCLUSIONS: Study results show Ramelteon may have an antioxidant effect by reducing diabetes and inflammation-oxidative damage caused by diabetes.

This study was supported by TUBITAK 1002-A (323S449) and 2211-A National PhD Scholarship Program.

Key Words: Ramelteon, Diabetes, Oxidative Damage, Melatonin.

PC-39

Inhibition of Transient Receptor Potential Ankyrin 1 Channels Reduces Renal Ischemia Reperfusion Injury

Semanur Fırat¹, Murat Çakır¹, Burak Bircan², Ali Aydın³, Güldeniz Şekerci⁴, Samet Öz⁵

¹Yozgat Bozok University, Faculty of Medicine, Department of Physiology, Yozgat, Türkiye

²Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Medical Services and Techniques, Osmaniye, Türkiye; ³Yozgat Bozok University, Faculty of Medicine, Department of Medical Biology, Yozgat, Türkiye

⁴Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

⁵Osmaniye Korkut Ata University, Vocational School of Health Services, Department of Veterinary Medicine, Osmaniye, Türkiye

AIM: Transient receptor potential ankyrin 1 (TRPA1), a calcium-permeable non-selective cation channel, has been shown to play a role in modulating inflammation after tissue injury and TRPA1 expression is altered in renal tissue after ischemia reperfusion (IR). In this study, we investigated the effects of TRPA1 agonist ASP7663 and TRPA1 antagonist HC-030031 on renal IR injury.

METHODS: A total of 40 male Sprague Dawley rats were divided into 4 groups (Control, IR, IR+ASP7663, IR+HC-030031). No surgical procedure was performed on the animals in the control group. Both kidneys of rats subjected to IR were subjected to 45 minutes ischemia followed by 24 hours reperfusion. One of the two IR groups received 3 mg/kg dose of ASP7663 and the other received 30 mg/kg dose of HC-030031. At the end of the experiment, urea and creatine (Cre) were measured from the serum of the animals. Toll-like receptor-4 (TLR4), phosphorylated nuclear factor-kappa B (p-NF-κB), phosphorylated IκB-α, tumor necrosis factor alpha (TNF-α), interleukin 1 beta (IL-1β), caspase-3 levels were measured immunohistochemically in the kidney tissue. Histopathologic examinations were also performed in the kidney.

RESULTS: Serum urea, creatinine levels and renal tissue TLR-4, p-NF-κB, phosphorylated IκB-α, TNF-α, IL-1β, caspase-3 levels were significantly increased in the IR group compared to the control group (p<0,05). Histopathologic examinations showed increased damage in the IR group compared to the control group (p<0,05). Renal tissue TLR-4, p-NF-κB, phosphorylated IκB-α, TNF-α, IL-1β, caspase-3 levels, histopathologic damage and serum urea, creatine levels were significantly decreased in the group treated with TRPA1 antagonist HC-030031 compared to the IR group (p<0,05).

CONCLUSIONS: In this study, we found that TRPA1 antagonist HC-030031 showed protective properties by reducing inflammation and apoptosis in renal IR injury. This study was supported by Yozgat Bozok University BAP unit (project no: TÇD-2023-1097).

Keywords: Ischemia-reperfusion, Kidney, TRPA1 channels, ASP7663, HC-030031.

PC-40

Evaluation of the Effect of Allium Tuncelianum (Tunceli Mountain Garlic) Plant Extract on Behavioral, Antioxidant and Metabolomic Parameters in Rats

Nigar Abbak¹, Emirhan Nemutlu², Tuba Reçber², Asli Şan Dağlı Gül¹, Hurrem Turan Akkoyun³, Mahire Bayramoğlu Akkoyun⁴, Gülderen Yılmaz⁵, Suat Ekin⁶, Ahmet Bakır⁶, Okan Arıhan¹

¹Hacettepe University, Faculty of Medicine, Physiology Department, Ankara, Türkiye; ²Hacettepe University, Faculty of Pharmacy, Department of Analytical Chemistry, Ankara, Türkiye

³Siirt University, Faculty of Veterinary, Department of Physiology, Siirt, Türkiye; ⁴Siirt University, Faculty of Veterinary, Department of Biochemistry, Siirt, Türkiye; ⁵Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Ankara, Türkiye

⁶Van Yuzuncu Yil University, Faculty of Science, Department of Biochemistry, Türkiye

AIM: Allium species are important plants in terms of nutrition and bioactivity. The aim of the study was to evaluate the effect of *Allium tuncelianum* (AT) (Kollmann) Özhatay, B. Mathew & Şiraneci ethanol extract on behavioral, antioxidant and metabolomic parameters in rats.

METHODS: A total of 24 Wistar albino male rats were divided into 4 different groups (n=6). The groups were determined as C, AT100, AT400 and diazepam. Ethanol extract was applied to AT groups at doses of 100 and 400 mg/kg, and distilled water was administered to the control. All administrations were performed orally for 10 days. Elevated plus maze, rotarod and hotplate tests were performed. Oxidative stress parameters were examined in brain, liver and kidney tissues. Untargeted metabolomic analyses were performed in plasma samples.

RESULTS: In liver tissue, diazepam group had significantly lower CAT and GSH-Px levels compared to control group; also, CAT activity was significantly lower compared to AT400 group (p<0.05). In kidney tissue, diazepam group had significantly lower CAT enzyme activity compared to control group and AT400 group (p<0.05). In brain tissue, diazepam group had significantly lower GSH-Px enzyme activity compared to control group (p<0.05). According to GC-MS and LC-qTOF-MS metabolite analysis results, fumaric acid, malic acid, vanillic acid, quercetin-3-arabinoside, hydrocinnamic acid and gallic acid were determined in the extract. When AT100 and control groups were compared, significant differences were detected in trehalose degradation, phosphatidylinositol phosphate metabolism and spermidine biosynthesis. No significant difference was observed in behavioral tests.

CONCLUSIONS: The present results indicate that AT extract did not cause oxidative stress or bring about significant changes in behavioral parameters. However, it caused significant differences in plasma metabolites and pathways.

Keywords: Allium, antioxidant, Anxiety-like behavior, Hot plate, Metabolomics, Rotarod

PC-41

Effects of Chronic Cold Stress and Oxytocin on Anxiety-Like Behavior and Antioxidant System

Soner Bitiktaş, İsa Yesilyurt, Serpil Can

Kafkas University, Faculty of Medicine, Department of Physiology, Kars, Türkiye

AIM: The stress response is an essential survival strategy for adjusting to changing conditions. One model used to examine stress and its effects is exposure to cold environments. Oxytocin, which stimulates uterine contraction during labor and milk ejection during lactation, also participates in the control of anxiety, pain and stress responses by directly affecting neurons. Anxiety-like behaviors and locomotor activity in rodents are commonly assessed using open field tests. This study aimed to investigate the effects of chronic cold stress exposure and exogenous oxytocin administration on anxiety-like behaviors, locomotor activities and antioxidant systems.

METHODS: Control (CNT), oxytocin (OT), chronic cold stress (CS), and chronic cold stress + oxytocin (CSO) groups (n=5 for each) comprised 20 male Wistar Albino rats weighing 250–350 g. Rats in CS and CSO groups were placed in cold environment (4 °C) for 2 hours per day for 21 days. Beginning on day 17, rats in the OT and CSO groups administered intranasal oxytocin (1 µg/µl; 2x10 µl) once daily for 5 days. A 5-minute open field test was performed on day 22. Rats were sacrificed after the experiments. Plasma SOD and GSH levels were measured.

RESULTS: OT group's distance moved ($p<0.01$) and average speed ($p<0.02$) were higher than CNT group's in the open field test. OT group spent more time in the center than other groups, but the difference was not statistically significant. No significant difference between the groups was found when examining the number of defecations. There was no statistically significant difference in the levels of SOD and GSH between the groups in the ELISA assays.

CONCLUSIONS: Our findings showed that anxiety-like behaviors, locomotor activities and antioxidant systems in rats exposed to chronic stress were not different from controls. This suggests that, unlike acute stress, chronic exposure to cold provides homeostasis by strengthening the organism's stress coping mechanisms.

Keywords: Cold stress, Oxytocin, Anxiety, Antioxidant

PC-42

Measuring the Electrodermal Activity Level in University Students Using the Beck Anxiety Test

Ahmet Ergun, Berkay Öz, Büşra Fadime Aksoy

Baskent University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Electrodermal activity (EDA), originating from sweat glands and adjacent epidermal and dermal layers, indicates sympathetic activity and can be recorded from the skin surface using electrodes. Stress from various stimuli increases sympathetic activity, causing anxiety symptoms. Increased eccrine sweat gland activity due to sympathetic stimulation can be observed by measuring EDA levels. EDA measurements were conducted with the Biopack system on students aged 17-25 took the Beck Anxiety Scale. This study aims to examine EDA test results by gender and through questions stimulating cognitive activity during measurements at certain moments.

METHODS: The study sample included 69 participants (40 females and 28 male) agreed to participate the research from Başkent University Faculty of Medicine. Participants completed a demographic information form and the Beck Anxiety Scale, with scores categorized as mild (5-9 points), moderate (10-14 points), and severe (15+ points). Electrodes were attached to the index and middle fingers of the using the Biopack MP36R device. A pulse oximeter device was connected to the and pulse and oxygen saturation (SpO₂) changes were recorded. During the measurements, the participants were asked three questions from a sample of questions prepared by the researchers at 90th, 120th and 150th seconds and the participants were asked to answer yes or no to these three questions only with eye movements.

RESULTS: The average age of participants was $20.4 \pm SD1.9$ years. An increase in EDA frequency from 0.02 to 0.06 Hz ($p<0.001$) was observed. There was no significant difference between genders or between participants with moderate and severe anxiety levels.

CONCLUSIONS: According to the findings in gender-differentiated students obtained with the EDA circuit, it was determined that the EDA frequency measured after asking questions was higher than the basal frequency. In the study, an increase in sympathetic activity was demonstrated through EDA measurement in participants with stimulation of cognitive activity.

Keywords: Electrodermal activity, Beck anxiety test, Sympathetic arousal, Pulse

PC-43

Poster was not presented at the meeting.

PC-44

**Effect of Spexin on Cell Viability in a Diabetic Neuropathy Model:
An *in vitro* Study**

Mehmet Refik Bahar¹, Seval Ülkü Orhan², Mete Özcan², Suat Tekin³

¹Osmaniye Korkut Ata University, Faculty of Health Sciences, Osmaniye, Türkiye

²Firat University, Faculty of Medicine, Department of Biophysics, Elazig, Türkiye

³Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Diabetic neuropathy (DN), which targets sensory, autonomic, and motor neurons of the peripheral nervous system, is one of the most common chronic complications of diabetes. Nociceptors sense pain stimuli in the DN, and the cell bodies of nociceptors are located in the dorsal root ganglion (DRG). Spexin (SPX) is a peptide hormone involved in many metabolic processes, such as nociception, nutrition, and reproduction. However, it shows activity in the brainstem, trigeminal ganglia, and cerebral cortex, which are known to be closely related to nociceptive transmission. The effects of SPX, which has been emphasized as having antinociceptive activity in previous studies, on cell viability in diabetic DRG neurons are unknown. The aim of this study was to investigate the efficacy of SPX in an *in vitro* model of DN.

METHODS: DRG neurons used in the study were isolated from 2-3-day-old Wistar Albino rats by enzymatic and mechanical procedures. An *in vitro* model of DN was established using DRG neurons exposed to high glucose (45 mmol/L) for 24 hours. SPX was administered to DRG neurons at various doses (0.1, 1, 10, 100, and 1000 ng/ml) with high glucose for 24 hours to see how it affected the viability of cells. The MTT assay was used to determine cell viability. Cell viability (EC50) was calculated using Graphpad Prism 8 software. In comparisons between groups, the IBM SPSS-24 package program was used, and a $p < 0.05$ value was considered statistically significant.

RESULTS: It was determined that 1, 10, 100 and 1000 ng/ml concentrations of SPX administered together with high glucose significantly increased the cell viability of DRG neurons ($p < 0.05$).

CONCLUSIONS: As a result of this study, SPX was found to increase cell viability in DRG neurons. SPX may show potential as a new therapeutic target in DN. This study was supported by the TUBITAK with project number 124S122.

Keywords: Spexin, Diabetic Neuropathy, Dorsal Root Ganglia

PC-45

The Neuroinflammatory and Neuroprotective Roles of Apelin-13 in D-Glutamic Acid-induced Excitotoxicity in SH-SY5Y Cell Line

Kadriye Yağmur Oruç¹, Gökhan Ağtürk³, Aykut Oruç², Karolin Yanar⁴, Hakkı Oktay Seymen²

¹Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Physiology, İstanbul, İstinye University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

²Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

³Haliç University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

⁴Istanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, Department of Biochemistry, İstanbul, Türkiye

AIM: Excitotoxicity, resulting from the excessive accumulation of glutamate in the extracellular space, leads to neuronal cell death. This study investigates the protective effects of Apelin-13 on D-glutamic acid-induced excitotoxicity in SH-SY5Y human neuroblastoma cells, an *in vitro* model for neurodegenerative diseases. Unlike the commonly studied L-glutamic acid, this research focuses on understanding the specific impacts of D-glutamic acid.

METHODS: SH-SY5Y cells were treated with varying concentrations of D-glutamic acid and Apelin-13, followed by cell viability tests (MTT) and imaging at 12th and 24th hours. DT, KYN, T-SH, AOPP, and AGE were analyzed using biochemical methods. IL-10, IL-1 β , TNF- α , TGF- β 1 and BDNF were determined using ELISA. GraphPad-Prism was used for statistical analysis. Data normality assessed with Shapiro-Wilk test and homogeneity with Levene-test. One-way-ANOVA and post-hoc Tukey tests were used comparisons. Kruskal-Wallis and post-hoc-Dunn tests were used for non-normal data. $P < 0.05$ was considered statistically significant.

RESULTS: MTT analyses revealed that D-glutamic acid exhibited significant cytotoxic effects at doses of 10 mM and 20 mM, reducing cell viability by over 50%. However, Apelin-13 treatment, especially at 2 μ g/mL, mitigated these effects, increased cell viability, and reduced inflammatory cytokine levels (IL-1 β , TNF- α). Additionally, Apelin-13 increased the levels of anti-inflammatory cytokines (IL-10, TGF- β 1) and brain-derived neurotrophic factor (BDNF), demonstrating its neuroprotective role. The oxidative stress markers significantly elevated by D-glutamic acid were effectively reduced by Apelin-13.

CONCLUSIONS: The neuroprotective effects of Apelin-13 are associated with the regulation of cAMP/PKA and MAPK signaling pathways, increased BDNF synthesis, and the reduction of oxidative stress and inflammatory responses. This study is the first to demonstrate the effects of D-glutamic acid on SH-SY5Y cells. It highlights the potential of Apelin-13 as a therapeutic agent against excitotoxicity-induced neuronal damage and emphasizes its ability to modulate critical molecular pathways involved in inflammation and oxidative stress. Further *in vivo* studies are needed to explore the long-term neuroprotective effects of Apelin-13 in the treatment of neurodegenerative diseases. This study was supported by Istanbul University-Cerrahpaşa Scientific Research Projects Unit (Project-Number: TSA-2023-37359).

Keywords: Apelin-13, Excitotoxicity, D-Glutamic Acid, Neuroinflammation, SH-SY5Y cell line

PC-46

Effects of Zinc Deficiency and Supplementation on Molecular Functions in Hippocampus Tissue in a Rat Experimental Multiple Sclerosis (MS) Model

Adem Atacak¹, Elif Gülbahçe Mutlu², Gözde Acar¹, Saltuk Buğra Baltacı³, Rasim Mogulkoc¹, Abdulkerim Kasim Baltacı¹

¹Selcuk University, Medical Faculty, Department of Physiology, Konya, Türkiye

²KTO Karatay University, Medical Faculty, Department of Medical Biology, Konya, Türkiye

³Medipol University Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: The aim of this study was to investigate how dietary zinc status affects hippocampal ZnT3, NOGO-A, IL-6 and SESN2 gene expression levels and hippocampal MDA and GSH levels in a rat experimental MS model.

METHODS: The study was conducted on 46 adult male Wistar rats and was approved by the local ethics committee. The animals used in the study were divided into 5 groups (G) (Control 6, other groups 10). G1, Control. G2, Sham-MS: Carboxy-methyl-cellulose (CMC) solution in which Cuprizone was dissolved was administered to the rats via gavage daily for 8 weeks. In order to create MS, animals in G3, 4 and 5 were administered cuprizone in CMC solution via gavage daily for 8 weeks at a rate of 1% of their feed intake. G4 was fed a zinc deficient diet (50 µg/kg zinc). G5 was given zinc sulfate (5 mg/kg/day) intraperitoneally (ip). At the end of the applications, ZnT3, NOGO-A, IL-6 and SESN2 gene expressions were determined by Real-Time-PCR method and MDA and GSH levels were determined by ELISA method in hippocampus tissue samples of sacrificed animals.

RESULTS: The highest MDA and lowest GSH levels and the lowest ZnT3 and highest NOGO-A gene expression were obtained in Groups 3 and 4 ($p<0.05$). Zinc supplementation significantly decreased MDA and NOGO-A gene expression values in Group 5 ($p<0.05$) and significantly increased GSH and ZnT3 gene expression values ($p<0.05$). The highest IL-6 and SESN2 gene expression values were obtained in G3 and G4 ($p<0.05$). Zinc supplementation significantly decreased IL-6 and SESN2 gene expression values in Group 5 ($p<0.05$).

CONCLUSIONS: The results of the current study show that dietary zinc status significantly affects some molecular parameters in the hippocampus tissue in a rat experimental MS model. Zinc supplementation may be effective in preventing pathological processes occurring in hippocampal tissue in an experimental MS model.

Keywords: Multiple sklerosis, Cuprizone, zinc hippocampus, oxidative stress.

PC-47

Investigation of the Effects of Dapagliflozin in an Experimental Cerebral Ischemia-Reperfusion Model in Rats

Asiye Beytur, Engin Korkmaz, Kevser Tanbek, Suat Tekin

İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Stroke is among the most common neurological disorders worldwide and is a leading cause of mortality and disability. The aim of this study is to investigate the effects of the SGLT2 inhibitor Dapagliflozin (Dapa) in the middle cerebral artery occlusion (MCAO) model in rats.

METHODS: *Sprague Dawley* male rats (weighing 280-320 grams) were divided into four groups ($n=10$): Sham, cerebral ischemia (CI), CI+Dapa1mg/kg and CI+Dapa10mg/kg. For 7 days prior to the surgical procedure, sham and CI groups received oral saline, while CI+Dapa1mg/kg and CI+Dapa10mg/kg groups received two different doses of Dapa (1 and 10 mg/kg) by oral gavage. Rats were trained for 3 days before the surgical procedure to perform motor/sensorimotor tests (rotarod, sticky tape removal and grip strength test). Subsequently, the sham group underwent a sham operation and CI, CI+Dapa1mg/kg and CI+Dapa10mg/kg groups underwent a 60-minute MCAO procedure. During the 72-hour reperfusion period, all groups were assessed for neurological deficits and motor/sensorimotor performance. Following this, the animals were euthanized and the infarct area in the brain was determined using the triphenyltetrazolium chloride (TTC) staining method. BDNF and TrkB protein levels were assessed using western blotting.

RESULTS: Comparisons between groups indicated that Dapa facilitated the recovery of motor and sensorimotor deficits caused by CI ($p<0.05$). Dapa treatment resulted in a reduction in the infarct area compared to the CI group ($p<0.05$). Additionally, it was determined that Dapa activated the BDNF/TrkB signaling pathway ($p<0.05$).

CONCLUSIONS: This study demonstrates that Dapa administration reduces neuronal damage caused by ischemic stroke.

Acknowledgements: This study was supported by Inonu University Scientific Research Projects Unit (Project no: TDK-2024-3557).

Keywords: Cerebral ischemia, Dapagliflozin, Neuroprotection

PC-48

Erythropoietin Exerted an Anxiolytic Effect by Regulating Monoaminergic Neurotransmitters and Brain-Derived Growth Factor in Young and Aged Rats

Hasan Çalışkan¹, Ekin Çelik², Seda Koçak³, Erhan Nalçacı⁴

¹Balikesir University, Faculty of Medicine, Department of Physiology, Balikesir, Türkiye

²Kırşehir Ahi Evran University, Faculty of Medicine, Department of Medical Biology, Kırşehir, Türkiye

³Kırşehir Ahi Evran University, Faculty of Medicine, Department of Physiology, Kırşehir, Türkiye

⁴Ankara University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Erythropoietin (EPO) is a hormone that has hematopoiesis and cell protective effects. The present study aimed to investigate the effects of Darbepoetin alfa on anxiety-like behaviors, locomotor activity, and brain neurotransmitter-neurotrophic factor mRNA levels in young and aged rats.

METHODS: Adult 32 male Wistar Albino rats were used. They were divided into 4 groups young adult control (12-week-old, n=8), EPO-treated young adult (12-week-old, n=8), aged control (2-year-old, n=8), and EPO-treated aged (2-year-old, n=8). Darbepoetin alfa (EPO-derivation) 2 microgram/kg was administered intraperitoneally once a week for four weeks. Behaviors were analyzed in open field test and elevated plus maze test. Serotonin, noradrenaline, dopamine, and brain-derived neurotrophic factor (BDNF) mRNA levels in the prefrontal cortex and striatum were analyzed by RT-PCR. Anova and Tukey tests were performed as statistical tests.

RESULTS: Anxiety-like behaviors (freezing-grooming time, stretched-attend posture, anxiety index) were significantly decreased in aged rats receiving EPO treatment ($p < 0.05$). While there was no difference between EPO-treated young adults and young controls in terms of freezing and itching duration, stress-induced tense posture and anxiety index decreased in EPO-treated young adults ($p < 0.05$).

Time spent in the open field and time spent in the open arm increased in the groups receiving EPO ($p < 0.05$). It was observed that locomotor activity was impaired in old rats, and this was improved by EPO treatment ($p < 0.05$). Serotonin, dopamine, noradrenaline, and BDNF mRNA levels were significantly increased in both the prefrontal cortex and striatum in young and aged subjects after EPO treatment ($p < 0.05$).

CONCLUSIONS: Darbepoetin alfa, a derivative of erythropoietin, was found to reduce anxiety-like behaviors in young and aged subjects by regulating brain neurotransmitters and BDNF. Locomotor activity in the vertical and horizontal direction, which deteriorates with age, was also significantly improved. Although 2 mcg of darbepoetin alfa showed positive effects on the central nervous system in elderly subjects, more studies are needed to examine its long-term effects.

Keywords: Anxiety-like behaviors, BDNF, Erythropoietin, Monoaminergic neurotransmitters, Aged rats

PC-49

Analysis of Dopamine Signalling in the Nucleus Accumbens of Opioid Dependent Rats Using Biosensors and Fibre Photometry

Yasin Ali Çimen¹, Aysu Şen², Raviye Özen Koca², Canan Eroğlu Güneş³, İsmihan İlknur Uysal⁴, Mehmet AK^{5,7}, Ömer Faruk Akça^{6,7}, Ercan Kurar^{3,7}, Selim Kutlu^{2,7}

¹Bezmizlem Vakıf University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

²Necmettin Erbakan University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

³ Necmettin Erbakan University, Faculty of Medicine, Department of Medical Biology, Konya, Türkiye

⁴Necmettin Erbakan University, Faculty of Medicine, Department of Anatomy, Konya, Türkiye

⁵Necmettin Erbakan University, Faculty of Medicine, Department of Psychiatry, Konya, Türkiye

⁶Necmettin Erbakan University, Faculty of Medicine, Department of Child and Adolescent Psychiatry, Konya, Türkiye

⁷Necmettin Erbakan University, Neuroscience Research Center, Konya, Türkiye

AIM: G protein coupled receptor activation-based (GRAB) biosensors are a novel method in experimental neuroscience research. Overactivation of dopamine, a major neurotransmitter in the central nervous system, in the nucleus accumbens (NAC) plays an important role in the physiopathology of main addiction mechanisms. In this study, we aimed to record dopaminergic activity in the NAC using GRABDA sensors and fibre photometry system in rats with experimental opioid addiction and to provide methodological standardisation.

METHODS: Two groups of adult Wistar rats were used in this study. GRABDA sensors were microinjected stereotactically into the left NAC region of anaesthetised animals and fibre photometric ferules were placed in the same area. After the 15th day, physiological saline was subcutaneously injected into the control group and morphine at a dose of 10 mg/kg was subcutaneously injected into the addiction group for 5 days. Dopaminergic signal activity from GRABDA biosensors was recorded using a fibre photometer system. The effect of opioid antagonist naloxone on basal dopamine signal activations was also determined. One-way analysis of variance was used for statistical evaluation of the findings.

RESULTS: Basal dopaminergic activity level was significantly higher in the morphine dependence group compared to the control period ($p < 0.001$). Naloxone administration significantly decreased the signalling activity compared to the morphine dependence groups ($p < 0.01$).

CONCLUSIONS: At the end of this study, the analysis of dopaminergic activity in the central nervous system was performed using a fibre photometer system and GRABDA biosensors. The significantly higher detection of dopaminergic activity in NAC in opioid dependence, which was chosen as a model, shows that the method can be standardised in terms of the efficiency of the biosensor and recording system, stereotaxic localisation of the site of application, dosology, suitability of the fibre.

Keywords: Biosensor, Dopamine, Fibre photometry, Nucleus accumbens, Opioid addiction, Rat

PC-50

Memory Performance in Female Rat Offspring Born to Mothers Fed a Zinc-Deficient Diet is Associated with Dietary Zinc Status

Buse Günaydin Türker¹, Omer Unal², Saltuk Bugra Baltaci³, Nilufer Akgun Unal⁴, Rasim Mogulkoc⁵, Abdulkirim Kasim Baltaci⁵

¹Erciyes University, Faculty of Medicine, Department of Physiology, Kayseri, Türkiye

²Kirikkale University, Faculty of Medicine, Department of Physiology, Kirikkale, Türkiye

³Istanbul Medipol University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

⁴Ondokuz Mayıs University, Faculty of Medicine, Department of Biophysics, Samsun, Türkiye

⁵Selcuk University, Faculty of Medicine, Konya, Türkiye

AIM: The aim of this study was to investigate the possible effects of maternal zinc deficiency and dietary zinc status on cognitive performance in offspring female rats born to mothers fed a zinc-deficient diet.

METHODS: The study was conducted on 40 female Wistar rats and was approved by the local animal ethics committee. The first three groups in the study were obtained from mothers fed a zinc-deficient diet during pregnancy and until they were separated from their offspring. Group 1 was fed a zinc-deficient diet (2.8 mg/kg zinc). Groups 2 and 4 were fed standard rat chow. The animals in Group 3 were provided with zinc supplementation (5 mg/kg/day intraperitoneal zinc sulfate). Group 4 was used as the control group. Memory performance in the study was evaluated with the Morris water maze test.

RESULTS: At the beginning of the study, no significant difference was observed between the groups in terms of memory performance in the platform finding training for the purpose of accustoming the animals to the tests. In the intragroup comparisons of the tests performed from the 1st day to the 4th day for training purposes, it was determined that the animals showed better memory performance on the other days compared to the first day as the tests were repeated ($p < 0.05$). In the measurements made at the end of the applications; the memory performance impairments in the parameters of "time until the target quadrant is first reached, time until the platform is first reached, total swimming distance and swimming speed" in the rats fed with a zinc deficient diet (G1) were prevented with zinc supplementation ($p < 0.05$).

CONCLUSIONS: The present study has shown that the impaired memory performance in female rats fed a zinc-deficient diet after maternal zinc deficiency was induced can be corrected with zinc supplementation.

Keywords: Maternal zinc deficiency, Memory performance, Zinc deficient diet

PC-51

Can the Right Brain Hemisphere's Rapid Sensory Processing Capability Speed up the Reaction Time of the Left Hand?

Işinsu Karaoğlu¹, Lamia Pınar²

¹Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

²Okan University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Based on the knowledge that different types of auditory stimuli are integrated with different brain hemispheres in cerebral lateralization, in our study we aimed to investigate the effect of the known superiority of the right hemisphere in the process of processing non-verbal sounds on reaction time. For this purpose, we tested the right and left hand reaction times against a non-verbal auditory stimulus in sympathetic activation generated through exercise in sedentary young people.

METHODS: Thirty right-handed volunteer students participated in this study, which received ethics committee approval. Participants' blood pressure and heart rate were measured before and after exercise, and a treadmill exercise was performed in the form of doubling the resting heart rate and continuing the exercise for 5 minutes in this way. The finger tapping test against a non-verbal sound stimulus was tested separately for each hand before and after exercise. The sound stimulus was applied in 2 different ways, at fixed and random intervals. The data were analyzed using the paired t-test for time-dependent comparisons, as they have a normal distribution.

RESULTS: In both stimulus types, right and left hand reaction speeds increased significantly after exercise compared to before exercise. In the sound stimulus given at fixed intervals; although the right hand reaction speed was higher than the left hand; the difference between the two hands was not significant before and after exercise. In the sound stimulus given at random intervals, the left hand reaction speed was found to be faster than the right both before and after the exercise ($p < 0.01$).

CONCLUSIONS : Although the left hemisphere is more competent than the right hemisphere for motor control, in this study, it was evaluated that the speed of the right hemisphere in sensory processing and its increased activation with excessive attention applied to the left hand accelerated the left hand reaction time.

Keywords: Exercise, Cerebral Lateralization, Right Brain, Attention, Auditory Reaction Time

PC-52

Transgenerational Effect of Nicotine Consumption on the TCF7L2 Signalling Pathway and Glucose Metabolism

Ibrahim Halil Citci¹, Ramazan Can Gökmen², Ayşe Çekin¹, Ege Sevinç Yeşil³, Ersin O. Koylu², Lütüye Kanit², Oğuz Gözen², Buket Kosova¹

¹Ege University, School of Medicine, Department of Medical Biology, Izmir, Türkiye

²Ege University, School of Medicine, Department of Physiology, Izmir, Türkiye; ³Ege University, School of Medicine, Department of Medical Biology, Izmir, Türkiye; Istanbul Health and Technology University, School of Medicine, Department of Medical Biology, Istanbul, Türkiye

AIM: The role of the TCF7L2 signaling pathway in glucose metabolism is known for the pancreas, its precise function in different brain regions remains largely unknown. Therefore, the aim of this study was to elucidate the transgenerational effect of nicotine consumption on the TCF7L2 pathway and glucose metabolism.

METHODS: Selectively bred high nicotine preferring rats (F30), and naive controls were divided into four groups (n=10/group, all male). The nicotine consumption was measured using a two-bottle-free-choice-paradigm, containing tap water with or without nicotine. Nicotine was administered at 10 mg/L for the first two weeks and increase to the 20 mg/L for the next four weeks. Food was removed 12 hours before animals were as decapitated, and the mRNA expression levels of Tcf7l2, Bdnf, Gsk3 β , Glp1-r, and Chrna7 genes in the NAc, VTA, mHb, and pancreas were analyzed using qRT-PCR. Fasting blood glucose levels were determined using strips, while insulin and glucagon levels were measured via ELISA.

RESULTS: Nicotine consumption resulted in a decrease of Tcf7l2, Glp1-r and Bdnf; and an increase of Gsk3 β and Chrna7 gene expressions in the NAc, VTA and mHb brain regions. Nevertheless, although no difference could be detected for Gsk3 β ; Tcf7l2 and Glp1-r gene expression levels showed an increase in the pancreas (all, p<0.05). Nicotine consumption also resulted in elevated fasting blood glucose and insulin levels (p<0.05); and, reduction in circulating glucagon levels.

CONCLUSIONS: Nicotine decreases Tcf7l2, Glp1-r, and Bdnf while increasing Gsk3 β and Chrna7 gene expression in the NAc, VTA, and mHb brain regions. Concurrently, it increases Tcf7l2 and Glp1-r, and decreases Gsk3 β in the pancreas. These changes elevate fasting blood glucose and insulin levels, highlighting nicotine's potential role in disrupting glucose metabolism. This work was supported by Ege University Scientific Research Projects Coordination (TS-DKT-2023-2852-to-B.K.) and approved by Ege University Animal Experiments Ethics Committee (EUHADYEK-2022-072R1).

Keywords: Nicotine, Nicotine Prefer Rat Lines (NP), Glucose Metabolism, TCF7L2, Brain, Pancreas.

PC-53

Evaluation of Pathophysiological Processes in Neuronal Cells in an Experimental Cerebral Ischemia Reperfusion Injury Model

Kevser Tanbek, Suleyman Sandal

Inonu University, Faculty of Medicine, Department of Physiology Malatya, Türkiye

AIM: Ischemia-reperfusion (IR) is a comprehensive pathophysiological process in all tissues, many of whose molecular steps have not been adequately elucidated. This study aimed to determine new targets for the treatment of cerebral IR by comparing different ischemia and IR processes.

METHODS: In the study, 50 Sprague-Dawley rats were divided into Sham, SI(60), SI(90), SI(60)+R, SI(90)+R groups. Different ischemia groups were created as 60 and 90 min focal SI (except Sham group) and 24-hour reperfusion processes. At the end of the IR processes, the infarct area was determined with triphenyltetrazolium chloride (TTC). Mitophagy, autophagy, apoptosis, inflammation and oxidative stress markers from brain tissues were determined in ischemic and ipsilateral lobes by Western Blot and ELISA method.

RESULTS: There was no significant change in the ischemic area in the SI groups compared to the Sham group. The increase in the ischemic areas of the SI/R groups is statistically significant (p<0.05). When the SI and SI/R groups are compared, the increase in oxidative stress, mitophagy and autophagy markers during the reperfusion process is statistically significant (p<0.05). When the 60 and 90-minute SI and SI/R groups are compared, the increase in apoptosis and inflammation markers in the long-term ischemia groups is statistically significant (p<0.05).

CONCLUSIONS: Our study findings indicate that the reperfusion process in SI/R injury triggers oxidative stress, mitophagy and autophagy pathways. The increase in the SI process causes an increase in apoptosis and inflammation. Therefore, the use of protective agents before the reperfusion process in SI treatment may affect the treatment results and processes. This research was supported by Inonu University Scientific Research Projects Unit with project number TOA-2024-3716.

Keywords: Cerebral ischemia, Reperfusion, Mitophagy, Autophagy, Apoptosis, Inflammation

PC-54

Gallic Acid Protects SH-SY5Y Cells Against MPP+-Induced Neurotoxicity by Reducing Apoptosis

Hasan Ulusal¹, Hatice Kübra Yiğit Dumrul², Sibel Dağlı³

¹Gaziantep University, Graduate School of Health Sciences, Department of Medical Biochemistry, Gaziantep, Türkiye

²Gaziantep University, Faculty of Medicine, Department of Physiology, Gaziantep, Türkiye

³Hatay Mustafa Kemal University, Faculty of Medicine, Department of Medical Microbiology, Antakya, Türkiye

AIM: Gallic acid (GA), a type of phenolic acid, has been associated with a wide range of neurological disorders. The aim of this study was to investigate the protective effect of GA against 1-methyl-4-phenylpyridinium (MPP+)-induced toxicity in human neuroblastoma SH-SY5Y cells, which are widely used in molecular studies related to Parkinson's disease.

METHODS: In this study, human neuroblastoma cell line SH-SY5Y cells were used to investigate the protective effect of GA. SH-SY5Y cells were treated with predetermined concentrations of GA (100, 50, 25 µM) and MPP+ at 2mM and 1mM concentrations, followed by incubation for 24 and 48 hours. At the end of 24 and 48 hours of incubation, CCK-8 viability test was performed. To examine the effects on apoptosis in the cell, the protective effect of 100, 50, 25 µM GA against 1mM MPP+ exposure was measured using the Annexin-V apoptosis test with flow cytometry.

RESULTS: CCK-8 results show that GA prevents MPP+-induced cell death in a concentration-dependent manner. In cells treated with 1mM MPP+, it was found that 25µM GA application increased cell viability by 34.7% and 55% at 24 and 48h incubations, respectively. In SH-SY5Y cells, 1mM MPP+ was used for apoptosis test since 2 mM MPP+ killed nearly 80% of the cells. According to apoptosis results, 25 µM GA was found to be the most protective against MPP+-induced apoptosis. While the live cell rate was 11.1% and 8.4% for 24h and 48h in MPP+ application, the live cell rate was found to be 14.8% and 13.4%, respectively.

CONCLUSIONS: Our results showed that GA exerted neuroprotective effects against MPP+-induced neurotoxicity in SH-SY5Y cell line in a dose-dependent manner. GA also suppressed apoptosis by reducing MPP+-induced cytotoxicity in SH-SY5Y cells. Therefore, our research reveals a new alternative with potential protective effects for neurons in PD.

Keywords: Apoptosis, Gallic acid, MPP+, Neuroprotective, Parkinson

PC-55

Deciphering the Role of Optogenetic Manipulation of A11 Neurons on Motor Activity After Spinal Cord Injury

Ayşenur Özpinar¹, Buse Balaban², Pelin Dilsiz³, Serdar Altunay⁴, Enes Doğan¹, Saltuk Buğra Baltacı⁴, Mustafa Çağlar Beker⁵, Ertugrul Kilic⁵

¹Istanbul Medipol University, Research Institute for Health Sciences and Technologies (SABITA), Istanbul, Türkiye

²Istanbul Sağlık Bilimleri University, School of Medicine, Department of Medical Biology, Istanbul Türkiye

³Istanbul Technical University, School of Science and Letters, Department of Molecular Biology and Genetics, Istanbul, Türkiye

⁴Istanbul Medipol University, School of Medicine, Department of Physiology, Istanbul, Türkiye; ⁵Istanbul Medeniyet University, School of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Spinal cord injury is a neurodegenerative condition with high mortality risk, leading to loss of motor, sensory, and autonomic functions. Dopamine, a key modulator of the spinal cord, is primarily provided by the diencephalospinal pathway from dopaminergic A11 neurons. This study aims to examine the impact of cell type-specific optogenetic manipulation of tyrosine hydroxylase-expressing A11 neurons, the primary source of spinal dopamine, on motor coordination and locomotor activity after spinal cord injury.

METHODS: In this study, we used 8–12-week-old male Th-cre transgenic mice (Jackson Laboratory Stock No: 008601) were injected with cre-dependent rAAV2/1-EF1α-FLEX-hChR2(H134R)-EYFP-WPRE-HGHpA (n=6), rAAV2/1-EF1α-DIO-iChLoC-2A-dsRed (n=6) or rAAV2/1-hSyn-DIO-mCherry (n=6) recombinant adeno-associated viruses and fiber optic implantation was performed. After completion of transgene expression, motor coordination and locomotor activities of Th-cre mice before and after spinal cord injury and after optogenetic stimulation were observed by Basso mouse scale, horizontal ladder rung walking test and open field test. For optogenetic manipulation, 20-Hz photoexcitation was applied at 473 nm wavelength with 10-ms pulses per second repeated every 4 seconds. Statistical differences between the groups were analyzed by independent sample t-test and p<0,05 was considered statistically significant.

RESULTS: Motor coordination and locomotor activity were significantly (p<0,05) decreased in all mice with spinal cord injury model. Optogenetic stimulation of tyrosine hydroxylase-expressing dopaminergic A11 neurons increased motor coordination and locomotor activity, whereas inhibition of these neurons suppressed motor activity (p<0,001).

CONCLUSIONS: Our results show that endogenous dopamine innervation of the spinal cord by optogenetic stimulation of cell type-specific and recombinant adeno-associated viruses-mediated tyrosine hydroxylase-expressing A11 neurons significantly improves impaired locomotor activity after spinal cord injury and sheds light on the therapeutic effect of the diencephalospinal pathway on spinal cord injury.

Keywords: A11 neurons, Dopamine, Spinal cord injury, Optogenetics, Tyrosine hydroxylase

PC-56

Effects of SIRT2 Inhibition on Inflammation and Autophagy in Different Brain Regions in a D-Galactose-Induced Accelerated Aging Model

Hatice Kavak¹, Arzu Keskin Aktan², Kazime Gonca Akbulut¹

¹Gazi University, Faculty of Medicine, Department of Physiology, Ankara

²Afyonkarahisar Health Sciences University, Faculty of Medicine, Department of Physiology, Afyonkarahisar

AIM: Aging is associated with increased inflammation and decreased autophagic activity in the brain. In this study, we aimed to investigate the effects of the SIRT2 inhibitor AGK2 on the expression of proteins related to inflammation and autophagy in different brain regions in a D-Galactose (D-Gal)-induced accelerated aging model.

METHODS: A total of 32 three-month-old male Sprague-Dawley rats were used and divided into four groups: Control, D-Gal, D-Gal+DMSO, D-Gal+AGK2. For the accelerated aging model, D-Gal (150 mg/kg/day, 0.5 mL 0.9% saline) was administered subcutaneously for 10 weeks. The control group received only saline, and the experimental groups received D-Gal, D-Gal prepared with 4% DMSO:PBS, AGK2 (10 µM/bw) and D-Gal prepared with 4% DMSO:PBS. In the brain, hippocampal, frontal, and temporal cortex tissues were isolated. SIRT2 and LC3 protein expression were analyzed by Western Blot, and TNF-α and IL-1β by ELISA. SIRT2 mRNA expression was shown by q-PCR. One-way ANOVA or Kruskal-Wallis H was used for statistical analysis (p<0.05).

RESULTS: D-Gal increased SIRT2 mRNA expression in the hippocampus and frontal cortex (p<0.001), and SIRT2 protein expression only in the hippocampus (p=0.009). In the D-Gal+AGK2 group, hippocampal LC3 expression was significantly lower (p=0.006, p=0.006, p=0.006) and higher in the frontal cortex (p=0.006, p=0.006, p=0.033) compared to the other groups (control, D-Gal+DMSO, D-Gal). D-Gal administration increased TNF-α and IL-1β levels in the hippocampus, while AGK2 administration reversed this in the hippocampus and frontal cortex (p<0.05). No significant differences were found between groups in the temporal cortex.

CONCLUSIONS: Our current findings suggest that SIRT2 may play a region-specific role in the regulation of pro-inflammatory cytokine levels and autophagy in the aging brain.

This study was supported by the Scientific Research Projects Coordination Unit of Gazi University (Project ID: 7926, Project Code: TYL-2022-7926).

Keywords: D-Galactose, Aging, Inflammation, LC3, Autophagy

PC-57

The Role of Myeloid Derived Growth Factor in a Model of Parkinson's Disease in Mice

Halil İbrahim Koç¹, Enes Doğan¹, Ayşenur Özpinar¹, zehra değirmenci¹, Mustafa Beker², Ertugrul Kilic²

¹Istanbul Medipol University, Research Institute for Health Sciences and Technologies (SABITA), Istanbul, Türkiye

²Istanbul Medeniyet University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Parkinson's disease (PD) is the second most common neurodegenerative disorder in the elderly. Current treatments primarily alleviate symptoms by restoring striatal dopamine levels. Recent studies suggest that Myeloid Derived Growth Factor (MYDGF), secreted by bone marrow-derived monocytes and macrophages, may offer a potential treatment for neurodegenerative diseases. In this study, we aimed to investigate the neuroprotective effects of MYDGF in an in vivo PD model by increasing or decreasing its protein level via lentiviral vectors.

METHODS: The study was approved by Istanbul Medipol University Animal Research Ethics Committee (13.02.2023-08). In our study, 32 male C57BL6/J mice aged 8-12 weeks were anaesthetised with isoflurane (1.5%). Lv-MYDGF (to increase MYDGF expression), Lv-GFP (control of Lv-MYDGF), sh-MYDGF (to inhibit MYDGF expression) or scRNA (control of sh-MYDGF) produced after molecular cloning were injected intrastrially (n=8/group). An in vivo PD model was established by injection of 10 µg 6-hydroxydopamine 7 days after lentivirus injection. Rotation, open field and light/dark field tests were performed on days 7, 14, 21, 28 after the experimental PD model. After the mice were sacrificed on day 28, dopaminergic neuron survival was examined from coronal brain sections. Student's t-test was used for statistical analysis and p<0,05 was considered statistically significant.

RESULTS: As a result of our study, dopaminergic neuron survival decreased, motor asymmetry increased, locomotor activity, anxiety and exploratory drive decreased in the Lv-MYDGF group compared to the Lv-GFP group (p<0,001). Furthermore, in the sh-MYDGF group in which MYDGF expression was inhibited, dopaminergic neuron survival was increased (p<0,05), motor asymmetry was decreased, locomotor activity, anxiety and exploratory drive were increased (p<0,05) compared to the scRNA group.

CONCLUSIONS: The data of our study show that inhibition of MYDGF expression has a neuroprotective effect in an in vivo PD model. It is thought that MYDGF may play a role in the development and pathophysiology of the clinical symptoms of PD and the development of new strategies targeting MYDGF may provide an important advance in the treatment of PD.

Keywords: MYDGF, Parkinson's Disease, Neuroprotective Effect

PC-58

Investigation of Antiepileptic Activity of Ambroxol Hydrochloride in Pentylene-tetrazole Kindling Epilepsy Model

Hatice Doğan Göçmen¹, Selda Kabadere², Enver Ahmet Demir³, Okan Tutuk¹, Duygu Seren Özyılmaz¹, Cemil Tümer¹

¹Hatay Mustafa Kemal University, Faculty of Medicine, Department of Physiology, Hatay, Türkiye

²Eskişehir Osmangazi University, Faculty of Medicine, Department of Physiology, Hatay, Türkiye

³Ankara Etlik City Hospital, Department of Cardiology, Ankara, Türkiye

AIM: It was aimed to evaluate the antiepileptic activity of ambroxol hydrochloride in experimental temporal lobe epilepsy induced by pentylene-tetrazole kindling epilepsy model.

METHODS: 55 male Wistar albino rats were divided into 4 groups as Control Group (C; n=10; per oral (p.o.) physiological saline was administered every day and intraperitoneal (i.p.) physiological saline was administered every other day), Epilepsy Group (PTZ; n=15; i.p. 40 mg/kg PTZ was administered every other day), Valproic Acid Group (VPA+PTZ; n=15; p.o. 300 mg/kg VPA was administered every day and i.p. 40 mg/kg PTZ dose was administered 30 minutes after VPA application every other day), Ambroxol Hydrochloride Group (AH+PTZ; n=15; p.o. 800 mg/kg AH was administered every day and i.p. 40 mg/kg PTZ dose was administered 30 minutes after AH administration every other day). AH was dissolved in physiological saline. Animal behavior in PTZ, VPA+PTZ and AH+PTZ groups were recorded for 30 minutes post-pentylene-tetrazole injection, and the convulsion stage was assessed using Racine's scale. All animals were subjected to open field and social interaction tests. One-way ANOVA and Tukey post hoc tests were used for statistical analysis. P<0.05 was considered significant.

RESULTS: The challenge dose was administered after 10 days following 14 injections of 40 mg/kg i.p. PTZ given every other day. The challenge dose was scored in stage 4/5 (p<0.001) in the PTZ group, stage 1/2 (p<0.05) in the VPA+PTZ group, and stage 2/3 (p<0.05) in AH+PTZ group. Locomotor activity did not decrease in PTZ group compared to control group (p=0.051). The mobility of AH+PTZ group was found to be considerably reduced in comparison to control group (p=0.035). In comparison to control group, frequency of social interactions was found to be considerably reduced in PTZ and AH+PTZ groups (PTZ: p<0.05; AH+PTZ: p<0.05).

CONCLUSIONS: The findings of study indicate that Ambroxol Hydrochloride can partially mitigate hyperexcitability in a kindling model of epilepsy.

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Keywords: Epilepsy, Seizure, Ambroxol hydrochloride, Behaviour.

PC-59

Investigation of Semaphorin 7A Protein Role in Temporal Lobe Epilepsy Model

Hatice Doğan Göçmen¹, Okan Tutuk¹, Enver Ahmet Demir², Duygu Seren Özyılmaz¹, Selda Kabadere³, Cemil Tümer¹

¹Hatay Mustafa Kemal University, Faculty of Medicine, Department of Physiology, Hatay, Türkiye

²Ankara Etlik City Hospital, Department of Cardiology, Ankara, Türkiye

³Eskişehir Osmangazi University, Faculty of Medicine, Department of Physiology, Hatay, Türkiye

AIM: This study aimed to evaluate semaphorin (Sema) 7A protein in rats induced experimental temporal lobe epilepsy model.

METHODS: Fortyfive male Wistar albino rats were divided into 4 groups: Control Group (C; n=10), which received daily oral administration of physiological saline for 47 days, and intraperitoneal physiological saline for the first 36 days (every other day) and on the 47th day; Valproic Acid Group (VPA; n=10), which received daily oral administration of 300mg/kg VPA for 47days; Suppressed Epilepsy Group (VPA+ pentylene-tetrazole, PTZ; n=10), which received daily oral administration of 300mg/kg VPA for 47 days and intraperitoneal administration of 40 mg/kg PTZ for the first 36 days (every other day) and on the 47th day; and Epilepsy Group (PTZ; n=15), which received intraperitoneal administration of 40mg/kg PTZ for the first 36 days (every other day) and on the 47th day. Behaviors of animals in the PTZ and VPA+PTZ groups were recorded for 30 minutes post-administration of PTZ, and the convulsion stage was assessed using Racine's scale. All animals were subjected to marble burying and nestlet shredding tests. Semaphorin 7A was evaluated using ELISA, and gene expression levels were assessed via qRT-PCR in tissue samples from the cerebral cortex and hippocampus. One-way ANOVA and Tukey post hoc tests were used in the statistical analysis. P<0.05 was considered significant (HMKÜ HADYK 2020/04-8).

RESULTS: No significant difference was seen between groups in the levels and expression of Sema 7A in the cerebral cortex and hippocampus, as determined by ELISA and qRT-PCR studies. The PTZ group experienced a notable reduction in the duration of cotton exploration and identified fewer marbles than the Control (p=0.05; p<0.01), VPA (p<0.01) and VPA+PTZ (p<0.01) groups.

CONCLUSIONS: The non-significant increase of Sema7A protein in cerebral cortex and hippocampus induces synthesis of inflammatory cytokines, leading to inflammatory reactions that may provoke neuronal hyperexcitability and repeated seizures. The overall levels of Sema 7A protein were analyzed in study. Sema7A needs to be evaluated with cell typing in advanced molecular analysis.

Keywords: Epilepsy, Seizure, Semaphorin 7A, Behaviour.

PC-60

Myrtenal Exhibits Protective Effects in Rats with Acute Ischemic Stroke

Engin Korkmaz¹, Asiye Beytur¹, Kevser Tanbek¹, Suat Tekin¹,
Çiğdem Tekin²

¹Inonu University, Faculty of Medicine, Department of Physiology,
Malatya, Türkiye

²Inonu University, Health Services Vocational School, Malatya,
Türkiye

AIM: The majority of strokes are caused by cerebral ischemia (CI) due to cerebral embolism. Oxidative stress and inflammation play a significant role in the pathophysiology of stroke. Myrtenal (Myrt) is a monoterpene derivative found in the essential oils of various plants. In preclinical studies, Myrt has been reported to possess antioxidant, anti-inflammatory and neuroprotective properties. The aim of this study was to investigate the protective effect of Myrt in the CI model induced by middle cerebral artery occlusion (MCAO) in rats.

METHODS: *Sprague Dawley* male rats (3 month) were divided into three groups: Control (n=10), CI (n=12) and Myrt+CI (n=12). Myrtenal (40 mg/kg) or a vehicle (Tween 80 (0.05%)) was administered intraperitoneally to the animals daily for 28 days prior to surgery. Rats were trained to perform motor/sensorimotor tests (rotarod, adhesive removal and grip strength test) for 3 days prior to the surgery. After the training period, a 60-minute MCAO operation was performed on the CI and Myrt+CI groups, while a sham operation was performed on the control group. During the 24-hour reperfusion period, neurological deficit scoring and motor/sensorimotor tests were conducted in all groups. Subsequently, the animals were euthanized and the infarct area in the brain was evaluated using the triphenyltetrazolium chloride staining method.

RESULTS: Group comparisons revealed that Myrt pretreatment resulted in an improvement of the motor and sensorimotor deficits induced by CI (p<0.05). Additionally, Myrt administration led to a reduction in the infarct area caused by CI (p<0.05).

CONCLUSIONS: These findings demonstrate that Myrt exerts a neuroprotective effect against ischemic stroke.
Acknowledgement: This study was supported by the Health Institutes of Türkiye (Project no: 36022).

Keywords: Stroke, Cerebral Ischemia, Myrtenal

PC-61

The Effects of Levetiracetam Treatment with Probiotic and Prebiotic Supplements on Motor and Cognitive Behaviors in a Post-Traumatic Epilepsy Model

Uğur Aykın, Sezin Kiroğlu Uzun, Cumaali Demirtaş, Mehmet Yıldırım

University of Health Sciences, Hamidiye Faculty of Medicine,
Department of Physiology, Istanbul, Türkiye

AIM: Post-traumatic epilepsy (PTE) leads to various behavioral and neuropsychiatric dysfunctions like depression, learning-memory deficiencies, anxiety and motor coordination impairments. This study aims to investigate effects of prebiotic, probiotic, and synbiotic supplements on behavioral changes caused by PTE and levetiracetam(LEV) treatment using a rat model of PTE.

METHODS: Male, 10-12 weeks old, 200-240 grams Sprague-Dawley rats were divided into 6 groups(n=8). Except for control group, all groups were subjected to traumatic brain injury using weight-drop method. Seven days later, PTE was induced with intraperitoneal injections of subconvulsant doses of pentylenetetrazol(PTZ, 30+15+15 mg/kg) at 30-minute intervals. For 28 days, 100 mg/kg LEV or LEV+1g/kg inuline; LEV+10x109/kg VSL#3, or 1g/kg inuline+10x109/kg VSL#3 were administered orally. PTZ-induced seizure induction was performed once a week for 4 times. In last week of treatment, locomotor activity and anxiety changes were assessed using open field and elevated plus maze, learning and memory performance using radial arm maze and passive avoidance, motor coordination using rotarod and pain threshold using dynamic and thermal plantar tests. Data were statistically analyzed using Kruskal-Wallis followed by Mann-Whitney U test.

RESULTS: Compared to control group, significant increase in anxiety levels was observed in LEV group (p<0.05). It was found that application of probiotics with LEV reversed this effect. When examining data on motor coordination, no significant difference was observed in LEV alone or prebiotic and probiotic combination groups compared to control group. Similarly, no significant difference was detected in learning and memory performance analysis between any group and control group.

CONCLUSIONS: In the experimental PTE model, it was observed that administration of probiotics with LEV prevented anxiety due to LEV, and both probiotics and prebiotics applied for PTE treatment did not adversely affect motor functions, cognitive performance, or pain threshold levels.

Acknowledgement: The presented study was approved as ethically by SBU-HADYEK at the meeting dated 09/03/2023.

Keywords: Behavior, Post-traumatic epilepsy, Prebiotic, Probiotic,

PC-62

Effect of 3',4'-Dihydroxy Flavonol (DiOHF) Treatment on Retinal Neurogenesis and Damage in Experimental Focal Brain Ischemia-Reperfusion in Rats

Osman Çetin¹, Gözde Acar¹, Tuğçe Aladağ¹, Ümmügülsüm Önal²,
Esra Gülsüm Danış¹, Rasim Mogulkoc¹, Abdulkirim Kasim Baltacı¹

¹Selcuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

²Selcuk University, Faculty of Medicine, Department of Histology and Embryology, Konya, Türkiye

AIM: The reduction or disappearance of blood supply to a part of the body for various reasons is defined as ischemia. Neurons are deprived of oxygen and energy after an ischemic stroke, resulting in cell death. 3', 4'-dihydroxyflavonol (DiOHF) is a synthetic flavonoid and its protective effect has been determined in different ischemia-reperfusion studies. This study was conducted to determine the effect of 1 week of 3',4'-Dihydroxyflavonol supplementation on neurogenesis in retinal tissue following cerebral ischemia-reperfusion in rats.

METHODS: This study was carried out on male Wistar-albino rats to be obtained from Selçuk University Experimental Medicine Research and Application Center. In the study in which a total of 28 rats were used, the groups were formed as Control (n=6), Sham (n=6), Ischemia-Reperfusion (n=8) and Reperfusion+DiOHF (n=8) and DiOHF was administered for 1 week after the carotid arteries of the rats were ischemized by ligation for 30 minutes. At the end of the study, retinal tissue from animals sacrificed under general anaesthesia was frozen and immunofluorescence labelling was performed with H&E and DAPI staining to evaluate the possible retinal damage after IR with carotid artery occlusion and the therapeutic effect of DiOHF drug.

RESULTS: After ischemia/reperfusion, histologic changes in the retinal morphology of rats were minimal, whereas disruption in the laminar architecture of the retina was observed. After IR injury, irregular cell borders and occasional cell loss were observed in the retinal ganglion cell layer. While these ganglion cell losses were reversed after 1 week of DiOHF treatment, the irregularity between the retinal layers persisted.

CONCLUSIONS: The study shows that focal cerebral ischemia in rats causes significant retinal structure deterioration, but 1 week of DiOHF treatment is effective in preserving the morphological structure by reversing ganglion cell losses.

Keywords: Brain ischemia-reperfusion, DAPI immunostaining, H&E staining, 3' 4'-Dihydroxyflavonol (DiOHF), Neurogenesis, Retina

PC-63

The Effect of 2-Week Naringin Administration on Neurogenesis After Cerebral Ischemia- Reperfusion in Ovariectomized Rats

Ayşenur Keskin¹, Gözde ACAR¹, Tuğçe Aladağ¹, Ümmügülsüm Önal², Saltuk Bugra BALTACI³, Rasim Mogulkoc¹, Abdulkirim Kasim Baltacı¹

¹Selcuk University, Faculty of Medicine, Department of Physiology, Konya

²Selcuk University, Faculty of Medicine, Department of Histology and Embryology, Konya

³Medipol University, Faculty of Medicine, Department of Physiology, Istanbul

AIM: Cerebral ischemia-reperfusion is a condition that occurs when blood flow is restored after a transient interruption and can lead to impaired brain function. The aim of this study was to determine the effect of 2-week naringin supplementation on neurogenesis after cerebral ischemia-reperfusion in ovariectomized female rats.

METHODS: Experimental groups consisting of 36 female Wistar-albino rats with Ethics Committee Approval (Ethics Committee No: 2023-03) were formed as follows: 1-Control group: No anaesthesia or surgical procedure was performed. 2-Ovariectomy-Sham Brain I/R Group: After ovariectomy under general anaesthesia, carotid artery regions were opened and closed and sham I/R was performed, followed by vehicle administration for 2 weeks. 3-Ovariectomy-I/R Group: After ovariectomy, carotid arteries were ligated for 30 minutes under general anaesthesia and reperused for 2 weeks after ischemia. 4-Ovariectomy-I/R Sham Treatment Group: After ovariectomy, carotid arteries were ligated under general anaesthesia and ischemia was performed for 30 minutes, followed by reperfusion and carrier administration for 2 weeks. 5-Ovariectomy-I/R Naringin Treatment Group: After ovariectomy, carotid arteries were ligated and ischemia was applied for 30 minutes under general anaesthesia, followed by reperfusion and Naringin administration for 2 weeks. NeuN levels were determined by immunohistochemical staining and anti-NeuN antibody labelling in hippocampus tissue samples taken from anesthetized animals. Kruskal-Wallis variance analysis was used for group comparisons. Mann-Whitney U test was applied for p<0.05 level. P<0.05 level was considered statistically significant.

RESULTS: When the anti-NeuN antibody level was examined, the anti-NeuN antibody levels decreased in the I/R and I/R+Solvent groups (P<0.01). In the I/R+Naringin group, which was subjected to 2 weeks of naringin application, a significant increase was observed compared to the ischemia groups (P<0.01), but did not reach the levels of the control and sham groups.

CONCLUSIONS: The results of the study showed that NeuN levels, which are effective in neurogenesis, were significantly suppressed as a result of I/R-induced damage; however, 2-week intraperitoneal naringin supplementation had a positive effect on neurogenesis in ovariectomized rats.

Keywords: Brain ischemia-Reperfusion, Naringin, NeuN, Neurogenesis

PC-64

Increased Release of Inflammatory Cytokines in Spinal Cord Tissue in a Cuprizone Induced Rat Multiple Sclerosis (MS) Model Is Prevented by Zinc Supplementation

Saltuk Buğra Baltacı¹, Gözde Acar², Ayşenur Feyza Bayıroğlu², Ebru Kübra Uzdil², Rasim Moğulkoc², Abdülkerim Kasım Baltacı²

¹Istanbul Medipol University, Faculty of Medicine, Department of Physiology, İstanbul, Türkiye

²Selçuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: MS is a chronic autoimmune disease of the central nervous system characterized by neuroinflammatory processes, leading to demyelination and neurodegeneration. There is no study investigating the relationship between zinc, which plays a critical role in the immune system, and inflammatory cytokines that occur in MS. The aim of this study was to investigate the effect of dietary zinc status on inflammatory cytokine release in spinal cord tissue in a rat Multiple Sclerosis model induced by Cuprizone.

METHODS: The study was carried out on 46 adult male rats of the genus Wistar. The animals used in the study were divided into 5 groups (G) (Control 6, other groups 10). G1, Control. G2, Sham-MS: Carboxy-methyl-cellulose (KMS) solution in which Cuprizone was dissolved was given to rats by gavage daily for 8 weeks at the rate of 1% of daily feed consumption. MS was formed by giving 1% of the daily feed consumption cuprizone in KMS solution by gavage to the animals in G3, 4 and 5 for 8 weeks. G4 was fed with a zinc deficient (50 µg/kg zinc) diet. G5 was given intraperitoneal (ip) zinc sulfate (5 mg/kg/day) supplementation. MS formation in animals was determined by Rotarod tests and Myelin Basic Protein (MBP) gene expression analysis. TNF-α, IL-1β and IL-6 levels were determined in spinal cord tissue samples of animals by ELISA method (pg/g tissue).

RESULTS: The highest levels of TNF-α, IL-1β and IL-6 in spinal cord tissue were detected in G3 and G4 (P<0.05). Zinc supplementation prevented the increase in the parameters mentioned in G5 and restored them to control values (P<0.05).

CONCLUSIONS: The findings of the present study indicate that physiological doses of zinc supplementation in a rat experimental MS model may reduce the severity of the disease by regulating the release of inflammatory cytokines.

Keywords: Cuprizone, Inflammatory cytokines, Multiple sclerosis, Spinal cord, Zinc

PC-65

The Effect of 2-Week Naringin Administration on Frontal Cortex Calbindin and Tubulin Values After Cerebral Ischemia-Reperfusion in Ovariectomized Rats

Ayşenur Keskin¹, Gözde Acar¹, Tuğçe Aladağ¹, Ümmügülsüm Önal¹, Saltuk Buğra Baltacı², Rasim Moğulkoc¹, Abdülkerim Kasım Baltacı¹

¹Selçuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

²Istanbul Medipol University, Faculty of medicine, Department of Physiology, İstanbul, Türkiye

AIM: Cerebral ischemia-reperfusion is a condition that occurs when blood flow is restored after a temporary interruption and can lead to impaired brain function. This study aimed to determine the effect of 2-week naringin supplementation on frontal cortex calbindin and tubulin after brain-ischemia reperfusion in ovariectomized female rats.

METHODS: Experimental groups consisting of 36 female Wistar-albino rats were formed as follows: 1-Control group: No anesthesia or surgical procedure was performed. 2-Ovariectomy-Sham Brain I/R Group: After ovariectomy under general anesthesia, carotid artery regions were opened and closed and sham I/R was performed, followed by vehicle administration for 2 weeks (2 weeks, 1 ml 0.25% carboxymethylcellulose). 3-Ovariectomy-I/R Group: After ovariectomy, carotid arteries were ligated for 30 minutes under general anesthesia and reperfusion for 2 weeks after ischemia. 4-Ovariectomy-I/R Sham Treatment Group: After ovariectomy, carotid arteries were ligated under general anesthesia and ischemia was performed for 30 minutes, followed by reperfusion and carrier administration for 2 weeks. 5-Ovariectomy-I/R Naringin Treatment Group: After ovariectomy, carotid arteries were ligated and ischemia was applied for 30 minutes under general anesthesia, followed by reperfusion and Naringin administration for 2 weeks. PCR determined calbindin and alpha/beta-tubulin levels in frontal cortex tissue samples obtained from anesthetized animals. Results were defined as mean ± standard deviation. Kruskal-Wallis analysis of variance and Mann-Whitney U test for p<0.05 level were used for intergroup comparisons. P<0.05 level was considered statistically significant.

RESULTS: Frontal cortex calbindin and alpha/beta-tubulin levels were significantly reduced by I/R. However, 2 weeks of naringin administration was observed to increase calbindin and alpha/beta-tubulin levels.

CONCLUSIONS: Our results show that the impairment of neurogenesis in the frontal cortex in brain I/R after ovariectomy in female rats was significantly improved by 2 weeks of naringin supplementation.

Keywords: Brain ischemia-reperfusion, Calbindin, Tubulin, Naringin

PC-66

The Effect of Idebenone in Rats with Neuropathic Pain Model Induced by Sciatic Nerve Ligation

Sinan Şafak¹, Rümeyşa Abdullahoğlu², S.Sırrı Bilge¹

¹Ondokuz Mayıs University, Faculty of Medicine, Department of Pharmacology, Samsun, Türkiye

²Ondokuz Mayıs University, Faculty of Medicine, Department of Physiology, Samsun, Türkiye

AIM: Idebenone is a drug used in the treatment of symptoms of vascular and degenerative cerebral pathologies due to its antioxidant and anti-inflammatory effects. There is limited data regarding the efficacy of idebenone on pain. The aim of our study was to investigate the effect of idebenone on neuropathic pain, in which oxidative stress and inflammation play a role in the pathogenesis, in a rat sciatic nerve ligation model.

METHODS: In our study, a total of 42 adult male Sprague-Dawley rats were used, with seven rats in each group. For the neuropathic pain model, the rats' left sciatic nerve was ligated at three separate points, spaced 1 mm apart, using chromic catgut. The rats in the sham group underwent the entire surgical procedure except sciatic nerve ligation. The rats were administered 50, 100, 200 mg/kg idebenone (IDE), 10 mg/kg pregabalin or physiological saline by oral gavage for 14 days starting from the 1st day after sciatic nerve ligation. Mechanical pain (Randall-Selitto Claw test) and thermal pain (Hot-Plate test) were evaluated 24 hours after the last application. One-way analysis of variance (ANOVA) test was used for statistical analysis and Tukey-Kramer post-hoc test was used for multiple comparisons between groups.

RESULTS: Sciatic nerve ligation significantly decreased mechanical and thermal pain thresholds compared to the sham group ($p<0.001$ and $p<0.05$, respectively). Administration of 100 and 200 mg/kg idebenone and 10 mg/kg pregabalin attenuated the decrease in mechanical threshold ($p<0.01$ - 0.001) and completely prevented the decrease in thermal threshold ($p<0.001$). 50 mg/kg idebenone administration did not change the decrease in both pain thresholds with SSL.

CONCLUSIONS: Our findings show that idebenone has a decreasing effect on mechanical and thermal hyperalgesia induced by sciatic nerve ligation in rats. Further studies are needed to determine the mechanisms through which idebenone exerts its antihyperalgesic effect.

Keywords: Hyperalgesia, Idebenone, Neuropathic pain, Pain, Rat, Sciatic nerve ligation

PC-67

Curcumin and Ascorbic Acid's Neuroprotective Efficacy Against Rotenone-Induced Parkinson's Model in SH-SY5Y Cells

Işinsu Atıcı¹, Özlem Yılmaz¹, Mümin Alper Erdoğan²

¹Ege University, Faculty of Medicine, Department of Physiology, İzmir, Türkiye

²Katip Çelebi University, Faculty of Medicine, Department of Physiology, İzmir, Türkiye

AIM: Rotenone is a pesticide widely used to create experimental models of Parkinson's disease. This study aims to investigate the protective effects of curcumin and ascorbic acid in a rotenone-induced toxicity model in SH-SY5Y cells. While the effects of curcumin and ascorbic acid on Parkinson's disease have been studied individually, the combined neuroprotective effects of these agents in a rotenone-induced Parkinson's model have not been investigated.

METHODS: The human neuroblastoma cell line SH-SY5Y was used. Curcumin and ascorbic acid were applied as pretreatment agents for 2 hours. To induce neurotoxicity, a 24-hour rotenone application was performed. Cell condition was assessed using MTS cell proliferation and colony formation capacity assays. Statistical analyses were performed using one-way ANOVA with SPSS v15.0.

RESULTS: The neurotoxic dose determination study with rotenone established a 24-hour IC₅₀ dose of 500 nM, which was used for subsequent model applications ($p<0.0001$). In the MTS test, it was found that pretreatment with 10, 50, and 100 nM curcumin, and 50 and 100 nM ascorbic acid significantly preserved cell viability and proliferation capacity against 500 nM rotenone exposure ($p<0.0001$). Additionally, combinations of 10 nM curcumin + 50 nM ascorbic acid, 50 nM curcumin + 50 nM ascorbic acid, and 10 nM curcumin + 100 nM ascorbic acid also significantly preserved cell viability against rotenone toxicity ($p<0.0001$). Consistent with the MTS assay results, the colony formation capacity was also significantly preserved with 10 and 50 nM curcumin, 50 and 100 nM ascorbic acid, and their combinations against rotenone toxicity ($p<0.0001$).

CONCLUSIONS: The findings demonstrate that curcumin and ascorbic acid provide significant protection against rotenone-induced neurotoxicity in the SH-SY5Y cell line. These results suggest that the combination of these two agents could be a potential neuroprotective strategy in the treatment of Parkinson's disease.

Keywords: Neurotoxicity, Rotenone, Curcumin, Ascorbic Acid, Parkinson's Model

PC-68

Investigation of Depression-Like Behaviour of Maternal and Offspring Rats Exposed to Maternal Separation Stress

Özge Selin Çevik¹, Ümmühan Adam Utli¹, Ahmet Can Türkoğlu¹, Didem Derici Yıldırım², Leyla Şahin¹

¹Mersin University, Faculty of Medicine, Department of Physiology, Mersin, Türkiye

²Mersin University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Mersin, Türkiye

AIM: The connection established with the mother at a young age is extremely important for the child's development. A healthy bond with the mother contributes to the emotional, mental and social development of the child. The stress of separation from the mother is a natural stress response seen in humans as well as in other animal species. This stress can cause mental health problems such as anxiety disorders and depression. Investigating the effects of maternal separation stress not only on male rat pups but also on their mothers is beneficial in terms of examining the interaction between offspring and mother.

METHODS: Groups were determined as control pups (n=10); control mother (n=10); maternal separation pups (n=10); maternal separation mother (n=10). Maternal separation stress was induced between 08:00 and 12:00 in the morning. During the stress protocol, the mother was removed from the cage and placed in another cage and reunited with her offspring at the end of the procedure. At the end of the stress protocol, depression-like behaviours of the animals were examined by forced swimming test (porsolt). The data obtained were evaluated with one-way anova test.

RESULTS: According to the results obtained, there is a statistically significant difference between the groups for the swimming variable (p=0,030). When the post hoc test was performed to determine the source of this difference, there was a difference between the stressed pup and the control mother (p=0,048). There was also a difference between the stressed mother and the stressed male pup in the immobility time parameter (p=0,042).

CONCLUSIONS: 21-day maternal separation stress did not show a difference between stressed and control mothers in terms of depression-like behaviour, but the fact that we observed this difference between male pups and mother suggests that there is a difference in depression-like behaviour studies, especially in terms of interaction between mother and pups.

Keywords: Depression, Maternal separation, Stress, Mother, Infant

PC-69

Effects of Mitochondrial Transfer on Post-Stroke Brain Damage and Anxiety

Saltuk Buğra Baltacı¹, Sevban Bayırlı², Oğuzhan Baygöl³, Halil İbrahim Koç², Enes Doğan², Zehra Değirmenci², Çiğdem Bayraktaroğlu², Zeynep Aladağ², Emre Vatandaşlar², Serdar Altunay¹, Mustafa Çağlar Beker³, Ertuğrul Kılıç³

¹Istanbul Medipol University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

²Istanbul Medipol University, Research Institute for Health Sciences and Technologies, Istanbul, Türkiye

³Istanbul Medeniyet University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Stroke is the second leading cause of death worldwide. Mitochondrial dysfunction is among the main events occurring in pathophysiology of ischemia. The demonstration of mitochondrial transport from astrocytes to neurons after stroke suggests that providing healthy mitochondria to neurons after stroke may have therapeutic potential. This study aims to determine the effects of post-stroke mitochondrial transfer on neuronal survival, glial scar formation, brain atrophy and anxiety.

METHODS: C57BL-6 mice were induced with 30 minute ischemia using the middle cerebral artery occlusion model. After brain ischemia, the animals were divided into three groups: control, intrastriatal mitochondrial injection and intraarterial mitochondrial injection groups. Mitochondria isolated from healthy mice brains using Percoll density gradient. The number of isolated mitochondrial particles was determined by flow mitometry. For intrastriatal mitochondrial injection, 5×10^5 mitochondrial particles were administered by stereotaxic method. For intraarterial mitochondrial injection, 5×10^6 mitochondrial particles were administered via tail artery. To determine anxiety, elevated O maze and light-dark tests were applied to animals 3 days before ischemia and on days 7, 14, 28 and 42 after ischemia. On 55th day after ischemia, experimental animals were sacrificed and brains were collected. Neuronal survival and striatal atrophy occurring after stroke were determined by NeuN staining from brain sections, and glial scar was determined by GFAP staining.

RESULTS: Intraarterial mitochondrial injection in the light-dark test increased the time spent on the light side after stroke compared to control group (p<0.05). There was no difference between the groups in elevated O maze. Intraarterial and intraarterial mitochondrial injection increased neuronal survival after stroke compared to the control group (p<0.001). Intraarterial mitochondrial injection reduced striatal atrophy and glial scar formation after stroke (p<0.05).

CONCLUSIONS: The results show that providing healthy mitochondria to the ischemic tissue after stroke alleviates ischemic damage, reduces striatal atrophy and glial scar formation, and improves anxiety.

Keywords: ischemic stroke, Mitochondria transfer, Mitochondrial dysfunction

PC-70

Does Taurine Prevent Blood Brain Barrier Impairment in Rats Administered with Intracerebroventricular Amyloid Beta 1-42 Injection?

İlayda Numanoglu, Burak Kayabaşı, Sibel Dinçer

Gazi University Faculty of Medicine, Department of Physiology, Ankara, Türkiye

AIM: Blood brain barrier is an unit that protects brain parenchyma by restricting substance transport between blood and brain. Blood brain barrier breakdown in neurodegenerative disease causes an imbalance in substance transport between blood and brain. Blood barrier breakdown that occurs during Alzheimer's disease results in deterioration of removing amyloid beta from brain. This study aims to investigate the possible changes in tight junction molecule Zonula Occludens 1 (ZO-1) that is a part of blood brain barrier and astrocytic biomarker Glial Fibrillary Acidic Protein (GFAP) in neurodegenerative process induced by intracerebroventricular injection of Amyloid Beta 1-42 (A β 1-42) and taurine's effect on these changes.

METHODS: 250-300 gr Wistar rats were divided into four groups as Control (n=6), Taurine (n=6), A β 1-42 (n=6) and A β 1-42+Taurine (n=6). Stereotaxic injection of icv A β 1-42 (5 μ g/5 μ l) was performed for A β 1-42 and A β 1-42+Taurine, icv PBS injection (5 μ l) was performed for Control and Taurine groups for each ventricle. 300 mg/kg of Taurine was applied with oral gavage to the Taurine and A β 1-42+Taurine groups for 28 days. Morris Watermaze Test and Open Field Test were used to evaluate cognitive functions and locomotor activity and anxiety behaviour. In brain tissue, ZO-1 and GFAP levels were measured by Western blot. Non parametric tests were applied for statistical analyses. P<0.05 was considered as significant. (Ethical approval G.Ü.ET-23.043 and supported by Gazi University BAP TYL-2023-8731).

RESULTS: There were no significant differences in behavioural tests and brain GFAP levels among groups. In ZO-1 levels, there was a significant decrease in A β 1-42 group compared to Control group (p<0.05). Although taurine supplementation approximate ZO-1 levels to the control, it was found statistically non-significant.

CONCLUSIONS: In neurodegenerative processes like Alzheimer's disease, blood brain barrier disruption can occur without altering the cognitive behaviour. Although taurine's moderate improvement is seen on blood brain barrier, further studies are needed in this topic.

Keywords: A β 1-42, astrocyte, GFAP, Taurine, Tight junction protein, ZO-1

PC-71

Effect of Environmental Enrichment on Brain Inflammatory Response in a Chronic Unpredictable Mild Stress Model

Ece Durmuş, Hale Sayan Ozaçmak

Zonguldak Bülent Ecevit University, Faculty of Medicine, Department of Physiology, Zonguldak, Türkiye

AIM: Longterm exposure experimental animals various stressors causes neurobehavioural changes including learning and memory impairments. Chronic stress has been shown to cause functional and morphological impairments in various brain regions experimental animals such as hippocampus, prefrontal cortex and amygdala. Chronic unpredictable mild stress (CUMS) is reported to cause microglial activation in brain and increase production of inflammatory cytokines. Environmental enrichment (EE) environment can prevent brain aging mechanisms and increase in pro-inflammatory markers in experimental animals. This study, it was aimed to investigate the effects of environmental enrichment inflammatory responses in brain after CUMS.

METHODS: Approval of Zonguldak Bülent Ecevit University Animal Experiments Ethics Committee was received. It was supported by Zonguldak Bülent Ecevit University BAP unit as project number 2023-26259946-03. This study, 4 groups were formed with 8 rats in each group: Control, CUMS, environmental enrichment, environmental enrichment + CUMS. Rats in stress group were exposed to randomly applied stresses 7 days a week for 3 weeks to create a chronic mild stress model. The rats in EE and EE+CUMS groups were housed in special cages measuring 110 x 75 x 70 cm containing toys and tunnels that increase physical activity and social interaction. Interleukin (IL)-6, IL-1 β , Tumour necrosis factor (TNF)- α , Nuclear factor kappa B (NF- κ B) protein levels in hippocampus, prefrontal cortex tissue were analysed ELISA method. Statistical analyses were performed Kruskal Wallis and Bonferroni, and p<0.05 value was considered significant.

RESULTS: Chronic stress group had significantly higher IL-6 protein levels in hippocampus compared to EE group (p<0.05). IL-1 β level in hippocampus of control group was found to be significantly lower than in EE+stress group (p<0.05). No statistically significant difference was observed in terms of parameters measured in cortex tissue samples in all groups.

CONCLUSIONS: Environmental enrichment was found to be an effective method to reduce increased inflammatory response in hippocampus with CUMS. Results suggest that environmental enrichment applications are effective in preventing chronic stress-induced neurobehavioural changes by reducing neuroinflammatory response.

Keywords: Environmental enrichment, Rat, Stress

PC-72

Investigation of the Effect of Rupatadine on Oxytocin-induced Contractions of Isolated Human Myometrium

Niyazi Akkas¹, Ülfet Sena Metin¹, Ahmet Akkoca², Jule Eriç Horasanlı¹ Selim Kutlu³

¹Necmettin Erbakan University, Faculty of Medicine, Department of Obstetrics and Gynecology, Konya, Türkiye

²Necmettin Erbakan University, Faculty of Medicine, Department of Biophysics, Konya, Türkiye

³Necmettin Erbakan University, Faculty of Medicine, Department of Physiology, Konya, Türkiye

AIM: Rupatadine, a second-generation antihistamine with H1 receptor antagonist properties, is frequently used in allergic reactions. Histamine is known to be a moderately effective simulator of uterine contractions. This effect is evident in human myometrium contractions. Although H1 receptors are commonly found in the uterus as well as in many peripheral tissues, the effect of rupatadine on uterine contractions is unknown. The aim of this study was to investigate the effect of rupatadine on oxytocin-induced contractions in human myometrium.

METHODS: Myometrium strips obtained during caesarean section operations from individuals whose consent was obtained after ethics committee approval were used in this study. Isometric contractions were induced by applying 2 grams of tension to the strips placed in an isolated organ bath containing Krebs solution. Amplitude (mg), frequency (number of contractions in 30 minutes) and peak area (AUC) parameters of contractions induced by oxytocin (1nmol/L) recorded as control values. Following the 30-minute period, rupatadine at concentrations of 0.04mg/ml and 0.2mg/ml was administered to different groups and the changes on contraction parameters were determined. One-way analysis of variance was used for statistical evaluation of the findings.

RESULTS: Administration of 0.04mg/kg rupatadine produced a non-significant mild inhibition on oxytocin-induced contractions ($p>0.05$). While 0.2mg/ml rupatadine did not change the frequency of contractions, it significantly decreased the amplitude and AUC parameters ($p<0.01$).

CONCLUSIONS: The results of this study showed that rupatadine has an inhibitory effect on human myometrium contractions under in vitro conditions. This effect appears to be dose dependent.

Keywords: Isometric contractions, Myometrium, Rupatadine

PC-73

The Relationship Between CTRP Levels, Plasma Lipids, Trp64Arg Gene, and $\beta 3$ -AR in Preterm Birth

Dilan Aşkın Özek¹, Rauf Melekoglu², Hande Yüce³, Nesibe Zeyveli Çelik², Yasemin Şahin⁴, Kevser Tanbek⁵, Şeyma Yaşar⁶, İlker Ateş⁷, Songül Ünüvar³, Süleyman Sandal⁵

¹Firat University, Kovancılar Vocational School of Pharmacy Services, Elazığ, Türkiye

²İnönü University, Faculty of Medicine, Department of Obstetrics and Gynecology, Malatya, Türkiye

³İnönü University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Malatya, Türkiye

⁴Pamukkale University, Faculty of Medicine, Department of Medical Biology, Denizli

⁵İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

⁶İnönü University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Malatya, Türkiye

⁷Ankara University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Ankara, Türkiye

AIM: This study aimed to compare the Trp 64 Arg gene expression in beta-3 adrenoreceptors ($\beta 3$ -ADR) in pregnant women who gave preterm birth with that of healthy pregnant women and to determine relationship of gene levels with adipokines and plasma lipids.

METHODS: Forty pregnant women diagnosed with preterm labor and 40 healthy pregnant women who completed their pregnancies normally were included in this study. C1q/tumor necrosis factor-related protein levels and plasma lipid levels were determined in blood samples taken from all individuals participating in the study by ELISA method. Gene expressions were evaluated by the RT-PCR method. IBMSPSS Statistics 26.0 program was used in the analyses. Independent Samples t-test, Mann-Whitney U test, Pearson Chi-Square test, Yates's Corrected Chi-Square test and Fisher's Exact Chi-Square test were used in statistical analyses.

RESULTS: A significant decrease in $\beta 3$ -AR gene level and an increase in Trp64Arg gene frequency ($p<0.05$) were found in the study group compared to the control. A decrease in serum CTRP3 levels in the study group compared to the control ($p<0.05$), and the opposite increase in CTRP4 levels ($p<0.05$) were found. An increase in LDL levels ($p<0.05$) and a decrease in TC levels ($p<0.05$) were observed in the study group.

CONCLUSIONS: In this study, where the relationship between CTRP levels and preterm birth was investigated for the first time, it was observed that there was a relationship between CTRPs and HDL and LDL levels and that the decrease in CTRP3 levels in preterm birth cases ($p=0.026$) increased CTRP4 levels as a defense mechanism ($p=0.040$). Decreased $\beta 3$ -AR levels ($p=0.014$) and increased Trp64Arg gene frequency were detected in the placenta. The study was approved by the Inonu University Malatya Clinical Research Ethics Committee with approval dated 18.05.2022 and numbered 2022/43. This study was supported by Inonu University Scientific Research Projects Unit (Project No: TDK-2022-3013).

Keywords: CTRP, Preterm Birth, Lipids, Trp64Arg Gene, $\beta 3$ -AR.

PC-74

Examination of Serum Isthmin-1 Levels in Patients with Polycystic Ovary Syndrome

Zeynep Dila Öz¹, Ayşe Akmeşe Atlı², Mehmet Rıdvan Özdede¹, Ahmed Sait Bozyıl¹, Orhan Sayın¹, Mehtap Pervin¹, Hüsna Batmaz¹, Faruk Kılınç³, Emine Kaçar¹

¹Firat University, Faculty of Medicine, Department of Physiology, Elazığ, Türkiye

²Firat University, Faculty of Medicine, Department of Psychiatry, Elazığ, Türkiye; ³Firat University, Faculty of Medicine Hospital, Department of Endocrinology, Elazığ, Türkiye

AIM: Polycystic Ovary Syndrome (PCOS) is a common endocrine and metabolic disorder characterized by insulin resistance, affecting 8-13% of women of reproductive age and potentially causing infertility. A thorough understanding of the etiopathogenesis of PCOS is crucial for the development of effective treatment strategies. Adipokines are peptide hormones that regulate energy metabolism and play significant roles in the etiology of various metabolic diseases. Isthmin-1, a newly discovered adipokine, has been shown to play a role in glucose homeostasis, with recent studies demonstrating its beneficial effects, such as stimulating glucose uptake and improving insulin resistance. This study aims to elucidate the potential relationship between PCOS and Isthmin-1.

METHODS: The target population included women diagnosed with polycystic ovary syndrome (PCOS). Exclusion criteria encompassed severe psychiatric disorders, a history of malignancy, neurological diseases, and other endocrine disorders besides PCOS. A total of 30 women diagnosed with PCOS who met these criteria, along with 30 healthy female volunteers with similar demographic characteristics (age, height, weight, and body mass index), were enrolled as the control group. Serum Isthmin-1 levels were measured using the ELISA method. Student's t-test was employed for between-group comparisons, and Pearson's correlation test was used for correlation analyses. A p-value of <0.05 was considered statistically significant.

RESULTS: Compared to the control group, there was no significant difference in serum Isthmin-1 levels in PCOS patients (Control: 3.354 ± 0.3367 ng/mL and PCOS: 2.287 ± 0.2720 ng/mL, $p = 0.1828$).

CONCLUSIONS: The lack of insulin resistance among the PCOS patients in our study may have contributed to the absence of a significant difference in Isthmin-1 levels between the groups. Further comprehensive studies investigating the potential role of Isthmin-1 in the pathogenesis of PCOS may contribute to the development of innovative approaches for the diagnosis and treatment of this syndrome.

This study was supported by the Scientific Research Projects of Firat University (Project no: TF.23.17).

Keywords: Isthmin-1, Polycystic Ovary Syndrome, Adipokine

PC-75

Salivary Urea, Uric Acid and Creatinine Levels in Chronic Renal Patients

Hivda Ezgi Tursun¹, Bayram Berktaş², Faruk Dişli³, Sedat Yıldız³

¹Afyonkarahisar Health Sciences University, Faculty of Medicine, Department of Physiology, Afyonkarahisar

²İnönü University, Faculty of Medicine, Department of Nephrology, Malatya

³İnönü University, Faculty of Medicine, Department of Physiology, Malatya

AIM: Chronic Kidney Disease (CKD) is a disease that is common in older ages, is irreversible, progressive, has a high mortality rate and is characterized by loss of kidney function. In CKD, uremic metabolites such as urea, uric acid and creatinine accumulate in the blood. These metabolites can be reflected in body fluids such as saliva, but there is not enough information about their reflection levels in saliva. The aim of the study is to reveal the relationship between the blood and saliva levels of these metabolites (urea, uric acid, creatinine) that accumulate in the blood in CKD.

METHODS: Before starting the study, ethics committee permission numbered 2022/14 was obtained. Then, chronic kidney disease patients (n=35) and healthy individuals (n=35) were included in the study. Blood and saliva samples of the participants were taken in the morning (09:00-12:00) and measured using a spectrophotometric device. Non-normally distributed data were examined with the Mann-Whitney U test, and normally distributed data were examined with the Independent Sample T test. The correlation between blood and saliva was examined with the Spearmann Rho coefficient. A value of $p < 0.05$ was considered significant.

RESULTS: No relationship could be detected between blood and saliva creatinine levels in CKD. In CKD, urea levels ($r=0.370$) and uric acid levels ($r=0.414$) in blood and saliva were positively correlated ($p < 0.05$).

CONCLUSIONS: Findings reflecting the relationship between urea and uric acid levels in blood and saliva in CKD show that saliva may be a potential non-invasive marker in revealing uremia in CKD. It is also thought that it may be useful to investigate the possible reasons why creatinine in the blood is not reflected in saliva in CKD. This study was supported by İnönü University Scientific Research Projects Unit (No: 2022/2974).

Keywords: Chronic Kidney Disease, Creatinine, Saliva, Urea, Uric Acid

PC-76

Poster was not presented at the meeting.

PC-77

Histological Examination of the Effects of Agomelatine in an Experimental Abortion Model

Mehtap Pervin¹, Orhan Sayın¹, Ahmed Sait Bozyıl¹, Mehmet Rıdvan Özdede¹, Hüsnâ Batmaz¹, Busenur Yaşar¹, Zeynep Dila Öz¹, İhsan Serhatlioglu², Nevin Kocaman³, Emine Kacar¹

¹Firat University, Faculty of Medicine, Department of Physiology, Elazığ, Türkiye

²Firat University, Faculty of Medicine, Department of Biophysics, Elazığ, Türkiye

³Firat University, Faculty of Medicine, Department of Histology and Embryology, Elazığ, Türkiye

AIM: Early pregnancy complications often include abortion, which is typically treated with progesterone administration and bed rest. However, the efficacy of these treatments remains inconclusive. Therefore, it is important to explore new therapeutic approaches. In this context, the aim of this study is to histologically demonstrate the potential therapeutic effect of agomelatine, known for its beneficial effects on the female reproductive system, on abortion.

METHODS: Eighty intact female Sprague-Dawley rats, aged 8-10 weeks with regular estrous cycles, were used. Eight groups were formed: control, sham, abortion, melatonin, agomelatine, progesterone, melatonin + progesterone, and agomelatine + progesterone (n=10). Administration of agents via oral gavage began on the first day of pregnancy. Melatonin was administered at 10 mg/kg/day, agomelatine at 10 mg/kg/day, and progesterone at 3.02 mg/kg/day for 14 days. An experimental abortion model was created by administering mifepristone (50 mg/kg) on the 11th day of pregnancy. Decapitation was performed on the 14th day without anesthesia. Uterine tissues fixed in 10% formalin were subjected to Hematoxylin & Eosin staining for histological examination. Statistical analyses were conducted using One-Way ANOVA/Kruskal-Wallis and post-hoc Tukey tests.

RESULTS: Histological examinations of uterine tissues revealed statistically significant differences between the abortion group and the treatment groups. Parameters such as decidual inflammation, congestion, cytotrophoblast, and syncytiotrophoblast showed higher histological changes in the treatment groups compared to the abortion group (p<0.0001). Decidual necrosis was higher in the treatment groups compared to both the abortion and control groups (p<0.0001).

CONCLUSIONS: The findings of the study suggest that the administration of agomelatine, either alone or in combination with progesterone, could be considered a potential approach for the treatment of abortion. These findings may provide a significant foundation for future research and could shed light on the development of treatment protocols. This study was supported by TUBITAK (Project No: 123S215).

Keywords: Abortion, Agomelatine, Histology, Pregnancy, Rat

PC78

Investigation of the Efficacy of Agomelatine on Depression-like Behaviors in an Experimental Abortion Model

Mehmet Rıdvan Özdede¹, Mehtap Pervin¹, Orhan Sayın¹, Ahmed Sait Bozyıl¹, Hüsnâ Batmaz¹, Abdullah Yaşar², İhsan Serhatlioglu³, Salih Burçin Kavak⁴, Emine Kacar¹

¹Firat University, Faculty of Medicine, Department of Physiology, Elazığ, Türkiye

² Firat University, Vocational School of Health Services, Elazığ, Türkiye

³ Firat University, Faculty of Medicine, Department of Biophysics, Elazığ, Türkiye

⁴Firat University, School of Medicine, Department of Obstetrics and Gynecology, Elazığ, Türkiye

AIM: Abortion is a serious health issue associated with the risk of fetal loss in the early stages of pregnancy, leading to both physical and psychological effects. Classical treatments for abortion often result in side effects such as depression, which can negatively impact patients' quality of life. Agomelatine is an antidepressant classified as *Category B*, known for its positive effects on the female reproductive system. The primary aim of this study is to demonstrate the efficacy of agomelatine on depression-like behaviors in an experimental abortion model using the forced swim test (FST).

METHODS: Eighty female Sprague-Dawley rats were used in the study. The animals were randomly divided into eight groups (n=10). The groups were as follows: control group (K), abortion group (Ab)(mifepristone 50mg/kg/day), progesterone group (P)(3.02 mg/kg/day), melatonin (10mg/kg/day)(M), melatonin + progesterone (MP), agomelatine (10mg/kg/day)(A), agomelatine (10mg/kg/day)+ progesterone (3.02 mg/kg/day) (AP). With FST, each group's swimming times and inactivity periods were recorded. Statistical analysis was performed using one-way analysis of variance(ANOVA), and the Tukey test was used for post-hoc evaluation.

RESULTS: According to the results of the FST; Swimming times were found to be higher in the M, MP, A and AP groups compared to the control group. In addition, the swimming times of A and AP were found to be higher than in the other treatment groups compared to Ab (p<0.01). In terms of duration of inactivity, a decrease was observed only in the agomelatine group compared to the control group (p<0.01).

CONCLUSIONS: Agomelatine was found to have positive effects on depressive behaviors, which are a cause of abortion. In particular, it has been shown to improve depression caused by progesterone. In this context, we think that agomelatine may be a potential agent in further studies in abortion cases where depression-like behaviors are included in the etiopathogenesis. This study was supported by TÜBİTAK (grant # 123S215).

Keywords: Abortion, Agomelatine, Forced swimming test, Pregnancy, Rat

PC79

Investigation of the Effects of Agomelatine on Cyclophosphamide-Induced Testicular Toxicity

Engin Korkmaz, Asiye Beytur, Suat Tekin

Inonu University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Cyclophosphamide (CP) is an agent used in the treatment of cancer and certain autoimmune diseases, known to induce various side effects including testicular toxicity. This study aims to evaluate the role of agomelatine against CP-induced testicular toxicity.

METHODS: Three month old male *Sprague Dawley* rats were randomly divided into four groups (n=10): i) control group received oral saline for 14 days, ii) CP group received oral saline for 14 days and a single dose of CP (200 mg/kg, intraperitoneally) on the 14th day, iii) Agomelatine group received agomelatine (40 mg/kg, orally) for 14 days, iv) CP+Agomelatine group received agomelatine (40 mg/kg, orally) for 14 days and a single dose of CP (200 mg/kg, intraperitoneally) on the 14th day. Levels of FSH, LH and testosterone in the plasma, as well as the levels of TNF- α , IL-1 β and NF- κ B in the testes were measured using the ELISA method; levels of SOD, GSH, CAT, MDA and GSH-Px in the testes were measured using spectrophotometric methods.

RESULTS: CP significantly decreased SOD, GSH, CAT and GSH-Px levels in testicular tissue, while increasing MDA, TNF- α , IL-1 β and NF- κ B levels (p<0.05). Pretreatment with agomelatine significantly attenuated these adverse changes induced by CP (p<0.05). CP administration resulted in a significant reduction in plasma FSH, LH and testosterone levels (p<0.05). In the CP+Agomelatine group, FSH, LH and testosterone levels were further reduced compared to the CP group (p<0.05). Additionally, agomelatine administration in healthy animals decreased FSH, LH and testosterone levels compared to the control group (p<0.05).

CONCLUSIONS: In conclusion, the findings suggest that agomelatine may mitigate CP-induced testicular damage through its antioxidative and anti-inflammatory properties. Additionally, it is hypothesized that agomelatine administration may inhibit the secretion of FSH, LH and testosterone by affecting the hypothalamic-pituitary axis.

Acknowledgements: This research was supported by Inonu University Scientific Research Projects Unit (Project no:TDP-2023-3373).

Keywords: Agomelatine, Cyclophosphamide, Oxidative stress,

PC-80

Effects of Humanin on Spermatogenesis and Mitochondrial Membrane Potential in Male Rats

Sinan Canpolat¹, Ebru Gökdere¹, Eda Çoban Ercan¹, İbrahim Halil Güngör², Rümeysa Esra Köm¹, Mehmet Emre Akipek¹, Ahmet Tuluhan Atmaca¹, Gaffari Türk²

¹Firat University, Faculty of Medicine, Department of Physiology, Elazığ, Türkiye

²Firat University, Faculty of Veterinary Medicine, Department of Reproduction and Artificial Insemination, Elazığ, Türkiye

AIM: Spermatogenesis is a lifelong process that requires coordinated mitochondrial and metabolic activities. During the stages of spermatogenesis, mitochondria play an important role in male fertility. Humanin, a mitochondrial-derived peptide that is abundantly expressed in the testes of many species, has been suggested to play a role in spermatogenesis. The aim of this study was to determine the effect of humanin on sperm parameters.

METHODS: Male Sprague-Dawley rats, 21 days old, weighing 35±2 grams, were divided into 2 groups (n=10) as control and humanin. Humanin were administered intraperitoneally at a dose of 1mg/kg/day for sixty days. At the end of the experiment, sperm motility, abnormal sperm ratios, and flow cytometric analyses were determined from the left epididymis and sperm density was determined from the right epididymis. The normal distribution of the data was confirmed by the Shapiro-Wilk test; Student's t-test was used for parametric data and Mann-Whitney-test for non-normally distributed data.

RESULTS: Humanin administration increased sperm density and motility compared to the control group. The head anomaly and total abnormal sperm rate were found to be decreased in the humanin group. (p<0.05). There was no difference in tail abnormality in both groups. The high mitochondrial membrane potential ratio was higher in the humanin group, while the normal and low mitochondrial membrane potential ratios were lower in the control group (p<0.05). There was no difference between the ratio of dead to live spermatozoa and the ratio of total acrosomal damage between the two groups.

CONCLUSIONS: The data obtained in our study suggest that humanin may play a role in spermatogenesis and in improving the abnormal spermatozoon ratio. It also showed that it may be effective in increasing mitochondrial membrane potential, which is an indicator of intact mitochondrial functionality for sperm to maintain motility.

This study was supported by TÜBİTAK (Project no:122S419).

Keywords: Humanin, Sperm Parameters, Mitochondrial Membrane Potential

PC-81

Investigating the Relationship Between Nitric Oxide Activity in the Brain and Reproductive Organs During the Estrous Cycle

Tuğba Kırboğa¹, Fatma Töre²

¹Bolu Abant İzzet Baysal University, Faculty of Medicine, Department of Physiology, Bolu, Türkiye; Erciyes University, Faculty of Medicine, Department of Physiology, Kayseri, Türkiye

²Atlas University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

AIM: Nitric oxide (NO), a versatile biological messenger, is an effective molecule in modulating many functions in the ovarian and uterine cycle of the female reproductive system. This study investigated the relationship between NO activity in the brain and reproductive organs during the stages of the rat estrous cycle.

METHODS: A total of 32 Wistar Albino female rats were sacrificed at different stages of the estrous cycle, 8 animals in each group (proestrus, estrus, metestrus, and diestrus) following vaginal smear monitoring. Plasma, brain, uterine, and ovarian tissues were collected. Nitrate and nitrite concentrations, the stable end products of NO, were measured using a colorimetric method to determine NO concentration. Plasma LH, FSH, and estradiol levels were measured using the ELISA method. The data were analyzed using the GraphPad Prism statistical program. Normally distributed data were analyzed with One-way ANOVA, while non-normally distributed data were analyzed using the Kruskal-Wallis test.

RESULTS: The total brain tissue NO level was significantly higher in the metestrus phase compared to the estrus phase ($p<0.05$). The NO level in uterine tissue was significantly higher in the estrus phase compared to other phases ($p<0.01$). NO levels in ovarian tissue and plasma showed no statistically significant difference. Plasma FSH levels were significantly higher in the proestrus phase compared to the diestrus phase ($p<0.01$). Plasma estradiol levels were significantly higher in the proestrus phase compared to other phases ($p<0.001$).

CONCLUSIONS: This study indicates that the high levels of uterine NO during the estrus phase suggest that NO is involved in the menstrual cycle. The increase of NO in brain tissue during the metestrus phase could be associated with premenstrual syndrome in women and, particularly, with migraines that occur with premenstrual attacks.

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Keywords: Nitric oxide, Estrus cycle, Rat

PC-82

Effects of Different Doses of Lavender (*Lavandula angustifolia*) on Pubertal Development and Hormones in Male Syrian Hamsters (*Mesocricetus auratus*)

Emine Inci Balkan¹, İlke Ceren Kırıl², Bülent Gündüz²

¹Demiroğlu Bilim University, Vocational School of Health Services, Department of Medical Laboratory Techniques, Istanbul, Türkiye

²Çanakkale Onsekiz Mart University, Faculty of Science, Department of Biology, Çanakkale, Türkiye

AIM: The effects of lavender, known for its calming effect, on the nervous system and reproductive system are being investigated. This study examines the development of male offspring exposed to different doses of lavender extract from the pregnancy period onwards.

METHODS: Eight adult female and forty adult male offspring Syrian hamsters in a long photoperiod (16L) were assigned to four groups: the control group, the groups that received 50 mg/kg, the groups that received 100 mg/kg, and the groups that received 200 mg/kg lavender extract applied. Lavender extract was injected to the pregnant females in the experimental group during the last week of pregnancy and throughout the lactation period. From the 15th day after birth, male offspring were separated into groups of 5, with blood samples taken at midday and midnight. The doses were injected for 40 days. Weekly testis measurements were taken. Changes in serum leptin and testosterone hormones taken at the end of the experiment were determined. Testis histology was examined.

RESULTS: The experimental groups showed no significant difference in leptin levels ($p>0.05$), although testosterone levels remained lower than in the control group ($p<0.05$). Testicular weights in the 100 mg/kg and 200 mg/kg groups were significantly lower than in the control group ($p<0.05$). Additionally, there was a decrease in Leydig cells and spermatogenesis in testicular histology in these groups.

CONCLUSIONS: The physiological effects of plant extracts are not well studied, despite the fact that lavender is being used more and more in various fields. However, it is also known that higher dosages lower testosterone hormone levels and suppress the reproductive system in mature animals. This study evaluated the effects of various doses of lavender on the reproductive development of pubertal offspring from pregnancy onward, and for the first time, it was found to have negative impacts on development.

Keywords: Lavender, Leptin, Syrian hamster, Pubertal development, Testosterone

PC-83

The Effect of Calorie Restriction on Testicular Tissue During Aging Process

Esra Toker¹, Ayça Coşkun², Arzu Keskin Aktan³, Saadet Özen Akarca Dizakar⁴, Kazime Gonca Akbulut¹

¹Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye; ²Sakarya University of Applied Sciences, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Sakarya, Türkiye; ³Gazi University, Faculty of Medicine, Department of Physiology, Ankara, Türkiye; ⁴Afyonkarahisar University of Health Sciences, Faculty of Medicine, Department of Physiology, Afyonkarahisar, Türkiye; ⁵Izmir Bakircay University, Faculty of Medicine, Department of Histology and Embryology, Izmir, Türkiye

AIM: Aging is associated with free radical damage. Calorie restriction (CR) reduces oxidative stress. This study, aimed to examine the effect of CR on physiological and histological changes in the testicular tissue during the aging.

METHODS: In the study, young (3 months old) (n=12) and old rats (20 months old) (n=12) were divided into two groups as control and experimental groups. While the control group was fed ad libitum, CR group were given a diet containing about 1/3 (~1,303 kcal/kg) of the daily calorie intake of dietary content (14% fat, 52% protein, 34% carbohydrates). Weight change and organ index [(Testicular weight/body weight) × 100] were calculated. Plasma testosterone levels were measured by Chemiluminescent Immunoassay method at the end of 10 weeks. Malondialdehyde (MDA) and glutathione (GSH) was measured in testicular tissue by TBARS method and modified Ellman method respectively. Histological analyses were also performed by hematoxylin-eosin staining. Data were analyzed using one-way ANOVA, paired sample t test, and Pearson's r.

RESULTS: Body weight changes were different in all groups (p<0.05). Aging decreased organ index, plasma testosterone and testicular GSH level, while increasing MDA level (p<0.05). CR decreased body weight and testosterone levels in young and old rats, increased organ index, decreased testicular weight and MDA level in old rats (p<0.05). Plasma testosterone level and weight change were positively correlated, while testicular MDA level and organ index were negatively correlated. Aging caused irregularities and atrophic changes in seminiferous tubules and interstitial space. In the aged group, CR increased seminiferous tubule degeneration and impaired structural integrity in the peritubular space.

CONCLUSIONS: Our present results suggest that young and old rats, CR may positively affect the aging process by reducing oxidative stress although it could increase organ index and decrease testosterone levels.

This project was supported by Gazi University Scientific Research Project Unit (Project No: TCD-2023-8842/Project ID: 8842).

Keywords: Aging, Calorie Restriction, Testosterone, Oxidative Stress

PC-84

Investigation of the Protective Effect of Lacticaseibacillus casei and Its Postbiotic on Liver Tissue in Rats

Buse Nur Sülük¹, Nurhan Gumral², Tugba Kök Taş³, Rahime Aslankoç², Cahide Aslan¹, Oğuzhan Kavruk²

¹Suleyman Demirel University, Health Sciences Institute, Department of Physiology, Isparta, Türkiye

²Suleyman Demirel University, Faculty of Medicine, Department of Physiology, Isparta, Türkiye

³Suleyman Demirel University, Faculty of Engineering, Department of Food Engineering, Isparta, Türkiye

AIM: The gut-liver axis, which supports the immune and neuroendocrine system interaction, plays a role in the regulation of symbiosis between intestinal microbiota and liver. Probiotics and their metabolites have been shown to have direct or indirect antioxidant capacities. Postbiotics are defined as non-living microorganisms or their components that provide health benefits to humans. In our study, the possible effects of the probiotic Lacticaseibacillus casei (L. casei) bacteria and its postbiotic culture on rat liver tissue were investigated.

METHODS: Rats were divided into three groups as control (n=8), probiotic (n=12) and, postbiotic (n=12). For 42 days; 0.5 ml/day tap water was given to control group, 0.5 ml/day (9.6 log cfu/rat) of L. casei culture supplement prepared as 10 log cfu/ml was given to probiotic group, and 0.5 ml/day of the liquid prepared by inactivating live bacteria by heat treatment at 121°C for 20 minutes was given to postbiotic group. At the end of the experiment, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin were analyzed in the serum, and malondialdehyde (MDA), superoxide dismutase (SOD) and catalase (CAT) were analyzed in the liver tissue (Ethics Number:2024-310).

RESULTS: In serum AST values, a significant decrease was observed in both probiotic and postbiotic groups compared to the control group (p<0.05). No significant difference was detected in ALT and albumin values. In liver tissue analyses, it was determined that postbiotic supplementation reduced the MDA level, an oxidative stress marker, more compared to the probiotic group (p<0.05). Probiotic supplementation was observed to significantly increase the SOD value compared to the control group (p<0.05). No significant difference was detected between the groups in CAT values.

CONCLUSIONS: In conclusion, we think that probiotic L. casei and postbiotic application produced from it may be effective in preventing liver damage by protecting hepatocytes against oxidative damage and that further studies on the gut-liver axis are necessary.

Keywords: Probiotic, Postbiotic, Microbiota, Liver, Antioxidant

PC-85

Evaluation of the Effect of HMW-PVC Microplastic on rat Internal Organs and Gene Expression level

Ayper Boğa Pekmezekmek, Mustafa Emre², Erdal Tunç³, Seda Ilgaz⁴, Hale Öksüz⁴, Seyda Erdoğan⁵, Tuğba Toyran⁵, Toygar Emre⁶, Yasar Sertdemir⁷, Betül Kalay⁸, Nesrin Emre⁹, Yılmaz Emre⁹

¹Çukurova University, Faculty of Medicine, Department of Physiology, Adana, Türkiye; ²Çukurova University, Faculty of Medicine, Department of Biophysics, Adana, Türkiye; ³ Mardin Artuklu University, Faculty of Medicine, Department of Medical Biology and Genetics, Mardin, Türkiye; ⁴Çukurova University, Faculty of Medicine, Department of Medical Biology and Genetics, Adana, Türkiye; ⁵Çukurova University, Faculty of Medicine, Department of Pathology, Adana, Türkiye; ⁶Boğaziçi University, Faculty of Engineering, Industrial Engineering, Istanbul, Türkiye; ⁷Çukurova University, Faculty of Medicine, Department of Biostatistics, Adana, Türkiye; ⁸Çukurova University, Faculty of Medicine, Department of Pharmacology, Adana, Türkiye; ⁹Akdeniz University, Faculty of Education, Department of Mathematics and Science Education, Antalya, Türkiye

AIM: Our study aims to investigate the effects of 8-week chronic exposure to High Molecular Weight Polyvinyl Chloride (HMW-PVC) microplastic specially added to the pellets of young rats.

METHODS: A total of 40 young Wistar male rats were used in the study, 30 in the experimental groups (Group 1:15, Group 2:15) and 10 in the control group. Their weights were recorded every 15 days. At the end of the eight week, rat intestines, kidneys and livers were dissected under ketamine-xylazine anesthesia. Intestine, kidney and liver were examined histopathologically. Real-time quantitative PCR was used to examine mRNA expression rates of Cyp3A2, Pepck and Fasn genes in the liver; UT-A1, UT-A2, Renin and Cyp27B1 genes in the kidney; and Muc2, Fabp2 and PepT1 genes in the intestine. For homogeneous and non-homogeneous data, one-way ANOVA with Tukey test and Kruskal-Wallis with Man-Whitney U tests were used.

RESULTS: Our weight analysis revealed that there was no significance between the first group and the control group ($p > 0.05$), but the significance between the second group and the control group was quite high ($p < 0.001$). In the experimental groups, there were different levels of portal inflammation in the liver tissue, interstitial nephritis in the kidney and inflammation in intestinal tissue. Additionally, surface epithelial loss, mucus loss, and edema were observed. In RT-PCR analysis; compared to the control group, it was found that muc2, fab2 gene expression decreased in the intestine, while pept1 gene expression increased. While the expression of Cyp3a, Pepck and Fasn decreased in the liver in Group2, UT-A1, UT-A2 gene expression and Cyp27B1 gene expression increased in the kidney in Group1; renin gene expression decreased.

CONCLUSIONS: Since microplastics can enter our organs and cause harmful effects, precautions must be taken against this situation for our health.

Keywords: HMW-PVC, mRNA genes, UT-A, Cyp27B1, Muc2, Fabp2, Pep1, Cyp3a, Pepck, Fasn

PC-86

Effects of Gel-like Cell Protection Matrix Formulation on Cell Homeostasis

Reyhan Coban, Ozlem Yesil-Celiktas

Ege University, Faculty of Engineering, Department of Engineering, Izmir, Türkiye

AIM: The failures and various disadvantages associated with animal models in preclinical studies have led to a search for more humanized systems. Among these, humanized cell models have emerged as powerful tools for investigating particular disease mechanisms. However, the transportation of these cells to geographically distant locations still remains as a challenge. This study aims to synthesize a biocompatible hydrogel to ensure the stability and homeostasis of cells, enabling their transportation.

METHODS: Two distinct gelatin-based hydrogel materials were synthesized for the transportation of cells at two different temperatures. Experimental setups were designed for each condition, aiming to maintain cell homeostasis for embedded cells within the gel for up to 7 days under both conditions. To validate the viability of cells within the gel, a negative control group was also established. In the negative control groups, cells were kept in their native environment under the two different conditions, allowing the impact of the gel on cell viability to be assessed. Both quantitative and qualitative analyses were performed at five designated time points.

RESULTS: Viability of the different cell types in the gel was assessed at different time points during 7 days. The findings show that, while there was no significant difference in viability compared to the negative controls during the initial 24 hours due to the adaptation process to the environment and gel, a significant increase in viability was observed in the cells embedded in the gel at the 48-hour mark and beyond, compared to the negative controls ($p < 0.05$). This increase was substantiated through both qualitative and quantitative analyses. Additionally, it was demonstrated that the cells maintained viability in the gel at both conditions throughout the 7-day period ($p < 0.05$).

CONCLUSIONS: The developed gel effectively maintained the stabilization and homeostasis of the cells during the 7-day period at the transportation process simulated at both conditions.

Keywords: Gel-like cell protection matrix, Cell homeostasis, Hydrogel formulation, Cell transportation, Gelatin-based hydrogel

PC-87

Investigation of the Effects of Mononuclear Leukocytes on Platelet Functions and Hemostasis

Öznur Gürel¹, Fatma Özer¹, Sueda Güneş¹, Didem Çakırsoy Akyöney², Digidem Yoyen-Ermis³, Engin Sagdilek⁴

¹Bursa Uludag University, Institute of Health Sciences, Department of Medicine-Physiology, Bursa, Türkiye

²Bursa Uludag University, Institute of Health Sciences, Department of Medicine-Immunology, Bursa, Türkiye

³Bursa Uludag University, Faculty of Medicine, Department of Immunology, Bursa, Türkiye

⁴Bursa Uludag University, Faculty of Medicine, Department of Biophysics, Bursa, Türkiye

AIM: Hemostasis is the first response that occurs in the process of repairing tissue damage, and it is a complex event that proceeds primarily through the interaction of platelets, then other cell groups. In addition to indirect communication through secreted factors, platelets have been reported to cluster primarily with monocytes, neutrophils, and to a lesser extent with lymphocytes to form heterogeneous complexes. Our aim in this study is to study the interaction of mononuclear cells (monocytes/lymphocytes) with platelets and hemostasis.

METHODS: In order to evaluate the effect of mononuclear cells on the hemostasis process, thromboelastogram, and aggregometer devices were used. Assessments were made immediately after the mononuclear cells were separated from the blood (0th hour) and after 22 hours of being kept waiting without and with LPS stimulation. The effect of mononuclear cells added to platelet-rich plasma on platelet aggregations stimulated by ADP and collagen and on thromboelastogram parameters were investigated. Paired t-test and Bonferroni Test was used for comparisons.

RESULTS: In ADP and collagen-induced experiments, mononuclear cells significantly decreased maximum aggregation values in both 0th and 22nd hour stimulated and unstimulated conditions. In 0th hour, mononuclear cells did not affect thromboelastogram parameters, while mononuclear cells incubated with and without LPS stimulation for 22 hours significantly changed thromboelastogram parameters and activated hemostasis.

CONCLUSIONS: While mononuclear cells inhibited platelet aggregation in all cases, mononuclear cells incubated with and without stimulation for 22 hours showed hypercoagulant effects in thromboelastogram experiments. It was observed that the effects of mononuclear cells on platelets and hemostasis may differ depending on time. Contradictory findings between thromboelastogram and aggregometer suggested that the measurement system in thromboelastogram should be considered more accurate and reliable because it simulates in-vivo conditions better and is more compatible with other hemostasis tests and clinical situations.

Keywords: Hemostasis, Platelets, Platelet-monocyte aggregation.

PC-88

Comparison of the Cytotoxic Activities of *Stachys Lavandulifolia* and *Stachys Cataonica* Species

Hande Yüce¹, Rıdvan Özgen², İsmet Gürhan², Dilan Aşkın Özek³, Yasemin Şahin⁴, Kevser Tanbek⁵, Turan Arabacı², Songül Ünüvar¹, Süleyman Sanda⁵

¹İnönü University, Faculty of Pharmacy, Department of Pharmaceutical Toxicology, Malatya, Türkiye; ²İnönü University, Faculty of Pharmacy, Department of Pharmaceutical Botany, Malatya, Türkiye; ³Fırat University, Kovancılar Vocational School of Health Services, Department of Pharmacy Services, Elazığ, Türkiye

⁴Pamukkale University, Faculty of Medicine, Department of Medical Biology, Denizli, Türkiye; ⁵İnönü University, Faculty of Medicine, Department of Physiology, Malatya, Türkiye

AIM: Our study evaluated the essential oil components and cytotoxic activities of two plant species of the genus *Stachys* found in Türkiye, *Stachys lavandulifolia* and *Stachys cataonica* to investigate their potential for use in the treatment.

METHODS: The composition of the essential oils obtained from both plants was determined using a GC-MS system. The essential oil samples were applied to human neuroblastoma cells (SH-SY5Y) and fibroblast cells (L929) at increasing concentrations (0.125, 0.25, 0.5, 1, 2.5, 5 µM) to assess their cytotoxic activities using the MTS method. Using the ELISA method, cell viability was measured in 24 and 48 hours.

RESULTS: *S.cataonica* contains 41.11% α-pinene, while *S.lavandulifolia* contains 16.57% α-pinene. In *Stachys cataonica*, 52 different compounds were determined except α-pinene. The main ones are caryophyllene, humulene and bicyclogermacrene. In *S.lavandulifolia*, 90 compounds were determined. The main ones are sabinene, myrcene and spathulenol. After 24 hours of application, the IC50 values for the essential oil of *S. cataonica* were found to be 0.630 µM for L929 cells and 0.251 µM for SH-SY5Y cells. After 48 hours, the IC50 values were 0.627 µM for L929 cells and 0.359 µM for SH-SY5Y cells. For the essential oil obtained from *S.lavandulifolia*, the IC50 values after 24 hours of application were 0.650 µM for L929 cells and 0.160 µM for SH-SY5Y cells. After 48 hours, the IC50 values were 0.690 µM for L929 cells and 0.240 µM for SH-SY5Y cells. IC50 values were calculated using the GraphPad Prism 8 program.

CONCLUSIONS: Both essential oils demonstrated cytotoxic activity by reducing cell viability in neuroblastoma cells at lower concentrations than healthy cells. However, the cytotoxic activity of *S. lavandulifolia* on neuroblastoma cells was found to be higher than that of *S. cataonica*. This study was supported by the Scientific Research Projects Unit İnönü University (Project # TCD-2024-3690).

Keywords: *Stachys lavandulifolia*, *Stachys cataonica*, Essential oil, Anticancer activity.

PC-89

The Effect of Different Zinc Doses on Uterine Contractions and the Possible Roles of the Zinc Finger Protein, ZEB1, in this Effect

Serife Dokuyucu¹, Aylin Üstün², Elif Gülbahçe Mutlu³, Nilüfer Akgün Ünal⁴, Rasim Mogulkoc¹, Abdulkerim Kasim Baltaci¹

¹Selçuk University, Faculty of Medicine, Department of Physiology, Konya, Türkiye; ²Selçuk University, Vocational School of Health Services, Konya, Türkiye; ³KTO Karatay University, Faculty of Medicine, Department of Medical Biology, Konya, Türkiye; ⁴Ondokuz Mayıs University Faculty of Medicine, Department of Biophysics, Samsun, Türkiye

AIM: The aim of this study is to investigate the effect of different zinc doses on uterine contractions and the possible roles of ZEB1, a zinc finger protein, in this effect.

METHODS: The protocol of the study conducted on adult female Wistar rats was approved by the local ethics committee. Measurement of uterine contractions of a total of 20 rats in the isolated organ bath was completed in 5 days, 4 animals per day. The doses to be administered during uterine contractions were as stated below. One of the two uterine muscles removed from the first rats brought to the electrophysiology laboratory for the recording of uterine contractions was used for spontaneous contraction (right uterus) and the other (left uterus) was used for zinc chloride application at a dose of 1 micromol/L. Likewise, one of the removed uterine muscles of the next rats brought to the laboratory (right uterus) was used for zinc chloride application at a dose of 10 micromol/L, and the other (left uterus) was used for zinc chloride application at a dose of 100 micromol/L. Levels of ZEB1, a zinc finger protein, in the uterine tissues of rats used for contraction parameters in isolated organ baths were determined by ELISA method.

RESULTS: In our study, cumulative 1µM and 10µM in vitro zinc applications did not differ from the control group in terms of contraction strength, contraction force and contraction frequency in the uterine muscles, but caused a limited increase in ZEB1 levels (p<0.05). However, 100 µM in vitro zinc application resulted in suppression of the same parameters (p<0.05).

CONCLUSIONS: The results of the current study show that a 100 µM in vitro zinc dose causes a toxic effect on uterine muscles, suppressing both contraction parameters and ZEB1 levels. In vitro zinc administration has a dose-dependent effect on uterine contractions.

Keywords: Uterine Contractions, Zinc, ZEB1, Rat

PC-90

Evaluation of Exercise Capacity and Quality of Life in Individuals Recovered from COVID-19

Demet Erdogan¹, Tijen Acarkan¹, Meltem Yalçın³, Burçin Tuvana Us², Banu Musaffa Salepci⁴, Mehtap Kaçar¹

¹Yeditepe University, Institute of Health Sciences, Department of Pathophysiology, Istanbul, Türkiye

²Yeditepe University, Institute of Health Sciences, Department of Physiology, Istanbul, Türkiye

³Yeditepe University, Faculty of Medicine, Department of Physiology, Istanbul, Türkiye

⁴Yeditepe University, Faculty of Medicine, Department of Chest Diseases, Istanbul, Türkiye

AIM: This study aimed to evaluate cardiopulmonary exercise endurance, autonomic nervous system function, inflammatory status, and quality of life in individuals recovered from COVID-19 compared to those not infected.

METHODS: A total of 100 volunteers, 50 with a history of COVID-19 and 50 without, participated in the study. Cardiopulmonary Exercise Testing (CPET), Spirometry, Heart Rate Variability (HRV), inflammatory markers, and Copeptin levels were assessed. Fatigue Severity Scale (FSS) and Short Form-36 (SF-36) questionnaires were administered. Normality of data was evaluated using the Shapiro-Wilk test; between-group differences were analyzed using the Student's t-test or Mann-Whitney U test. Correlation analysis was used to investigate the relationship between fatigue score and spirometry and CPET parameters in the COVID-19 group. Pearson's correlation coefficient was used for normally distributed variables, and Spearman's for non-normally distributed ones. Correlation coefficients (r) and significance levels (p<0.05) were reported.

RESULTS: No significant differences were found in CPET results between groups. Among the COVID-19 group, 56% terminated the test due to fatigue compared to 34% in the control group (p<0.05). A significant negative relationship was found between fatigue severity and MVV in those with COVID-19 (r=-0.326, p=0.021). Weak negative correlations between fatigue severity and FEV1, VO2peak, and PEF were observed but were not statistically significant. HRV analysis revealed lower HF values and higher LF/HF ratios in the COVID-19 group (p<0.05). While hsCRP, ferritin, LDH, fibrinogen and D-dimer showed no significant change, lymphocyte counts were significantly lower in the COVID-19 group (p<0.05). **CONCLUSIONS:** Individuals who recovered from COVID-19 exhibited reduced exercise capacity, respiratory dysfunction, and low-grade inflammation. The significant negative correlation between MVV and fatigue suggests a lasting impact on respiratory capacity. Autonomic dysfunction may also persist post-COVID-19. This study was supported by Yeditepe University Research Projects and Scientific Activities (Project number: YAP-AP-SAB-22035).

Keywords: COVID-19, CPET, Spirometry, HRV, SF-36, Fatigue

PC-91

Ultrasonography in Embryological Animal Research: A Proposal for a Scoring System

Aylin Gökhan, Kubilay Doğan Kılıç

Ege University, Faculty of Medicine, Department of Histology and Embryology, İzmir, Türkiye

AIM: This study aims to evaluate the efficacy of abdominal ultrasonography (USG) in monitoring embryogenesis in pregnant rats and to establish a standardized scoring system for assessing developmental toxicity caused by exposure to various agents, enhancing the precision and reliability of developmental toxicity assessments.

METHODS: Copulation was predicted based on vaginal plug/smear results, with the noon following the mating night designated as embryonic day 0 (E0) for positive results. Minimal sedation was administered prior to the ultrasound, and ample gel was applied to avoid abdominal shaving. USG was performed using the Edan Dus 60 ultrasound device during the first trimester with a high-frequency probe to locate the uterus and embryos. Images and videos were captured in multiple planes (sagittal, transverse, and coronal) for comprehensive visualizations. A scoring system was developed to evaluate the severity of findings, incorporating specific criteria for each developmental stage. Both maternal and embryonic anomalies were systematically recorded.

RESULTS: Ultrasound scans at embryonic day 9 (E9) revealed small fluid-filled sacs with detectable heartbeats, neural tube formation, and initial somite segmentation. By embryonic day 13 (E13), more complex structures such as limb buds, organ formations, and dense vascularization were observed. The scoring system effectively identified normal milestones, such as well-defined neural tube and somite formation at E9, and strong heartbeats and proper limb formation at E13. It also highlighted abnormalities, including weak heartbeats and irregular somite segmentation at E9, and slowed growth and organ dysfunction at E13.

CONCLUSIONS: Abdominal ultrasonography is a valid and reliable method for non-invasive daily monitoring of rat embryo development. The scoring system represents a significant advancement in embryological studies, offering a framework for assessing developmental toxicity. USG can identify critical stages and detect abnormalities due to intrauterine exposure, improving experimental protocols and developmental toxicity assessments.

Keywords: Abdominal Ultrasonography, Embryogenesis, Developmental Toxicity, Prenatal Imaging, Embryo Development, Ultrasonographic Scoring

PC-92

Coenzyme Q10 and the Number of Pregnancies: Investigating the Effects of the Coenzyme Q10 Supplementation on Learning-Memory Impairment and Anxiety Associated with Increased Number of Births

Ahmet Furkan Gezer¹, Elif Türkdönmez Ak²

¹Ondokuz Mayıs University, Faculty of Medicine, Department of Physiology, Samsun, Türkiye; ²Ordu University, Faculty of Medicine, Department of Physiology, Ordu, Türkiye

AIM: Women can experience intense physiological and psychological changes during pregnancy and the postpartum period. The present study aimed to investigate whether coenzyme Q10 (Q10) supplementation affects learning memory, and anxiety, which may worsen with an increasing number of pregnancies.

METHODS: Following ethical approval (OMÜ-HADYEK 2024/11, with support from TÜBİTAK), 3-month-old female Wistar rats (n=72) were divided into four groups as virginal and breeding groups—that is, one, two, and three times breeding. Each group consisted of solvent (soybean-oil)- and Q10 (200mg/kg)-applied groups with naive controls. 24 hours after the 10-day administration, subjected to y-maze and elevated-plus-maze test. Statistically, according to the Shapiro-Wilk test, t-test, one-way ANOVA test were applied.

RESULTS: According to y-maze test, breeding rats spent longer in the first arm than virgins (p<0.05). Staying time in the first arm was not changed by the drug in the virgins, but it was prolonged in both the naive-control and breeding-drug groups (p<0.05); this effect was more pronounced in the three-time breeding group (p<0.001). In addition, the parameters of the total number of entries in all arms and the number of alternations decreased in the drug-treated breeding groups (p<0.01). In the elevated plus-maze test, there was no significant change in the closed-arm entry in the solvent-given-virgins compared to the naïve group. However, in breeding rats, the number of entries into the closed-arm was significantly increased compared to virgin-naïve controls (p<0.05). While the time-spent in the closed-arm was short in controls of each group, among the drug-treated groups, only the three-time-breeding group showed a statistically significant difference (p<0.05).

CONCLUSIONS: According to behavioral tests, there were no significant differences between single or multiple births; however, there are statistically significant differences between the virginal and breeding groups. Furthermore, contrary to expectations, the Q10 was adversely affected. We speculate that the dose in the literature or the solvent may be toxic.

Keywords: Anxiety, Co-enzyme Q10, Learning-memory, Number of births, Pregnancy

PC-93

The Effect of Maternal Sleep Quality on Newborn Anthropometric Parameters

Elif Selin Karanfil¹, Rahime Aslankoç¹, Sena Üner Karaköse¹, Ayça Coşkun¹, Adnan Karaibrahimoğlu²

¹Süleyman Demirel University, Faculty of Medicine, Department of Physiology, Isparta, Türkiye

² Süleyman Demirel University, Faculty of Medicine, Department of Biostatistics and Medical Informatics, Isparta, Türkiye

AIM: Poor maternal sleep quality may cause adverse postnatal outcomes such as low birth weight on the fetus. In this study, we aimed to investigate the effects of sleep quality of healthy pregnant women in the third trimester on anthropometric measurements of the newborn.

METHODS: A total of 35 pregnant women and their newborns were included in the study. Participants were recruited from designated family health centers and met the following inclusion criteria: age 18 years or older, willingness to participate, and gestational age between 28 and 32 weeks. Ethical approval for the study was obtained from the Clinical Research Ethics Committee of Süleyman

Demirel University Faculty of Medicine. Verbal consent was obtained from all participants. Data was collected using a two-part questionnaire including the Pittsburgh Sleep Quality Index (PSQI) and demographic information. Data was presented as median and p-values less than 0.05 were considered statistically significant.

RESULTS: PSQI score was 6.44, and the median was 6. The mean birth weight of the infants was 3260 grams, length was 49.25 cm, and head circumference was 34.6 cm. No significant correlation was found between the PSQI and newborn anthropometric measurements. A negative correlation was found between infant birth weight and the PSQI score, but this correlation was not statistically significant ($r=-0.299$; $p=0.115$). There was no significant difference in maternal PSQI scores based on mode of delivery ($p=0.128$). However, mothers who underwent cesarean delivery had a higher mean PSQI score (6.62) compared to those who had vaginal births (4.40).

CONCLUSIONS: Our findings suggest a potential association between poor maternal sleep quality and decreased birth weight in newborns. However, larger-scale studies are required to confirm this relationship and explore underlying mechanisms.

Keywords: Sleep quality, Pregnant women, Newborn, Anthropometric Parameters

PC-94

The Effects of Living Apart from Their Families on Mood and Eating Habits of Pamukkale University Medical Faculty Students

Dilek Sayın¹, Tunahan Anber¹, Hasan Akça¹, Özgen Kılıç Erkek¹, Fatih Altıntaş¹, Hande Şenol², Edanur Delibaşoğlu¹, Nurcan Doğan¹, Melek Bor Küçükatay¹

¹Pamukkale University, Faculty of Medicine, Department of Physiology, Denizli, Türkiye

²Pamukkale University, Faculty of Medicine, Department of Biostatistics, Denizli, Türkiye

AIM: Anxiety, depressive disorders and impaired eating behaviors are interconnected. Macro and micro-nutritional disturbances alter body composition and levels of elements like zinc (Zn), copper (Cu), and magnesium (Mg). Medical students frequently suffer from anxiety and depression due to intense coursework and exam stress, particularly those living away from their families. At Pamukkale University Faculty of Medicine (PAUMF), the Problem-Based Learning (PBL) system encourages active participation in disease scenarios and learning objectives in groups for 4-8 hours weekly, emphasizing social interaction and including courses on communication. Clinical education, such as psychiatry is provided from the first year. This study aims to investigate the effects of living away from family on trace element levels, anxiety, depressive mood and neuritin, BDNF levels in PAUMF students.

METHODS: Following approval from Pamukkale University Non-Interventional Clinical Research Ethics Committee (E-60116787-020-353819), 97 PAUMF students (61 female, 36 male) were categorized into two groups: those living with their families (LWF, n=23) and those living away (A, n=74). Participants were

administered the Dutch Eating Behavior Questionnaire (DEBQ), Hamilton Anxiety Rating Scale and Beck Depression Scale. Body composition was analyzed using TANITA BC 418 MA and BMI was calculated. Venous blood samples were collected and serum/erythrocyte Zn, Cu and Mg levels were measured via atomic absorption spectrometry (Perkin Elmer-Analyst400). Plasma BDNF and neuritin levels were determined by ELISA. Data were analyzed using SPSS package program.

RESULTS: There was no significant differences in eating behavior, anxiety or depression levels between the groups. No differences were also observed in body composition, serum/erythrocyte trace element levels or plasma BDNF and Neuritin levels.

CONCLUSIONS: Our findings show that students are successful in maintaining their general health levels under challenging conditions. The education system implemented in our faculty and the appropriate communication environment may contribute to this situation.

Keywords: Trace elements, Medical education, PBL, BDNF, Neuritin

PC-95

Evaluation of the Difference Between BAUN Faculty of Medicine 1st and 2nd Year Students in terms of Stroop, Visual and Auditory Digit Span and Cancellation Test performance

Yunus Emre Özer, Burak Şafak, Hüseyin Deniz, Çisem Çoşgun, Gülten Erken

Balıkesir University, School of Medicine, Department of Physiology, Balıkesir, Türkiye

AIM: Cognitive functions are affected by various factors. The aim of the study was to evaluate some cognitive functions in 1st (D1) and 2nd (D2) year students of the Faculty of Medicine.

METHODS: A total of 46 men and women D1 (n=23) and D2 (n=23) students studying at Balıkesir University Faculty of Medicine participated. Demographic characteristics of the participants were recorded. Stroop, Visual Auditory Digit Span (GISD) and Cancellation Test were applied to all participants to assess cognitive flexibility, memory and attention, respectively. Shapiro-Wilk and Mann-Whitney U tests were used to analyse the data and, $p<0.05$ was considered significant.

RESULTS: In the Stroop Test, no significant difference was found between the groups for the five parts of the test in terms of completion time, number of errors and number of corrections. According to GISD Test, no significant difference was found between the groups for auditory-verbal, visual-verbal, auditory-written and visual-written tests. The regular letters, regular shapes, irregular letters and irregular shapes forms in the Cancellation Test were evaluated in terms of test completion time, no significant difference was found between the groups; however, the number of targets marked was higher in D1 than D2 in the regular letters, irregular letters and irregular shapes forms ($p<0.01$). In the regular shapes form, no significant difference was found between the groups in terms of the number of marked targets.

CONCLUSIONS: No significant change was observed in terms of cognitive flexibility and memory. It was determined that the attention level of D1 students measured by the marking test was higher than that of D2 students. Considering that the stress level of D1 students may be higher than D2 students due to the adaptation process to new conditions, stress may have had moderate positive effects on attention. Further studies are needed.

Keywords: Cancellation test, Cognitive function, Stroop test, Visual auditory number strings test

PC-96

Psychological Distress Level of Cigarette User Students at Samsun University

Meryem Dilek Acar¹, İlayda Elitok², Zeynep Yaren Aydın², Burak Emirhan Çalışkan², Nazlı Hilal Ertekin²

¹Samsun University, Faculty of Medicine, Department of Physiology, Samsun, Türkiye

²Samsun University, Faculty of Medicine, Samsun, Türkiye

AIM: Free radicals caused by smoking leads oxidative stress-induced damage in the central nervous system. The aim of the research was to investigate the possible depression and anxiety levels that may develop as a result of smoking in undergraduate and graduate students.

METHODS: Depression and anxiety levels of n=310 non-smoker students (control group) and n=223 smoker students (17-30 years old) at Samsun University were determined by using the Kessler Psychological Distress Scale-K10. The Shapiro-Wilks test, the independent samples t-test, the One-Way ANOVA model were used for statistical analyses. Relationships between categorical features were examined by the Pearson chi-square test.

RESULTS: The mean age of non-smoking students was 19.60 and the mean age of smoking students was 20.65. Smoking rate was higher in man students (<0,001). The average score of the non-smokers and the smokers was respectively 25.31 and 29.10 points according to the Kessler Psychological Distress Scale-K10 (p<0.001). There were no significant linear relationship between age and psychological distress score in non-smokers (p=0,188) and in smokers (p=0,209). The duration (<2, 2-<5, ≥5 years) (p=0,358) and the amount (<10, 10-<15, ≥15 cigarette/day) (p=0,189) of smoking had not statistically effect on psychological distress. When non-smokers and smokers were excluded who consumes alcohol, who have serious chronic disease (cancer, diabetes, autoimmune disease etc.), who have first-degree relative with a psychiatric disorder (such as anxiety, depression, major depression, schizophrenia, bipolar disorder), who have fatal illness/dead/missing person from family members/close circle in last 12 months, the scores of the remaining 222 non-smokers were lower than the scores of 99 smokers (p<0.001). Probable well-being (32,4%) and propabl mild mental illness (23,9%) were higher in non-smokers (n=222), while propabl severe mental illness (45,5%) was higher in smokers (n=99) according to score ranges (<0,001). Propabl moderate mental illness was detected with similar frequency in two groups.

CONCLUSIONS: When different situations that may cause anxiety and depression were excluded, it was determined that smoking may cause depression and anxiety in students between the ages of 17-30. Acknowledgement: This study was approved by The Clinical Research Ethics Committee of Samsun University and supported by TUBITAK 2209-A (Project # 1919B012217842).

Key words: Cigarette, Neurodegeneration, Anxiety, Depression

PC-97

How Virtual Heart Ownership Influences Human Physiology?

Burak Erdeniz¹, Hasan Kazdağlı²

¹Izmir University of Economics, Department of Psychology, İzmir, Türkiye; ²Izmir University of Economics, Vocational School of Health Sciences, Izmir, Türkiye

AIM: Over the last decade a number of studies showed that by using a full-body ownership paradigm participants can feel ownership over virtual bodies. However, rather than using a full body ownership paradigm, the current study investigates the psychological and physiological changes associate with virtual organ ownership. We hypothesize that presenting a virtual heart in a virtual reality environment, such as the rhythmic visual representation of heartbeats along with synchronized heartbeat sounds and vibrations, can be used to manipulate participants' own heart rate.

METHODS: Sixty-five healthy participants who were all undergraduate student volunteered from İzmir University of Economics. Before the experiment all participants signed a written informed consent and filled a questionnaire about State-Trait Anxiety Inventory and Cardiac Anxiety Scale. During the experiment participants were exposed to controlled heart rhythms changes in a virtual reality setup, while they receive visual feedback from VR glasses, auditory feedback from headphones, and a haptic feedback device was attached to their chest. During the experiment, heart activities were recorded continuously via Photoplethysmogram and pulse-oximetry was attached to their fingers. After synchronous presentation of own and virtual heart, participants heart rates were adaptively manipulated (increased or decreased ±10 bpm) over a 2 min period. Then, every 2 min participants rated their synchronization with their heart rhythm on a seven-point scale. At the end of the experiment, participants filled a presence and interoceptive awareness questionnaire and repeated the STAI form based on their experience in virtual reality. **RESULTS:** The results regarding heart rate variability (HRV) and heart rate (HR) showed that for both increase and decrease manipulation and a significant effect on both the % SDNN scores, % RMSSD scores.

CONCLUSIONS: Manipulated heart rhythms not only affected heart rate but also influenced heart rate variability.

Keywords: Trypophobia, Immune system, Inflammation, Pro-inflammatory cytokines, Heart Rate Variability (HRV)