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Turkish Society of Physiological Sciences
45th National Physiology Congress

31 October– 03 November 2019

Palm Wings Ephesus Hotel Congress Center
Kuşadası, Aydın (TURKEY)

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Turkish Society of Physiological Sciences 45th National Physiology Congress
31 October– 03 November 2019 Kuşadası-Aydın TURKEY

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Conferences

Conference 1: Sodium Balance in Normal Man: Updates and Perspectives

Peter Bie

University of Southern Denmark, Institute of Molecular Medicine, Department of Cardiovascular and Renal Research, Odense, Denmark.

Several basic concepts of sodium metabolism are presently under scrutiny and may be subject to change. (i) For more than 60 years, total body sodium was believed to be present in two compartments. Soluble sodium ions in the body fluids and sodium trapped in the crystals of bones. Studies precipitated by Titze have revised this concept to include uneven distribution of sodium ions in soft tissues, but the magnitude and functional importance of soft tissue accumulation of remain uncertain. (ii) The direct relation between renal arterial pressure and sodium excretion ('pressure natriuresis') has been the key element of most models of sodium metabolism since the ground-breaking work of Guyton and colleagues in the late sixties. However, the results of a significant number of studies in dogs and man seem to disagree, and other primary controllers of sodium excretion may be more important components of sodium balance during daily day conditions. (iii) Are natriuretic peptides natriuretic? From the discovery by de Bold and coworkers in 1981 the natriuretic peptides ANP and BNP have been called powerful natriuretic and diuretic substances. Multiple studies of normal man seem to have confirmed this, but by high rates of peptide infusion. The physiological actions of ANP and BNP on renal function remain dubious at least in normal man. (iv) For decades the classical distal renal sodium transporters NCC and ENaC provided apparently inadequate mechanisms of regulation of sodium excretion. However, the placement of these transporters in series, NCC before ENaC, seem to be the background of functional collaboration in which the effects of the interstitial K^+ concentration on channel activities are key mechanisms. The status of these physiological concepts will be summarized, and some of the implications for future studies of sodium homeostasis and blood pressure regulation will be discussed.

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Assersen KB, Høilund-Carlsen PF, Olsen MH, Greve SV, Gam-Hadberg HC, Braad P-E, Damkjær M and Bie P. The exaggerated natriuresis of essential hypertension occurs independently of changes in renal medullary blood flow. *Acta Physiol.* 226: e13266, 2019.

Conference 2: Promoting Neuroplasticity in the Ischemic Brain

Dirk M. Hermann

Chair of Vascular Neurology, Dementia and Gerontology, Department of Neurology, University Hospital Essen, Germany

Recent laboratory findings suggest that it might be possible to promote cerebral plasticity and neurological recovery after stroke by use of cell-based or pharmacological treatments. Brain microvasculature and glial cells respond in concert to ischaemic stressors and treatment, creating an environment in which successful recovery can ensue. Neurons remote from and adjacent to the ischaemic lesion are enabled to sprout, and neural precursor cells that accumulate with cerebral microvessels in the perilesional tissue further stimulate brain plasticity and neurological recovery. These factors interact in a highly dynamic way, facilitating temporally and spatially orchestrated responses of brain networks. In view of the complexity of the systems involved, stroke treatments that stimulate and amplify these endogenous restorative mechanisms might also provoke unwanted side-effects, and stroke-associated risk factors may compromise treatment responses. Balancing the opportunities and possible risks, suggestions for the translation of restorative therapies from the laboratory to the clinic are provided, and recent successes and failures in the development of new therapies are presented.

Conference 3: The Ageing Muscle: From Stems Cells to Athletic Performance

Stephen D.R. Harridge

Professor of Centre for Human & Applied Physiological Sciences, King's College London, UK

The "typical" older persons muscle is smaller, weaker and more fatigue resistance (sarcopenia). This contributes substantially to the decline in ability to perform tasks of everyday living and increase the risk of falls in older people. The mechanisms by which this phenotype develops is multifactorial. Included among these factors in is an ability of the muscle stem cells (satellite cells) to effectively repair muscle following damage and the role of cellular senescence. However, the typical sarcopenic phenotype is not present in those older individuals who remain highly physically active. Thus, teasing out the contribution made by the inherent ageing process from ageing interacting with inactivity-mediated processes is key to understanding the changes in skeletal muscle in later life. Whilst important for many tissues, this is particularly important as regards muscle, which is uniquely sensitive to both metabolic and mechanical signals (i.e. physical activity) throughout the life course. The study of older exercisers provides unique insight into human ageing processes, free from disuse complications. Interestingly, world record performances of athletes show declines in ability and muscle performance which provide an interesting perspective on the physiology of human ageing. This presentation will thus discuss the typical ageing muscle, the role of muscle stem cells and cellular senescence and, using examples which extend through to master athletes, the role of physical activity in maintaining muscle function in old age.

Conference 4: Epigenome- and Transcriptome-wide Actions of Vitamin D: From *in vitro* to *in vivo*

Carsten Carlberg

School of Medicine, Institute of Biomedicine, University of Eastern Finland, Kuopio, Finland

Vitamin D_3 activates, via its metabolite 1,25-dihydroxyvitamin D_3 ($1,25(OH)_2D_3$, calcitriol), the transcription factor vitamin D receptor (VDR). Ligand-activated VDR binds genome-wide to thousands of genomic regions, interacts with the pioneer transcription factors PU.1 and CEPBA, changes the pattern of histone markers and increases chromatin accessibility, *i.e.*, vitamin D has a significant effect on the human epigenome. We demonstrated this most comprehensively in human monocytes (undifferentiated THP-1 cells) and confirmed it in an human *in vivo* setting, such as peripheral blood mononuclear cells obtained a vitamin D intervention study (VitDbol, NCT02063334) before and after a vitamin D_3 bolus (2000 µg). In general, epigenome changes in response to cellular perturbations create a memory, which is termed "trained immunity", *e.g.*, when monocytes/macrophages encounter microbes. Vitamin D modulates these epigenetic training events. Some the epigenome-wide effects of vitamin D are translated into changes of the transcriptome, *i.e.*, hundreds of genes are either up- order down-regulated in their expression (*e.g.*, nearly 600 genes in THP-1 cells). In context of our VitDbol study, we showed by RNA sequencing that *in vivo* in PBMCs 702 genes (4.7% of all) are significantly ($p < 0.05$) affected by the vitamin D_3 bolus. The expression pattern of vitamin D target genes differed significantly between individuals and the average expression changes can serve as a marker for vitamin D responsiveness. This allowed to the segregate the study participants into high, mid and low vitamin D responders. In conclusion, under *in vivo* conditions, vitamin D_3 supplementation results in significant changes of the human epigenome and transcriptome. The individual's molecular response to vitamin D requires personalized supplementation with vitamin D_3, in order to obtain optimized benefits in the prevention of osteoporosis, sarcopenia, autoimmune diseases, and possibly different types of cancer.

Conference 5: Descending Pain Modulatory Systems: Mechanisms, Significance and Translation

Bridget Lumb

President, The Physiological Society
Professor of Neuroscience, University of Bristol, UK

Descending pain modulatory systems (DPMS) that originate within the brain and modulate spinal nociception are a major determinant of acute and chronic pain. Investigations of these systems is critical to developing therapeutic strategies for the relief of pain. Despite our best efforts, something is lost in translation and we need to question if we are employing the right approaches.

Information about tissue damage is conveyed to the first synapse in pain pathways in the spinal cord by A-and C-fibre nociceptors. These nociceptors have different phenotypes, convey different qualities of the pain signal, and have different roles in acute and chronic pain. As such, they present different therapeutic targets. There is now good evidence that DPMS differentiate between information mediated by A- vs C-nociceptors. However, many studies that are designed to test analgesic efficacy do not distinguish between them. This is a potential shortcoming, and evidence will be presented that in acute pain, DPMS target responses to C-nociceptive inputs and that, in the transition to chronic pain, there is a shift to descending pro-nociceptive effects on responsiveness to A-nociceptive inputs. This extends to descending control of clinically relevant prostanoid systems that originate in the midbrain periaqueductal grey and which are modulated by non-steroidal anti-inflammatory drugs (NSAIDS).

A further confounding factor concerns the cutaneous structures stimulated in pre-clinical studies of acute and chronic pain. In humans and other mammals, the vast majority of the body surface is covered in hairy compared to glabrous skin. Evidence will be presented that DPMS has differential effects on inputs from glabrous versus hairy skin and yet, in the majority of pre-clinical studies of the analgesic efficacy of manipulating DPMS, effects are tested on responses to glabrous skin.

Finally, pain is a complex phenomenon that extends far beyond a sensory experience to include cognitive, emotional, affective and motor components. Increasingly, assessment of the holistic experience is being incorporated into pre-clinical studies with the aim of providing better models that are of translational relevance.

The take home message is that experimental approaches need to be carefully considered and re-assessed when designing pre-clinical studies that assess pain mechanisms and the analgesic efficacy of potential therapeutic agents in order for them to have translational validity.

Conference 6: Neurophysiology in the Age of Mind-Machine Continuum

Banu Onaral

School of Biomedical Engineering, Science & Health Systems, Drexel University, Philadelphia, PA, USA

Mobile, wearable and implantable technologies are poised to transform all aspects of our daily lives, from remedying physical, mental and cognitive deficits to enhancing physical function and performance. They augment learning, training, decision making and creativity. The convergence of the natural and the artificial alters how we heal, learn, work, play. Thus, the march of neurotechnologies seamlessly integrated within our daily lives is propelling neuroscience to the forefront of all human endeavors from neuro-learning to neuro-economics.

Now that the gap between the body, the brain and the technology shrinks, a better understanding of the 'human element' as a physiological and cognitive being becomes crucial. As the technology-driven 'industrial age' is setting, neurophysiology-centered era characterized by the mind-machine continuum is dawning. This next generation neurophysiology marks the onset of our co-evolution with technology.

We are complemented, extended or augmented, consequently modified and modulated by inanimate materials, mechanisms and machines. These artificial means range from wearable robot exoskeletons to learning algorithms and autonomous devices. Integrating natural intelligence with its artificial counterpart enable us to integrate high-performance human-in-the-loop systems that are safe, effective and efficient, hence neuroergonomic. Effective human-machine teaming is slowly but surely becoming a reality as mutual awareness and trust relationships are established between the animate and the inanimate.

The Cognitive Neuroengineering and Quantitative Experimental Research (CONQUER) is an interdisciplinary collaborative dedicated to the study of brain physiology and cognitive function. We design and develop wearable neurotechnologies amenable to natural settings and operational environments. This talk will provide an overview of our ongoing projects that illustrate the deployment of high-performance brain-in-the loop systems spanning healthcare, aviation and behavioral economics. On the dark side, we imagine a not-so-distant future when neuro-data will flow in hyper-connected automation networks and anticipate complex privacy and confidentiality challenges rising from data misuse and abuse, and attempts to behavioral modification. In closing, policies and regulations that may help preempt a 'neurotechnology winter' will be proposed.

Symposia

Symposium 1: Epilepsy and Calcium

S.1.1 *In vivo* Electrophysiological Methods in Epilepsy Research

Mehmet Yıldırım

Department of Physiology, Faculty of Medicine, University of Health Sciences, İstanbul, Turkey

Epilepsy is a chronic disease characterized by recurrent seizures. In approximately 70% of patients with epilepsy, seizures can be controlled by existing antiepileptic drugs. Experimental epilepsy models are needed to develop new antiepileptic drugs and to elucidate some pathophysiological processes related to seizures. Different experimental models generated by chemical, electrical and genetics are used in epilepsy research (1). In the present report, it is aimed to give information about frequently used *in vivo* electrophysiological methods in experimental epilepsy studies.

When considering the neurophysiological basis of epilepsy and the electrophysiological properties of neurons in the epileptic focus, the use of electrophysiological methods in experimental epilepsy studies is very important. When considering the neurophysiological basis of epilepsy and the electrophysiological properties of neurons in the epileptic focus, the use of electrophysiological methods in experimental epilepsy studies is very important. *In vivo* electrophysiological methods are used both in the development of experimental epilepsy model and in recording epileptic activity (2). Seizures generated by electrical stimulation are divided into two main types: induced by stimulation of the whole brain (electroshock seizures) and seizures induced by local stimulation of a particular brain structure (epileptic afterdischarges).

Electrophysiological methods are used not only in the development of experimental epilepsy model but also in recording and evaluating chemical, electrical or genetic models. Electroencephalogram (EEG) recording is an important method in determining the location, type, and severity of seizures in the experimental epilepsy models. EEG recording is frequently used in the experimental epilepsy models induced by proconvulsant agents such as pentylenetetrazole, picrotoxin, bicuculline and penicillin in different experimental animals (3). On the other hand, EEG recording in the genetic absence epilepsy models and posttraumatic epilepsy models provides quantitative data on the frequency, duration, and latency of the seizure.

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Keywords: Electrophysiology, experimental epilepsy, in vivo method

S.1.2 The Role of Calcium in the Central Nervous System

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Calcium is a fundamental ion that takes part in maintaining brain functions. In addition to regulating the synthesis and secretion of neurotransmitters, calcium plays a key role in important missions such as synaptic activity, cell-cell communication and adhesion. Properly controlled calcium signals not only support normal brain physiology, but also contribute to the maintenance of neuronal integrity and the prolonged maintenance of cell life. Intracellular free calcium concentration changes are usually compensated by strong mechanisms, however cell stress becomes unavoidable in case of overexcitation due to the excess calcium. Increased intracellular calcium triggers apoptotic response and causes neuronal losses and neurodegeneration in many neurological diseases such as Alzheimer's disease, amyotrophic lateral sclerosis, Parkinson's disease, brain ischemia and epilepsy. For this reason, inhibition of calcium influx constitutes the main defense mechanism of neuronal continuity.

Various calcium channels cause calcium influx to the neuron. Calcium channels are seperated into two main groups: ligand and voltage gated. Ligand gated channels such as glutamate-activated NMDA, AMPA, Kainate receptors, TRPV channels, ATP-activated P2X receptors and nicotinic acetylcholine receptors cause directly calcium influx. On the other hand, voltage gated T-, R-, N-, P/Q- and L-Type calcium channels are opened in response to action potentials and subthreshold signals, and play a key role in determining intracellular calcium levels. Recent experiments have demonstrated that functional changes or genetic mutations in calcium channels play an important role in the pathogenesis of neurological diseases. Consequently, maintaining neuronal calcium balance will shed light on the treatment of these diseases.

S.1.3 The Role of Calcium in Epilepsy

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Calcium is one of the most important elements in the human body. Most of the physiological functions that govern cellular activities, coordinate cell movements and exchange information between cells occur through signaling. These signal pathways cannot function properly without a small but multifunctional calcium ion.
Calcium ion plays a role in many physiological and pathophysiological mechanisms including epilepsy. Calcium ions can directly or indirectly affect calcium channels by binding to calmodulin and subsequently altering the activity of G-protein activated enzymes. Increased intracellular calcium concentration plays an important role in epileptogenesis. Intracellular calcium increasing or decreasing leads to excitation or inhibition by changing the activity of voltage-dependent calcium channels. Calcium causes the epilepsy by affecting the structures such as NMDA, AMPA, GABA, cannabinoid CB1 receptors and voltage gated calcium channels by presynaptic or postsynaptic pathway. Increased calcium ions have been shown to play a role in glia cell cytoplasm in seizure formation.
High voltage (HVA) and low voltage activated (LVA) calcium channels have been shown to be effective in idiopathic and focal epilepsies. T type Ca^{+2} channels plays a role in temporal lobe epilepsy, absence epilepsy and genetically generalized epilepsy. In our laboratory studies, flunarizine, nicardipine, nimodipine and NNC 550396 showed anticonvulsant effect on absence epilepsy and penicillin-induced epileptiform activity models.
It is known that calcium influences epileptogenesis using different mechanisms. Therefore, it is necessary to understand the role of calcium for new therapeutic approaches.

Symposium 2: Circadian Physiology and Sleep

S.2.1 Circadian Physiology and Sleep: Concepts and Definitions

Levent Öztürk

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Circadian physiology is a physiology branch that deals with temporal organization of bodily functions in the course of a day. The full set of rhythms and temporal changes in an organism is termed chronome. Many physiological processes in animals show circadian rhythm. Rhythms with a period length between 19-28 hours are circadian rhythms. Rhythms with lower oscillation frequency or longer periods such as estrus cycle are infradian rhythms. Cardiac and respiratory rhythms, intestinal smooth muscle contractions that repeat every 3-10 minutes, or REM/NREM cycles of sleep show shorter periods are ultradian rhythms. A circadian rhythm must meet three criteria: (1) must be generated endogenously, (2) must have a free-running period about a day and (3) must be entrained by external/environmental factors. Circadian rhythm evaluation is based on six characteristics: mean level, amplitude, phase, period, waveform and robustness. Besides the term circadian, diurnal and nocturnal are used for events that occur during daylight and night-time. Circadian physiology is a field with an increasing importance. Organization of activities as 5-6 days work and 1-2 days rest in weekly rhythms impact on our lives and biology. More traffic accidents occur on Fridays and Saturdays whereas suicide-related deaths peak on Mondays. Humans tend to eat more and sleep 1-2 hours longer on weekends. Due to increasing number of transmeridian flights, more people are suffering from jet-lag. Desynchrony between shift-work hours and circadian clock leads to workplace accidents which lead to increased economic burden. Considering circadian rhythms in the prevention and treatment of disease led to development of chronotherapy. Many clinical conditions including asthma, cardiovascular disorders, cancer, ulcer show circadian features and unveiling these characteristics are leading to new treatment approaches. Irregular timing of sleep leads to sleep disorders which have a wide-range of clinical consequences including obesity, metabolic syndrome, diabetes and Alzheimer's disease.

Keywords: Chronome, infradian, oscillation, ultradian

S.2.2 Ultradian Rhythm From Day to Night

Lamia Pınar

Professor of Physiology

Most of the mammals have nerve networks that generate rhythmic activities in their central nervous system. These systems produce ultradian rhythms which change between a few minutes to a few hours, and can regulate subconsciously the automatic functions such as, walking, breathing, sleep, wakefulness, arousal, motivation, addiction, and memory consolidation. The networks contain pacemaker neurons with the intrinsic ability to generate rhythmic activity in the form of action potentials. The most known rhythmic activity-produced by pacemaker cells, in the tegmental area of the brainstem, are the pre-Botzinger cells of the respiratory system. Pre-Bötzinger cells change their activity level due to norepinephrine which is adjusted by changes in environmental and behavioral conditions. Norepinephrine not only modulates the respiratory network, but is in fact one of the most prominent neuromodulators in the mammalian nervous system. The ultradian rhythm that affects all the bodily functions is claimed to be shifting due to cerebral dominance and the activation of the sympathetic or parasympathetic systems, and it continues with NONREM and REM phases of the sleep. It can be asserted that pontin-geniculo-occipital (PGO) waves in REM sleep can be triggered by increased Ca2+ conductivity of pontine tegmental neurons, during sympathetic activity of the brain, as seen in the dominance of the left hemisphere. NONREM sleep on the other hand may be a phenomenon of right brain activation.

Keywords: Ultradian rhythm, brainstem, hemispheric lateralization, REM and NONREM sleep

S.2.3 Circadian/Homeostatic Regulation of Body Temperature and Sleep

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Maintaining body temperature within a narrow range is essential for optimal maintenance of cellular functions and survival in harsh thermal conditions. Cutaneous blood vessels, salivary glands in rodents, sweat glands in humans, shaking response of skeletal muscles, metabolic energy released in brown adipose tissue, changes in body isolation play important roles in controlling body temperature. In addition, behavioral responses such as postural regulation, aggregation behavior, regulation of food intake, regulation of activity level and regulation of microenvironment help maintain body temperature. Homeothermic animals show a circadian rhythm of body temperature. Body temperature in both diurinal and nocturnal animals is higher in the active phase than the inactive phase. Despite the small amplitude of the circadian rhythm of body temperature (for example less than 1°C in humans), it is still important for energy conservation in the inactive phase. Maintaining high body temperature is expensive in energy, because more energy than total daily intake is used for heat generation. Therefore, the circadian rhythm of temperature can be important for energy saving in homeothermic animals when no energy is required. The rhythm of body temperature is not only a result of the circadian change in heat loss or production in the body. The rhythm of body temperature is due to the relationship between the circadian and the thermoregulation system. However, the mechanism is not yet fully known. Sleep in mammals is accompanied by changes in thermoregulatory effector activity and decreases in core body temperature. The circadian clock in the hypothalamic suprachiasmatic nucleus regulates the daily rhythms of both core body temperature and wakefulness. Anatomically and functionally, neural control of sleep and thermoregulation coincide with the preoptic anterior hypothalamus and adjacent brain structures. Experimental preoptic anterior hypothalamus damage that disrupts thermoregulation causes permanent insomnia. Mild preoptic anterior hypothalamus warming reduces sleep latency, increases NREM sleep and increases EEG slow wave activity during NREM sleep. Direct modulation of thermoefector pathways by warm sensing neurons active in sleep in the preoptic anterior hypothalamus may be important for sleep-related changes in core body temperature.

Keywords: Circadian, homeostatic, sleep, thermoregulation

S.2.4 Circadian Rhythms and Organ Physiology: From Center Clock to Peripheral Clocks

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The main controller of circadian timing in humans is suprachiasmatic nuclei (SCN) of hypothalamus. These nuclei couple are located above the optic chiasm and both sides of the third ventricle. SCN receives information of light via retinohypothalamic tractus. SCN uses this information to organize bodily functions. SCN synchronize sleep/wake cycles to light/dark cycles. An earth day is 24 hours while SCN day is about 25 hours. Therefore, environmental cues including light, activity, food intake and temperature adjust the biological clock of SCN every day and synchronize its function to earth day. Circadian oscillations are produced by a group of genes and a transcriptional feed-back loop. Clock, Bmal1, Period-1, Period-2, Cryptochrome-1 and Cryptochrome-2 are among these genes. CLOCK and BMAL1 activators promote Period (Per1, Per2) and Chryptochrome genes (Cry1, Cry2). Products of those genes increase in the cytoplasm, dimerize and form a complex which returns into nucleus. In nucleus, this complex interacts with CLOCK and BMAL1 in order to repress their own transcription. This loop takes 24 hours. These rhythms of clock genes and protein expressions are present in all cells. In fact, these rhythms remain in cell culture which verifies that each cell has its own endogenous circadian oscillator. However, cellular clocks of different tissues do not overlap. Thus, each cell needs a circadian control relevant to its functions. Circadian clock provides control of a wide spectrum physiologic processes. Among these, glucose, bile acid, lipid and cholesterol metabolisms in liver, heart rate, blood pressure and endothelial function in cardiovascular system, solute and water excretion in kidneys, gastrointestinal function and tissue regeneration may be mentioned. Conditions such as sleep and feeding irregularities due to shift-work, artificial light and technology may interrupt circadian control and have potential of impairing physiologic processes and leading to clinical consequences.

Keywords: Suprachiasmatic nucleus, gut clock, metabolic clocks, clock genes

S.2.5 Chronotype and Circadian Rhythm Disorders

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People's preferences for the timing of sleep behavior are defined as chronotype. Three chronotypes were identified as morningness (larks), eveningness (owls) and intermediate type. Larks are those who go to sleep early in the evening, both physically and mentally feel better in the morning, prefer to be active in the early hours of day. Owls prefer going to bed late, have difficulty in waking up early, feel better in the afternoon/evening and prefer to be active late in the day. Chronotype is affected by genetic, age, ethnicity and gender. The tendency towards morningness increases with age. Men are more prone to eveningness than women. The timing of sleep-wake behavior and circadian clock regulate temporal relationship of physiological functions. Circadian clock facilitates the adaptation of organism to life. Circadian rhythm sleep disorders refer to clinical conditions in which the timing of sleep-wake is impaired. Six syndromes have been identified according to the international classification of sleep disorders: Delayed sleep-phase, advanced sleep-phase, independent sleep-phase, irregular sleep-wake rhythm, jet-lag and circadian disorder of shift workers. The occurrence of circadian rhythm sleep disorders has been increasing due to the negative effects of technology and lifestyle. Circadian rhythm disorders were investigated by collecting data for one week in university students by using a sleep diary form (which is used in the pre-diagnosis of sleep disorders and applied for at least one week to obtain objective information about sleep rhythm). The sleeping time of students was quite variable and the average sleep time of 6.07 in the morning showed that the eveningness was prevalent. The mean sleep latency was 11.43 minutes and the average time to get out of bed was 10 minutes. Volunteers stopped alarm and continued sleep at least once. Average daily nap duration was 9.58 min. Average caffeinated beverage consumption was 1.6 cup. Volunteers scored their sleep quality 3.5 out of 5 points and their morning refreshment 5.7 out of 10. In general, there was no awakening before the alarm. According to the sleep log data, circadian rhythm disturbance, defined as delayed type phase shift, was common.

Keywords: Chronotype, circadian rhythm, circadian rhythm disorders

Symposium 3: Studying Neural Circuit Computations in Health and Disease

S.3.1 Integration of Sensory and Motor Information in Visual and Somatosensory Cortices

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We perceive the outside world as a result of continuous sensorimotor interactions. The relevance of continuous sensorimotor processing becomes particularly evident in brain injuries and diseases that disturb one or the other aspect of our interactions with the world. Traditionally sensory perception has been studied with passive stimulation of sensory modalities, however neuronal processing of even simple controlled stimuli varies greatly at different behavioral states. Therefore it is essential to study sensorimotor interactions in behaving models. We utilized in vivo electrophysiology and Two- photon calcium imaging to measure neuronal activity in head-restrained mice that are freely behaving in visual/tactile virtual realities to investigate sensorimotor integration. We found that active behavior, i.e. locomotion, changes spatial tuning of visual cortex neurons, such that surround suppression is reduced during running. Additionally our findings revealed that visual motion and locomotion were integrated linearly by visual cortex neurons. Although effects of locomotion on visual processing have been widely explored, findings cannot be generalized to other sensory modalities. Particularly vibrissae somatosensory processing during locomotion presents a challenging paradigm as running is almost always accompanied by whisking, which is by itself considered an active state. To investigate how locomotion modulates neuronal activity in somatosensory cortex and how it is integrated with whisker touch, we used two-photon calcium imaging of several classes of neurons in head-restrained mice running in a tactile virtual reality. About a third of excitatory neurons increased their activity during running and concomitant whisking, in the absence of touch. Fewer neurons were modulated by whisking alone (<10%). Layer specific responses arose during sensory stimulation: deep layer neurons responded transiently to touch during running whereas superficial neurons showed sustained activity. Consistently, neurons encoding running-with-touch were more abundant in superficial layers compared to deep layers, suggesting more integrative roles for superficial neurons in cortical computation.

S.3.2 Glia-Neuron Interactions During Epilepsy

Emre Yaksi

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Brain activity and connectivity alter drastically during epileptic seizures. Throughout this transition, brain networks shift from a balanced resting state to a hyperactive and hypersynchronous state, spreading across the brain. Glia-neuron interactions are proposed to be important for seizure generation, especially due to the direct role of astrocytes for the regulation of neuronal excitability and synaptic transmission. It is, however, less clear which mechanisms underlie these state transitions. To address this, we studied pharmacologically induced seizures in the zebrafish model. We performed in depth analysis of the activity of thousands of individual neurons and glia across the zebrafish brain. By studying neuronal and glia activity across the zebrafish brain, we observed striking differences between these networks. During the preictal period, neurons displayed a small increase in synchronous activity only locally, while the entire glial network was highly active and strongly synchronized across large distances. We observed that the transition from a preictal state to a generalized seizure leads to an abrupt increase in neuronal activity and connectivity, which is accompanied by a strong functional coupling between glial and neuronal networks. Finally, we showed that optogenetic activation of glia induced strong and transient burst of neuronal activity. We propose that changing interactions across glia-neuron networks is a potential mechanism for the manifestation of generalized seizures.

Symposium 4: Mechanisms of Neurodegenerative Diseases and Current Therapy Strategies

S.4.1 The Role of MYDGF in the Injury of Central Nervous System

Berrak Caglayan

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Increase in the production of “neurotrophic factors” following central nervous system injury was demonstrated with experimental systems. Especially, the presence or overexpression of growth factor proteins in the pathological conditions play an important role in the increased neuronal survival, neurogenesis and plasticity during recovery. Myeloid derived growth factor (MYDGF) is a newly-characterized growth factor protein. In proteomic analysis studies, it was shown that the protein was secreted by the bone marrow derived mouse macrophages and human synoviocytes and exerted cardiomyocyte protective effects in a myocardial infarction injury model. However, its role in nervous system injuries has not been studied before.

As MYDGF induced regenerative processes following myocardial infarction, we aimed to investigate whether this molecule encourages the endogenous repair mechanisms in the ischemic tissue in central nervous system injuries. To this end, lentiviral MYDGF overexpression or silencing vectors were used in spinal cord injury and cerebral ischemia models in mice. In these models, effects of MYDGF on neuronal survival and mediating potential signal transduction pathways as well as its effects on neuronal plasticity were studied. Mice were followed up for 60 days after the injury and behavioral tests performed at days 3, 15, 30 and 45 demonstrated statistically significantly improvement in motor function, sensory-motor coordination and functional recovery for MYDGF. In addition, somatosensory evoked potentials were analyzed and indicated a favorable effect for MYDGF. Although the role of MYDGF in central nervous system has not been identified before, these results indicate the contribution of this protein to regenerative processes. With the identification of its mechanism of effect, it is believed that our results will provide important insights for the use of MYDGF in neurodegenerative disorders.
This Project was supported by TÜBİTAK (117S124).

S.4.2 Effects of PDE10a and Bmal1 on Circadian Rhythm and Brain Injury

Mustafa Çağlar Beker

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Stroke is a remarkable disease, as the second most frequent cause of death in the world, following cardiovascular diseases. The unique time-of-day dependent distributions in cerebrovascular disorders were observed in several clinical observational studies since 1980s. Circadian rhythm, which plays an important role in the triggering of cerebral ischemia, has important effects on the injury mechanisms after ischemia. In our studies, phosphodiesterase 10A (PDE10A), which is found intensely at the striatum level, has been shown to oscillate like circadian proteins and has an important role in the pathophysiology of cerebral palsy. In addition, the effects of Aryl Hydrocarbon Receptor Carrier-1 (Bmal1) protein, which plays an important role in determining circadian rhythm, on neuronal damage mechanisms after in vivo and in vitro ischemia have been shown.
It is aimed to reveal the role of PDE10A and interacting mechanisms on the pathophysiology of stroke by inhibiting PDE10A via TAK-063 in C57BL6/J mice. 0,3 mg/kg or 3 mg/kg dosages of TAK-063 were determined to administer. From this view, in the proposed project; PDE10A was examined for its potential impacts on post-ischemic infarct volume, cytotoxic edema, blood-brain barrier permeability, DNA fragmentation, neuronal survival and intracellular signaling pathways first time in the literature. Effects of Bmal1 on cellular survival were investigated using oxygen glucose deprivation method in lentivirus mediated Bmal1 overexpression or Bmal1 silencing via shRNA in N2A cells. In addition, using targeted proteomics (immunoprecipitation combined with mass spectroscopy) effects of Bmal1 on intracellular signaling pathways were investigated.
In light of the results obtained in this study, it is believed to elucidate the unknown PDE10A and Bmal1 mechanisms as well as to contribute to the literature and development of novel targets and/or therapies for the clinical treatment of ischemia.
This study is supported by TUBITAK (218S453).

Keywords: Cerebral ischemia, Bmal1, PDE10A, Proteomics

S.4.3 Advanced Imaging Techniques in Neurological Diseases

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Advanced imaging techniques enable the monitoring of molecular and biological processes in the brain and systemically in non-invasive ways in vivo and in vitro. Advanced imaging technology appears to be both techniques that facilitate our understanding of the brain and the diagnosis of brain disease and disorders. By means of these techniques, differences between healthy and diseased tissues can be imaged and investigated in detail. It also allows us to compare the intracellular dynamics vividly when considered in the cellular dimension. Neurodegenerative diseases are conditions that affect millions of people, including both the patient and their family without a known cure. Neurodegenerative disorders include epilepsy, head trauma, cerebral palsy, spinal cord injury, Alzheimer's, Parkinson's, Huntington's, ALS. Some of these diseases are caused by the loss of function or death of nerve cells in the central or peripheral nervous system. In some, cell death occurs as a secondary injury and long-term permanent sequelae develops.

Today, the imaging equipment in many hospitals and research centers provides the opportunity to investigate the pathophysiology, underlying mechanisms and long-term changes of neurodegenerative diseases at the molecular level. Using a multi-photon microscope, all changes occurring in the brain of living animals; using spinning microscope intracellular dynamics in vitro or using light beam microscope normal and diseased tissues can be compared visualizing the whole tissue in 3 dimensional details. By moving these techniques further, F-techniques (FLIM, FRET, FRAP) can reveal protein-protein, protein-receptor, receptor-receptor relationships, intracellular transport systems.

As a result, neurodegenerative diseases reduce the quality of life of people and at the same time cause them to live in need of care. Advanced imaging techniques are a constantly evolving field and are among the most important infrastructures that can help improve the treatment of these diseases affecting millions of people.

S.4.4 Investigation of the Effect of Fetal Microchimeric Cell Following Brain Injury

Ahmet Burak Çağlayan

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Existence of genetically different cells from the host can be defined as microchimerism. Cell trafficking from fetus to mother during pregnancy is called fetal microchimerism. Although the existence of fetal microchimeric cells on the maternal tissue was shown by animal studies as well as by human studies, little is known about the role of these fetal microchimeric cells following brain injury. In this study, it was aimed to investigate the transition of fetal microchimeric cells from fetus to maternal tissues and the effect of fetal microchimeric cells on maternal brain following brain injury. Here, wild-type female mice were mated with green fluorescence protein (GFP) expressing transgenic male mice to study the transition of fetal cells. Brain injury was induced by middle cerebral artery occlusion or cold injury models on the different trimesters of the female pregnant mice (1., 2., or 3.). Respectively 72 hours or 48 hours after injury, the number of GFP positive cells on maternal brain and blood were analyzed by flow cytometry and immunofluorescence methods.

It was shown that induction of injury on the different trimesters affects the transition and the total number of GFP positive cells on the maternal brain and blood. It was also shown that the number of GFP positive cells on the maternal brain was statistically higher on the second trimester injury-induced group. With the elucidation of the transition mechanism to the injured tissue, the results obtained from this study can be useful for both stem cell therapy and cell-based therapy. In addition, identification of the cell types of fetal microchimeric origin on maternal tissue and the isolation of these cells can be used for the development of personalized therapy. This project was supported by TUBITAK (217S453).

Symposium 5: Vascular Tonus and Endothelium: Physiological Regulations in Ageing and Exercise

S.5.1 The Role of Endothelium on Regulation of Vascular Tonus

Oktay Kuru

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The vascular endothelium is represented by a single layer of flat cells acting as a barrier between the blood and underlying vascular tissue components, which is involved in numerous vascular regulatory functions as well. The close neighboring arrangement evolves interaction with other endothelial cells and surrounding smooth muscle cells. Taken together, these structural and functional features produce a dynamic and flexible way in control of vascular function. Vascular permeability and regulation of blood flow are important facts in regulation of delivery of nutrients and removal of cellular waste. The other processes like angiogenesis, inflammatory responses, coagulation and vascular remodeling are directly related with vascular endothelial tissue. Blood cells, microbial infections and proinflammatory cytokines, smooth muscle cells, pericytes, hormones and neurotransmitters provide an environment rich in signals to be interpreted by the endothelium. Endothelial cells generate paracrine regulators represented by different molecules. Prostacyclin, endothelium-derived relaxing factor - nitric oxide and endothelin are among the most popular investigated agents involved in vascular regulation. The impairment in physiological regulatory function of endothelium is related with diseases like hypertension and atherosclerosis. Therefore, the contribution of endothelial tissue in control of vascular tone is critically important in both physiological and clinical conditions.

S.5.2 The Changes in Vascular Tone Due to Aging

Günnur Koçer

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The extraordinary progress of science and technology in our century has greatly prolonged the average life expectancy and has increased both the number and proportion of elderly individuals in the population. Epidemiological data reveal that aging is the major risk factor for cardiovascular diseases and the morbidity and mortality related to cardiovascular diseases has increased in decades. Endothelium plays a key role in cardiovascular changes due to aging. Endothelium, which undertakes an important role in maintaining vascular structures and functions in physiological conditions, carries out these functions with autocrine and paracrine mediators produced and /or secreted. The loss of the normal endothelial function is known as endothelial dysfunction that plays a role in the pathogenesis of many diseases and is also associated with aging. Regardless of pathological conditions, aging has been reported to cause endothelial dysfunction in the aorta and resistance arteries. Aged dependent endothelial dysfunction is explained by the reduction of both production and bioavailability of various endothelial secreted vasodilatory agents, and in particular nitric oxide (NO). It has been shown that the amount of endothelial–nitric oxide synthase (eNOS) found in the endothelium in elderly individuals decreases and produces less NO in the existing eNOS. In the aging process, prostacyclin and endothelium-induced hyperpolarizing factor are the other two important relaxant mediators whose production and secretion are affected by endothelium. In addition to the reduction of vasodilators with aging endothelium derived vasoconstrictors such as endothelin-1, cyclooxygenase-derived prostanoids and reactive oxygen derivatives contribute to the increase in vascular tonus. In order to reduce the symptoms of vascular aging, minor changes in our lifestyle, such as healthy eating and regular exercise, will have positive effects on eNOS function and antioxidant capacity.

S.5.3 Vascular Adaptation to Regular Exercise

Seher Nasırcılar Ülker

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Many adaptations develop in various tissues in the organism as a result of regular exercise. In this process, the cardiovascular system is the main adapted structure. One of the most important evidences of cardiovascular adaptations is the decrease in resting blood pressure of both hypertensive and healthy individuals after regular physical activity. Another exercise-induced vascular adaptation is associated with endothelium, and endothelial function can be improved through several mechanisms. Primarily, exercise increases the production and bioavailability of endothelium-derived relaxing factor-nitricoxide (NO). Furthermore, it reduces reactiveoxygen species (ROS) by causing an increase in superoxide dismutase (SOD) and a decrease in nicotinamide adenine dinucleotide/nicotinamide adenine dinucleotide phosphate (NADH/NADPH) oxidase activity. Thus, NO bioavailability is increased by reducing NO inactivation. Exercise also leads to increased expression of eNOS through various pathways. Besides functional changes in the vessels, exercise causes vascular remodeling by inducing angiogenesis and arteriogenesis. These changes in vascular structure are likely associated with functional changes and improved organ blood flow. In addition to all these changes in the response of vascular smooth muscle to vasoactive agents may occur as a result of regular physical activity. Vascular tone is determined by the balance between vasoconstrictor and vasodilator factors. However, the response is not only related to external influences but also is related to the response capacity of the vascular wall. Although the data on how vasodilator or vasoconstrictor responses change as a result of exercise varies according to the subject, vessel type and vasoactive substance, especially it is observed that the relaxation response to vasodilators is increased and contraction response to vasoconstrictors decreased. The vasoactive responses of exercise-trained rats are varied in our studies as well. In conclusion, regular physical activity leads to significant changes both structural and functional in the vascular system.

Panels

Panel 1: Chronic Obstructive Lung Disease (COPD); Airways, Parenchymal and Vascular Physiopathology

P.1.1 Mucociliary Activity in COPD

Metin Baştuğ

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The lungs are highly resistant to pathogenic particles and toxic chemicals found in the breathing air, provided by the function of mucous secretion and cilia of the epithelial cell covering the airways. Mucus, which can be defined as extracellular gel, consists of water, protein and macromolecules. The most important macromolecules are mucin proteins in glycoprotein structure. These musin proteins are classified as polymerized, secreted gel forming and membrane related. Mucus secretion whose contents vary depending on the respiratory tract region and 12-16 beats per second of the cilia remove particles from the respiratory air towards the larynx.

Disruption of the secretion and ciliary functions of the respiratory tract epithelial cells cause significant problems in the defense mechanisms of the lungs. Excessive secretion of mucus causes deterioration of air flow and changes in the balance of proteins in the air, resulting in increased in air collapse in small airways, resulting in air trapping.

Smoking is the most important cause of COPD with clinical phenotypes such as chronic bronchitis and emphysema. In addition, α-1 anti-trypsin deficiency or excessive neutrophil products also play a role in the formation of COPD and dysfunction of airway mucociliary activity.

In this presentation, normal mucociliary activity and the mechanisms that cause dysfunction in COPD will be discussed in the light of the literature.

Keywords: Mucus structure, secretion mechanism, mucociliary activity, mucociliary dysfunction

P.1.2 Airways Physiopathology in COPD

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According to GOLD 2018 (Global Initiative for Chronic Obstructive Lung Disease), COPD is a common, preventable and curable disease that develops due to airway, alveolar and vascular abnormalities caused by exposure to harmful gases or particles. The prevalence of COPD is higher in smokers and higher in smokers than in non-smokers.

Airflow limitation and air trapping are very important in the pathophysiology of COPD. Bronchia with diameters larger than 2 mm make up the large airways, while bronchia smaller than 2 mm form the small airways. Mechanisms that cause flow restriction in small airways due to abnormal inflammatory response that play a major role in the pathogenesis of COPD; airway epithelial damage, mucociliary dysfunction, chronic airway inflammation, structural changes in the airway wall, decreased elastic recoil and lack of alveolar connections, activation of the airway smooth muscle and increased cholinergic tone. These physiopathological changes lead to the formation of small airway disease. Increased epithelial permeability due to irritant particles and gases in COPD exposes lower afferent nerve endings and irritant receptors to bronchoconstrictor and other proinflammatory agents. Neurogenic inflammation causes bronchoconstriction and airway inflammation in the airways. Airway inflammation in COPD is neutrophilic and is characterized by increased macrophages and CD 8+ T cells.

In COPD, the oxidative stres mechanisms are highly activated. Bronchial inflammation including phagocytes such as neutrophils and macrophages is the internal source of oxidants. Activation of various proteases within the airways is induced, while the effects of antiproteases are reduced. COPD is due to the effect of proinflammatory cytokines and oxidant stress in airway smooth muscles; cytokines and chemokines, proteases, and extracellular matrix components. The airway lumen is filled with fluid, cells and mucus, and acute exacerbations increase these responses. Thickening of the airway wall not only reduces the lumen of the airway, but also changes the mechanical behavior of the airways. Fibrosis in small airways and increase in airway resistance are very important in the development of small airway disease. Both hypertrophy and hyperplasia are seen in the airway smooth muscles. Airway obstruction causes ventilation and perfusion inequality and hypoxemia develops. As the airway wall thickens, the connected alveolar walls become shorter, the forces on the airway decrease, the external airway surface area increases, and the pressure applied to the airway decreases.

Elastic recoil has a primary effect on airway caliber. The primary formation of small airway remodeling is prebronchial fibrosis. This reduces airway elasticity, making COPD patients less susceptible to bronchodilator drugs. In addition, prebronchial fibrosis disrupts alveolar connections to the airway. This tends to expiratory closure of the airway. Closing volume increases and forced expiratory volume decreases in the first second (FEV1).

In order to develop new therapies in COPD, the cellular and molecular background of airway pathophysiology should be well understood.

Keywords: COPD, epithelial damage, airway inflammation, airflow limitation and air trapping

P.1.3 Parenchymal and Vascular Physiolopathology in COPD

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COPD is caused by pulmonary inflammation, tissue damage, perturbation in repair and defence mechanisms of lungs by chronic exposure to cigarette smoking, toxic gas and particles (esp., ≤2.5μ) and alfa-1 antitrypsin deficiency (GOLD, 2018). The major pathological changes are observed in both large and small airways, lung parenchyma and pulmonary vessels. Pulmonary parenchymal inflammation is more pronounced than that observed at chronic smokers.
Emphysema is the main parenchymal change determined in COPD. It is defined as abnormal and permanent widening of alveolar sacs beyond terminal bronchioles with wall damage but without prominent fibrosis. Additionally; small airway disease develops in the form of epithelial damage, structural changes in the airway walls, increased cholinergic tonus, bronchoconstriction and increased airway resistance. The most important reason for the limitation of expired airflow (air trapping or static hyperinflation) is the parenchymal damage which leads to loss of alveolar connections and elastic recoil.
There are different cells (macrophages, T lymphocytes – especially CD8+ and neutrophils) and various mediators (oxidants, proteases and toxic peptides) released from those cells which contributes to the developing inflammation in the lung parenchyma. Neutrophils directed to airways by chemotactile factors secrete neutrophil elastases and other proteases leading to increase in parenchymal damage and mucosal hypersecretion. Subsequently, inflammation in the lung develops further, since the balance between oxidant-antioxidant and protease-antiprotease is disrupted. Further along the process despite ceasing smoking inflammation continues to develop. The mechanisms of this persistent inflammation has not been understood, however there are studies reporting the development of auto-antibodies or changes in the microbiota as the responsible parties (GOLD, 2018).

As COPD progresses development of hypoxia in the alveolus causes medial smooth muscles of pulmonary arterioles spread towards distal vessels which are normally muscle free and vascular intima thickens. Besides, emphysema induces loss of pulmonary vascular network. Subsequently, developing pulmonary hypertension might result in right ventricular dilatation and hypertrophy (cor pulmonale). The occurrence of cor pulmonale in severe COPD signifies the increased load of pulmonary circulation and right ventricle. As the weakness of diaphragm and other respiratory muscles increases because of ongoing systemic inflammatory response, disease becomes more severe. In conclusion, when the whole physio-pathological processes in the occurrence and progressing of COPD considered ventilation/perfusion imbalance is the fundamental mechanism that distorts gas exchange and leads to arterial hypoxemia in all stages.

Keywords: COPP, emphysema, parenchymal inflammation, pulmonary hypertension

Panel 2. Cell Mechanics

P.2.1 Mechanical Response of Neurons to Axonal Injury

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Axonal injury and transection is a phenomenon that occur primary or secondary to nervous system traumas, stroke and neurodegenerative diseases. As consequences, partial or total degeneration of the proximal part and changes leading to survival or death of the neuron take place. Secondary neuronal death and consequent enlargement of the initial lesions and loss of function are among the expected results of such axonal injuries. Beside some well-known mechanisms, we have discovered that neurons respond to axonal injury also by contracting. The results of our studies in which we investigated the mechanical properties of this contraction, the routes of calcium entry required for contraction, the signaling mechanism and relationship of this phenomenon with the neuronal survival will be presented.

P.2.2 Detection of Mechanical Impulses and Molecular Mechanisms of Cell Response

Ramazan Bal

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Living cells are constantly subjected to mechanical stimuli originating from neighboring cells in contact and the surrounding extracellular matrix. In the context of cell mechanics, how mechanical stimuli affect the cell and the responses of the cell to it and how the mechanical stimuli are effective in controlling cell functions will be evaluated in the light of literature. Cellular mechanics in mammalian cells have been underestimated for many years. Recently, however, the molecular mechanisms related to the detection of the mechanical stimuli to which the cell is exposed and its conversion into signals (mecano-transduction) have been the subject of intense investigation. Mechanical stimuli are perceived by cells through diverse mechanically sensitive molecules present in the cell membrane. These mechanosensitive molecules include integrins, stretch-activated ion channels, G protein coupled-receptors and growth factor receptors. Mechanical signals, such as changes in cell volume, have been shown by many researchers to be important in events such as regulation of intracellular osmotic pressure, cell shape determination, cell proliferation, cell growth, cell death, cell migration, or regulation of intracellular metabolism.

When the cell volume increases or decreases due to the change in the osmolarity of the extracellular fluid, the cell activates many signaling pathways, and the intracellular / extracellular concentrations of K +, Cl–, Na + and organic osmolites are modified by active regulatory mechanisms to restore osmotic equilibrium. For example, if the osmolarity of the extracellular fluid decreases, the cell will swell as water enters the cell. In this case, in most animal cells, an active process known as **regulatory volume decrease** begins. In other words, K +, Cl–, Na + ions and organic osmolites are allowed to move out of the cell through channels and active pumps. Thus, the cell volume is reduced to normal values. On the other hand, in case of an increase in extracellular fluid osmolarity, it causes a decrease in cell volume. In this case, a mechanism called **regulatory volume increase** works to restore the osmotic balance between intracellular and extracellular. Hypertonic / hypotonic stress leads to increased expression of genes encoding ion channels that mediate the diffusion of ions and organic osmolyte transporters

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Panel 3. Exercise is Medicine

P.3.1 Respiratory System Diseases and Exercise

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It is known that the treatment of lung diseases, with increasing incidence, demonstrates serious problems for both patients and physicians. Contrary to many other diseases, the increasing death rate due to chronic obstructive pulmonary diseases also indicate that there are serious difficulties in identifying treatment strategies. The developments that follow the emergence of dyspnea in patients, forces them into a sedentary life style. However, the drop in physical capacity has further adverse effects on the life expectancy of the patients. On the other hand, detailed investigation of the relationship between chronic lung diseases and physical activity over the course of 70 years show that structured exercise programs are as effective as drugs used in the treatment of chronic lung diseases. This evidence made it possible to shape alternative treatment options. This classification is essential for the distinction of the efficiency of exercise as a treatment in lung diseases. In addition to the adverse effects over the functions of the lung, the increase in the frequency and severity of illness related symptoms, the emergence of skeletal muscle atrophy especially in the lower extremities and the subsequent increase in the length and recurrence of hospitalization are identified as the fundamental problems associated with chronic lung diseases. Furthermore, the coexistence of sedentary lifestyle associated comorbidities with lung problems in these patients is also significant. Diabetes, hypertension, heart disease, osteoporosis, systemic inflammation and malnutrition are some of the major problems seen in these patients. The prominence of exercise as a means of treatment of respiratory pathologies originates from the fact that it triggers a series of signal pathways that regulate above-mentioned diseases. As a matter of fact, in the long-term follow-up of chronic obstructive pulmonary patients, it has been shown that the addition of physical activity to medical treatment causes positive changes in the lung function. In addition to that, enhanced oxygen uptake, improvement in disease symptom scores, increase in exercise capacity, improvement of cardiac function after cardiovascular adaptation responses, decreased blood pressure, increased muscle tonus and strength, positive changes observed in bone tissue, stress reduction, increase in self-confidence and improved sleep quality are some of the positive results achieved in the treatment. With this in mind, it is possible to underline that correctly structured exercise programs have vital importance in the treatment of lung diseases. Multidisciplinary evaluation is essential for the treatment of these diseases. However, establishing further understanding of the issues related to the appropriate choice of exercise programs for varying patient groups, the mechanisms of the effects of exercise, patient compliance, symptom control, and strategies to maintain continuity in physical activity will be made possible with future studies.

Panel 4: Melatonin

P.4.1 Physiological Effects of Melatonin

Haluk Kelestimur

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Melatonin (MLT), one of the hormones that released by pineal gland, has wide variety of functions. Because its release is higher in dark, it is also known as “the hormone of darkness”. One of its well-known effect is its involvement in the regulation of biological rhythm according to the light-darkness rhythm. Signals related to the outside light-darkness state are transmitted to the suprachiasmatic nucleus (SCN) through retino-hypothalamic tract first to SCN in the hypothalamus. SCN is regarded as place of biological clock in the brain. Then, signals are transmitted to the paraventricular nucleus (PVN) in the hypothalamus. The signals travel in the nerve fibers in the intermediolateral column of spinal cord and reach to superior cervical ganglion (SGN) and finally arrive up to pineal gland and thereby regulates the gland secretion in accordance to light dark cycle. Melatonin release is higher in the darkness and its rhythm regulates rhythm of many physiological functions. In addition to its rather well-established roles in the regulation of circadian rhythms, sleep, and reproduction, melatonin has also been identified as an important regulator of glucose metabolism.

P.4.2 Cellular Mechanisms Regulating the Effects of Melatonin

Ahmet Ayar

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The pineal gland hormone melatonin was initially identified as an important regulator of sleep and circadian rhytm, but results from several *in vitro* and *in vivo* studies showed that physiological effects and functions of this hormone are a plethora ranging from acting as a strong antioxidant, antiapoptotic, anti-inflammatory, detoxification, circadian regulation of energy metabolism and many others crucial for homeostasis. Disruptions in release and effects of melatonin can lead to neurodegenerative diseases including Parkinson’s, Alzheimer’s, and Huntington’s, as well as sleep problems, reproductive and growth problems and premature aging. It has been documented that melatonin exerts its actions through both receptor-dependent (both cell surface and suggestive intracellular receptors subtypes namely: Mel1A, Mel1B and Mel1C) and receptor-independent mechanisms. Several second messengers including cAMP, cGMP, diacylglycerol, inositol trisphosphate, arachidonic acid, and free intracellular Ca^{2+} concentration ($[Ca^{2+}]i$) have been documented to mediate cellular actions and physiological functions of melatonin. Better understanding of these receptors and intracellular signaling mechanisms would provide important insights in role of melatonin in human health, also provide target for a wide range of diseases in which melatonin effect is impaired.

P.4.3 The Therapeutic Potential of Melatonin

Ertugrul Kılıç

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Melatonin exerts its effects through MLT1 and MLT2 receptors. These receptors have been documented to be highly expressed in the brain. Animal experimental studies have documented that MT1 receptors especially expressed in the SCN and pars tuberalis regions of the brain. The MT2 receptor expression is highly concentrated in bulbus olfactorius, frontal brain regions, hippocampus, amigdala and superior colliculus. All these strengthen the view that melatonin mediates important roles in the brain. In addition to regulatory role of melatonin on biological rhythm, its antioxidant and anti-inflammatory role have been subject to many studies. Recently its relation to regulation of energy metabolism has attracted attention. Thus, studies are concentrated on potential beneficial role of melatonin on prevention of neurodegenerative diseases and obesity and its complications.

Panel 5: Using Active Learning Methods in Physiology Education

P.5.1 Using Active Learning Methods in Elective Courses

Selma Arzu Vardar

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In recent years, traditional learning methods as well as student-centered active learning methods have been adopted in contemporary medical education. Physiologists also play a role in application of these methods as teachers. Physiology faculty members contribute individually in the preparation process of the elective course programs, which include individual or several disciplines. In recent years, methods such as presentations, projects, case discussions, PBL sessions, and impression reports are being frequently used in elective courses. Students describe such electives as encouraging for research and helpful for improving academic research skills.

According to evidence-based investigations, appropriately creating active learning environment increases examination performance and is important for conceptual learning. In order to ensure utilization of active learning methods, it may be useful for trainers to think individually about how to learn and follow the current approach on active learning methods.

Even if active learning methods cannot be included commonly in the faculty curriculum, elective courses can be used a field for application.

Along with the lecturer's delicate planning, coordination for cognitive processes can be achieved multiple and better in elective courses. Different activities can be added to lectures for improved learning and remembering processes. Elective courses can be used to create an active learning environment that enables students to remember. Environments in which students experience valuable and rich memories can be provided by elective courses. The small number of students in these courses can help to reach the desired objectives. Active learning methods used in elective courses can be effective in creating environments where students are emotionally supported, felt safe and valued.

P.5.2 Physiology Education in the Problem Based Learning Method

Cem Şeref Bediz

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Problem-based learning (PBL), an educational method in which the students are active, is based on the use of prior knowledge for the solution of health problems presented in a scenario, identifying, learning and discussing the subjects that the students need. This method is applied in small groups of students with a training guide. PBL sessions are student-centered and the training mentor does not transfer information; rather they support only with facilitating methods. With PBL, students take learning responsibilities and learn how to learn. The information used for understanding, comprehension, analysis, synthesis and evaluation processes are increased in persistency and can be questioned and adapted in professional life. PBL has a permanent contribution on wondering about human physiology where cause-effect relationships, interactions and balances are of great importance and education based on self-curiosity.

P.5.3 Multidisciplinary Approach to the Team Based Learning

Hande Yapışlar

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Small group studies are conducted in crowded classrooms in medical education with team-based learning (TBL), as an active educational method for students. The TBL is used as an effective method to ensure extensive learning of new information through teamwork and in-class discussions. As a method to support multidisciplinary and active learning in subjects covered by more than one basic science, it was seen that the TBL was able to effectively supply integration of the content.

Small rooms are not required for team-based learning. It can be applied in student groups more than twenty. Students should prepare the lesson and come to class after preparation period. Students should make contribution individually and also as a team member in small groups. Only one trainer is enough for TBL. The instructor must have expert of the subject. However, it does not need to be very specialized and experienced. Students do not need special training for team work, but they must be productive in the process. The time spent in the classroom is devoted to practical learning during TBL. Students can receive support from their friends when needed as well as the instructor.

Oral Communications

OC01

Blood Brain Barrier Dynamics and Antiepileptogenic Effects of Antiepileptic Drug-Bound Nanoparticle in Wag/Rij Rats as a Genetic Absence Epilepsy Model

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AIM: Epilepsy is a neurological disease that affects more than 65 million people worldwide. Absence epilepsy is seen in children and adolescents. The blood-brain barrier (BBB) constituted by the endothelial cells of the brain microvessels limits the passage of circulatory substances into the brain parenchyma. In this study, adult WAG/ Rij rats were used to show the effects of lacosamide (LCM) associated with gold nanoparticle (GNP) on seizures.
METHODS: All experimental animal procedures were performed after the approvement of the local ethics committee of Boğaziçi University and Koç University. One-way analysis of variance (ANOVA) followed by Tukey's HSD test was used to statistically evaluate the significance of four groups. To see the long-term effects of GNP on seizures, EEG recordings were obtained by electrodes placed in the right and left hippocampus, and an Elevated Plus Maze (EPM) test was performed. The presence of GNPs in the brain was determined by using Inductively Coupled Plasma Mass Spectrometry (ICP-MS) and electron microscopy. At the same time, hemogram analysis of the animals were performed at the end of the experiments.
RESULTS: Application of LCM with or without GNP caused significant decreases in amplitude, and seizure frequency values compared *with* baseline values ($p<0.01$). GNP+LCM injections significantly decreased anxiety levels as well ($p<0.01$). The findings obtained from in vivo imaging system (IVIS) showed that LCM reached higher levels of brain parenchyma in the presence of GNP ($p<0.01$). In ultrastructural examinations, GNPs were found in the neuronal structures after passing BBB endothelial cells. There were no significant changes in hemogram values.
CONCLUSIONS: Our results suggest that GNP is an effective transfer agent in terms of antiepileptogenic efficacy in the passage of LCM through the BBB, and more importantly, the application of low dose LCM as GNP+LCM strongly influences the amplitude, and frequency of seizures.

Keywords: Absence epilepsy, gold nanoparticle, electroencephalography, blood-brain barrier, lacosamide

OC02

The Effect of Resveratrol on Penicillin-Induced Epileptiform Activity

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AIM: Resveratrol (3,5,4'-tri-hydroxy stilbene; RESV) is *an* antioxidant polyphenolic compound. Studies have shown that resveratrol has neuron protective effects in various neurological diseases. The aim of this study was to investigate the effect of resveratrol on penicillin-induced epileptiform activity.
METHODS: Twenty-four male Wistar rats were used in our study (n: 6). Epileptiform activity was induced by administering 500 IU Penicillin-G to the cortex (intracortical) in a volume of 2.5 microliters with a Hamilton microinjector. Resveratrol was administered intraperitoneally at a dose of 25, 50, 100 mg/kg, respectively, after 30 minutes of penicillin injection. This study was approved by the Animal Experiments Local Ethics Committee (OMU HADYEK) and supported by OMU Project Office (PYO.TIP. 1904.17.019). One-way analysis of variance and Post Hoc Tukey tests were used for statistical analysis.

RESULTS: Compared *with* the control group, Resveratrol (50 mg/kg) reduces significantly in spike frequency in between 30-50 and 130-180 minutes ($p<0.05$). Resveratrol (25 mg/kg) significantly decreased spike frequency between 130-140 minutes and Resveratrol (100 mg/kg) significantly decreased spike frequency between 30 and 40 minutes ($p<0.05$). No statistically significant difference was found between the groups in terms of amplitude values ($p>0.05$).
CONCLUSION: Resveratrol showed anticonvulsant effect on penicillin-induced epileptic activity. Further studies are needed to explain the certain mechanism of anticonvulsant effect of resveratrol on epilepsy.

Keywords: Resveratrol, Epilepsy, Penicillin, Rat

OC03

Electroencephalographic Investigation of the Effects of *Ginkgo biloba* on Spike-Wave Discharges in Rats with Genetic Absence Epilepsy

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AIM: *Ginkgo biloba*, which is widely used in the treatment of some types of dementia and attention deficits, has been reported to cause epileptic seizures. The aim of the present study was to investigate the effects of chronic *Ginkgo biloba* extract (EGb 761) on absence seizures and locomotor behaviors in male WAG/Rij rats.

METHODS: 50, 100 and 200 or 400 mg/kg doses of EGb 761 were administered to male WAG/Rij rats with implanted EEG electrodes by oral gavage for 28 days. Absence seizures were evaluated on spike-wave discharges (SWDs) in EEG records that were obtained for 4 hours each week. The *number of*, mean duration and total duration of SWDs were determined for the analyzes. Electrophysiological data were analyzed by Wilcoxon test and locomotor data were analyzed by Mann-Whitney U test. The study was conducted with the permission of SBÜ Animal Experiments Local Ethics Committee 2017-1054.

RESULTS: In the group treated with 400 mg/kg EGb 761, the number and mean duration of SWD at the 1st and 7th doses and the total SWD duration at the 1st, 7th and 14th doses were significantly increased ($p < 0.05$). In *other* experimental groups treated with EGb 761 doses, there was no significant change in locomotor activity in the open field and the rotarod tests. CONCLUSION: *Ginkgo biloba* extract EGb 761 increased the epileptic SWDs parameters of WAG/Rij rats at high doses (400 mg/kg), causing a proconvulsant effect on absence seizures. It should be noted that *in epilepsy patients high-dose applications* of *Ginkgo biloba* extract EGb 761 may lead to an increase in neuronal excitability.

This study was supported by TÜBİTAK (Project no: 115S348).

Keywords: Absence epilepsy, EEG, {Ginkgo biloba}, spike-wave discharge, WAG/Rij rat

OC05

The Effect of Hemopressin Combined To CB1 Receptor Agonist and Antagonist on Epileptiform Activity in the Pentylenetetrazole Kindling Rat Model

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AIM: Hemopressin, α 9 amino acid nanopeptide derived from α chain of hemoglobin. However, it is not clear whatever hemopressin is agonist or antagonist of CB1 receptors. The aim of this study was examined its interaction between CB1 receptor agonist and antagonist in pentylenetetrazole kindling model.
METHOD: The animals were injected pentylenetetrazole (PTZ) sub-convulsive dose (35mg/kg/ i.p) for three days per week for a maximum 29 injections. Subsequently, combination injection of hemopressin (0.6 μg) + AM-251 (0.50 μg), AM-251 (0.50 μg) + hemopressin (0.6 μg) and, ACEA (7.5 μg) + hemopressin (0.6 μg) were administered. An ECoG recording was started when the PTZ injected and last for 30 minutes. The epileptiform activity frequency and amplitude were analyzed.

RESULTS: The administration of hemopressin (0.6 μg) + AM-251 (0.50 μg), significantly decreased the total number of spike wave discharges (SWDs), the number of spikes in each SWD and total SWDs time ($p<0.05$). While increased myoclonic jerk latency compared *with* the control group ($p<0.05$). The administration of AM-251 (0.50 μg) + hemopressin (0.6 μg), significantly increased the total number of SWDs and the number of spikes in each SWD ($p<0.05$), while no significant difference in total SWDs time, spike amplitude, seizure score and myoclonic jerk latency compared *with* the control group ($p>0.05$). The administration of ACEA (7.5 μg) + hemopressin (0.6 μg), significantly decreased the total SWDs, spike counts and total SWDs time ($p<0.05$), while significantly increased myoclonic jerk latency ($p<0.05$).

CONCLUSION: The hemopressin is acting as agonist of CB1 receptors in this model. When administered before the AM-251, homopressin decreased epileptiform activity, however when administered after AM-251 it increased epileptiform activity. When administrated with ACEA epileptiform activity was decreased suggesting that hemopressin acts as an agonist of CB1 receptor.

Keywords: Electrocorticography, Epilepsy, Hemopressin, AM-251, ACEA, pentylenetetrazole

OC06

Long-Term Dietary Probiotic Intake Ameliorates Pentylenetetrazole-Induced Epileptic Seizures by Reducing Oxidative Stress in Rats

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AIM: Pathophysiology of epilepsy isn't fully understood but the role of oxidative-stress in generation and progression of epilepsy is known. Intestinal microbiota modulates function of nervous system. A clinical case reported that fecal microbiota transplantation prevented epileptic seizures. This case reinforces hypothesis that microbiota may be protective in epilepsy. We investigated effects of long-term dietary probiotic-intake on seizures and oxidative-stress in pentylenetetrazole-induced seizure model in rats.
METHODS: Wistar male rat-weaners (30 days-old) were separated into 4 groups as control (n=7), probiotic (n=12), vehicle (n=12) and saline (n=12). Groups received 1ml/day saline, 109cfu/1ml/day probiotic mixture, 0,05mg/1ml/day inuline and 1ml/day saline by gavage for 60 days, respectively. 60 days later, except for control, groups received intraperitoneal injection of 50 mg/kg pentylenetetrazole and behaviors were videotaped for 30 min. Blood and brain samples were collected 24 hours after pentylenetetrazole injection. Seizures were assessed using Racine's scale. Oxidant (TOS, disulfide) and antioxidant (TAS, native and total thiol) parameters in plasma and brain samples were measured by automated-colorimetric method. Data were compared by Kruskal-wallis test.
RESULTS: In PTZ-treated groups, while 100% of rats in SF and vehicle groups entered generalized tonic-clonic seizure (stage-5), in probiotic group 91,6% of rats had generalized tonic-clonic seizure. Probiotic-intake extended onset-times of myoclonic-jerk and generalized tonic-clonic seizure (P=0,043; P=0,018), it shortened duration of generalized tonic-clonic seizure (P=0,009). Pentylenetetrazol increased plasma TOS and disulfide concentrations (P=0,001; P=0,007), it reduced native and total thiol concentrations (P=0,049; P=0,006), without changing TAS concentrations. Probiotic-intake decreased plasma TOS and disulfide concentrations (P=0,025; P=0,045), and it increased native and total thiol concentrations (P=0,035; P=0,046). Pentylenetetrazol increased brain TOS concentration (P=0,001) without changing TAS concentration. Probiotic-intake decreased brain TOS concentration (P=0,005).
CONCLUSION: When age-group of rats receiving probiotics is considered, long-term probiotic-intake from childhood demonstrated anticonvulsant effect on behavioral characteristics of epilepsy by improving epilepsy-impaired oxidant/antioxidant balance. Regular probiotic-intake from childhood may be a natural and effective approach for epilepsy prophylaxis. Grant-number: 2018.08.02.1370 (BAIBU-BAP).

Keywords: Epilepsy, microbiota, oxidative stress, probiotic

OC07

Effects of Selected Anti-epileptic Agents on Contractility of Gastric Fundus Strips Isolated from Control Wistar and Absence Epileptic WAG/Rij Rats

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AIM: Considering the high occurrence of gastrointestinal (GI) functional impairment including upper GI upset in epilepsy and GI-related side effects of anti-epileptic drugs, we aimed at investigating possible effects of valproic acid, levetiracetam and phenytoin on cholinergic agonist-induced contractions of gastric fundus isolated from healthy Wistar and absence epileptic Wistar Albino Glaxo/Rijswijk (WAG/Rij) rats.
METHODS: Fundus strips were mounted in organ bath containing Tyrode solution (pH=7.4, 95% O2 + 5% CO2 at 37°C), and contractile responses to cholinergic stimulation were tested with cumulatively-applied carbachol (CCh; 0.1, 0.3, 1 and 3 µM). In order to test the effects of anti-epileptics, valproate (100µM, 300µM, 1mM, 3mM), levetiracetam (100µM, 300µM, 1mM, 3mM) and phenytoin (10, 30, 100µM) were applied cumulatively on CCh (3µM)-induced contractions. Amplitude (mg) and area under the contraction curve (AUC) data were assessed as contraction parameters (AUC of 3µM CCh-induced contractions were regarded as 100% and drug effects were reported with reference to this). Data *were* analysed by using repeated measures ANOVA and Student's t-tests.

RESULTS: Mean amplitude (144.42%) and AUC values of contractions of fundus strips isolated from WAG/Rij rats were significantly higher than Wistars' ($n=21$, $p<0.05$). Considering the 3µM CCh-induced contractions; valproate [101±7, 82±12, 65±15, 53±16% (in Wistar group), 99±3, 103±5, 101±8, 97±11% (in WAG/Rij group)]; levetiracetam [96±5, 90±6, 83±6, 78±7% (Wistar), 104±4, 105±6, 105±7, 100±7% (WAG/Rij)] and phenytoin [87±4, 56±5, 28±8% (Wistar), 81±6, 56±6, 35±7% (WAG/Rij, n=7 for each subgroup)] exerted dose- and species-dependent effects. Phenytoin provided significant effects in both rat groups ($p<0.05$) and strongest relaxation effect ($p<0.05$).
CONCLUSION: The results from this *in vitro* study indicates that particularly phenytoin among the tested anti-epileptics agents caused relaxation of the fundus muscle. This effect may implicate impairment of gastric accommodation reflex and gastric emptying.
This study protocol was approved by Karadeniz Technical University Animal Research Ethics Committee.

Keywords: Antiepileptics, gastric fundus, gastric accommodation reflex, contractility, WAG/Rij rats

OC08

Effect of Thymoquinone on Ischemia/Reperfusion Injury in Isolated Hearts of Streptozotocin-Induced Diabetic Rats

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AIM: Diabetic patients have a high risk of cardiovascular diseases and cardiovascular complications which are the leading causes of morbidity and mortality. Thymoquinone, important bioactive component of black seed, has antioxidant and antidiabetic effects, and decreases blood glucose by increasing glucose use via increasing insulin secretion and preventing glyconeogenesis. This study was designed to investigate whether thymoqinone had protective effects against cardiac ischemia-reperfusion (IR) injury and oxidative stress in isolated hearts of diabetic rats.

METHODS: Thirty-five male Wistar albino rats (7 in each group) weighing 350-400 g were used. Animals were divided into control, IR, thymoquinone (10 mg/kg, 1 ml po, for 30 days), diabetes (streptozotocin 65 mg/kg, ip) and thymoquinone- or vehicle-treated diabetes+IR groups. After 20 minutes of stabilization; in control group 90 minutes perfusion, in IR groups 30 minutes ischemia and 60 minutes reperfusion were applied via Langendorff isolated heart system. Blood and heart tissue samples were taken for biochemical analysis and evaluated together with cardiodynamic parameters. The data were evaluated by Benforroni's multiple comparison test and $p<0.05$ was considered significant.

RESULT: Thymoquinone decreased blood glucose levels compared *with* diabetes group ($p <0.001$). End-diastolic pressure increased with ischemia, left ventricular developed pressure and max dp/dt decreased, thymoquinone treatment revealed a significant ($p <0.001$) return of all parameters compared to diabetic group. Thymoquinone also increased insulin levels, which decreased in diabetes ($p <0.01$). Diabetes increased cardiac injury markers CK-MB and NT-proBNP, inflammation markers CRP, TNF-α, IL-6 and IL-1β, endogenous antioxidants SOD and GSH, and these elevated levels were reduced by thymoquinone ($p <0.001$).

CONCLUSIONS: Diabetes activates inflammatory and oxidative mechanisms, causing cardiac damage and loss of function, thymoquinone has a positive impact on both glucose metabolism and cardiac performance, reducing the diabetes induced damage.

This project was supported by SRP unit of Bezmialem Vakıf University with the project number of 9.2017/8.

Keywords: Diabetes mellitus, heart, ischemia/reperfusion, oxidative damage, thymoquinone

OC09

Electrocardiographic and Histopathologic Evaluations on Possible Role of H3 Receptors in β-adrenergic Stimulation-Induced Myocardial Damage in Mice

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AIM: The present model deals with following questions: May the β-adrenergic stimulant "isoproterenol" leading to inflammatory/ischemic histopathologic changes in mice myocardium cause electrocardiographic alternations, as well? Additionally, may "isoproterenol" induced myocardial ischemia be prevented by H3 receptor (H3R) agonist "Imetit"?

METHODS: Four groups of Balb-c mice are *constituted* according to drugs given: Saline (SF), isoproterenol (ISO), Imetit (IMT), and a combination of IMT+ISO. Pre-condition lasted 7 days, for each days IMT and ISO+IMT groups were pretreated with oral 10 mg/kg Imetit. In both groups of ISO and ISO+IMT, 85 mg/kg isoproterenol was injected subcutaneously on the last two days to induce myocardial ischemia. At the end of pre-condition, two ECG leads are obtained (lead-I and "Z") under Na-Pentobarbital (75 mg/kg) + Fentanyl (0.2 mg/kg) anesthesia. Hearts were removed for histological evaluation: ventricular-wall sections were stained with Hematoxylin-Eosin (H&E) for morphological examination, and tissue level of inflammatory parameters IL-1β, TNF-alpha, MCP-1 were evaluated with indirect-immunoperoxidase staining. Data were compared with the t-test or Kruskal-Wallis test.

RESULTS: We found the J-wave area in lead-Z being a new ECG marker for ISO-induced myocardial ischemia. Both QJ interval and QRS duration increased due to ischemia (ISO), $p<0,001$ and $p<0,05$, respectively. H&E examination supported ECG findings, MCP-1 increased in ischemic myocardium ($p<0,001$) whereas IL-1β and TNF-α cytokines were unchanged. These ECG and histological alterations were not seen in pretreated animals with Imetit (IMT+ISO), except MCP-1. Imetit alone (IMT) decreased both atrial and ventricular conduction velocity therefore both PQ interval and QRS duration are increased, $p<0,05$, and $p<0,05$ respectively.

CONCLUSION: The J wave area in lead-Z seems to be sensitively correlated to the histological finding of ISO-induced myocardial ischemia in mice. We considered that H3 receptor might present on membranes myocardial cells, basing on increased PQ interval and increased QRS duration due to H3 agonist Imetit.

Keywords: ECG, fare, H3 receptor, imetit, isoproterenol, myocardial ischemia

OC10

Erythrocyte Derived Nitric Oxide Production in Pulmonary Arterial Hypertension

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AIM: Pulmonary arterial hypertension (PAH) is one of the rare fatal disease which is characterized by abnormally high blood pressure in the pulmonary artery. Major causes of the increased pulmonary artery pressure include decreased plasma NO (nitric oxide) levels due to decreased endothelial nitric oxide synthase (eNOS) enzyme activity in pulmonary artery endothelial cells. Erythrocytes have special importance that determining the vascular resistance in pulmonary circulation: NO released from endothelial cells in response to shear stress, that only occurs by the presence of erythrocytes. Erythrocytes constituently produce endothelial type NO under basal conditions and contribute to NO pool in the vascular system which has important roles on physiological systemic blood flow regulation. It is not known whether erythrocyte eNOS enzyme activation and NO production changes in PAH patients.

METHODS: Packed of erythrocytes were isolated from two different groups; healthy and PAH volunteers. Than packed were re-suspended in Hepes solution at a hematocrit of 0.01 l/l. Sampling protocols were approved by local ethical committees (06.02.2019/128). Intracellular NO, Ca+2 and ROS levels and eNOS activation measured by flow cytometry. Student-t test was used for evaluating the results. Statistical significance was $p<0.05$.

RESULTS: Intracellular NO and ROS levels decreased in PAH patients compared *with* healthy group ($p<0.001$; $p<0.01$). Phosphorylated eNOS level also diminished in PAH patients ($p<0.001$). However, there was no difference in intracellular Ca+2 levels between two groups.

CONCLUSIONS: The results of the study suggest that in PAH patients NO production in erythrocytes only diminished via eNOS phosphorylation decrement rather than intracellular Ca+2 changes.

Keywords: Erythrocyte, Hypertension, Nitric oxide, Pulmonary artery

OC11

The Effect of Heterochronic Parabiosis Model on Vascular Responses of Thoracic Aorta in Aged Mice

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AIMS: We aimed to determine effect of parabiosis model on vascular response of aged and young mice.

METHODS: In our study, young and old Balb/c mice were used and separated into 6 groups as isochronic old (IP-O), heterochronic old (HP-O), isochronic young (IP-Y), heterochronic young (HP-Y), control young (C-Y) and control old (C-O). While in the heterochronic parabiosis group, old and young animals were surgically combined through their skin, in the isochronic parabiosis groups, either young and young or old and old animals were combined too. After surgery, animals were sacrificed at 3rd, 5th, 7th and 9th weeks and then thoracic aortas were isolated. Vascular responses were determined by organ bath. To determine contraction responses, phenylephrine (10-9-3x10-5M) and potassium chloride Kkrebs (20 mM, 40mM and 80mM), and to determine vasodilation responses acetylcholine (10-9-3x10-5M), and sodium nitroprusside (10-9-3x10-4M) were used. While dose-response curves were evaluated by using repeated measure ANOVA, maximum contraction and relaxation responses were evaluated by using generalized linear model. LSD test was used as Post Hoc test. Data were shown as ±standard error and $p\leq0.05$ was obtained as significant difference.

RESULTS: Aging had a significantly lowering effect on maximum ACh relaxation responses ($p\leq0.01$). However, in the HP-Y group, the maximum ACh relaxation response at the 3rd weeks was significantly lower ($p\leq0.05$), but this significance disappeared at 9th weeks. Maximum ACh dilatation responses of groups; C-Y: 77,78±5,13, HP-Y; in 3rd week: 76,29±4,39, 5th week: 64,47 ±7,28, 7th week: 67,24 ±5,82, 9th week: 72,62 ±6,61, C-O: 60,79 ±6,25, HP-O; 3rdweek: 58,69±4,84, 5thweek: 57,14±2,98, 7th week: 60,19 ± 6,42, 9thweek: 73,28, IP-Y; 3rdweek: 70,48±7,16, 5thweek: 71,82±3,61, 7th week: 71,19±8,25, 9th: 76,62±5,61, IP-O; 3rdweek: 63,31±3,37, 5th week: 58,46±9,28, 7th week: 60,31±4,34, 9th week: 58,08±12. Maximum phenylephrine contraction responses were lower in the heterochronic parabiosis group ($p\leq0.05$).

CONCLUSION: The parabiosis model may have improving effect on endothelial disfunction.

Keywords: endothelium-dependent vasodilation, parabiosis, vascular tonus

OC12

Effects of Adropin and Spexin on Cardiac Inflammatory Markers; Chronic Renal Failure Model

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AIM: One of the most common cause of death in developed countries is cardiovascular diseases. Chronic renal failure (CRF) is an important risk factor for cardiovascular diseases such as pericarditis, hypertension, cardiomyopathy. In this study; the possible protective effects of newly identified spexin and adropin peptides on cardiovascular damage in adenine-induced chronic renal failure model were investigated.

METHODS: Wistar albino rats of both sexes divided as (180-220g, N=35) vehicle (5%CMC, 1 ml/kg, po) or CRF (adenine, 600 mg/kg, 5% CMC, 10 days/po) groups. CRF group was divided as saline (SF; 1 ml / kg, n = 7), adropin (2.1 g / kg / ml, n = 7), spexin (35 g/kg/ml, n=7) or adropin + spexin(n=7). Following the experimental procedure, rats were sacrificed at 4 weeks and serum and tissue samples were taken. Serum chemokines (eotaxin, group-alpha, IP-10, MCP-1, MCP-3, MCP-1a, MIP-2, rantes) and cytokines (G-CSF, IPN-g, IL- 2, IL-4, IL-5, IL-10, IL-12, IL-13 and IL-17α) were measured. Immunohistological staining was performed on aortic and cardiac tissues. Data were expressed as mean ± standard error, statistical analyzes were compared with ANOVA.

RESULTS: While eotaxin and rantes levels of chemokines increased in CRF (1247.0±130.2 vs 207.1±92.63; $p<0.05$) and spexin group (946.4±75.26; $p<0.05$), there was a decrease in Group-α levels (167.8±34.02 vs. 56.93±25.46; $p<0.05$). While MCP-1, MCP-2 and MIP-2 levels decreased in CRF group, it increased in adropin and adropin+spexin treated groups ($p<0.05$). In CRF group, G-CSF, IFN-γ, IL-4, IL-5, IL-10, IL-12 and IL-17α levels increased significantly (respectively: 20.15±1.86 vs 29.44±8.04; $p<0.05$, 20.15±1.86 vs 31.46±7.68, $p<0.05$, 7.46±2.71 to 14.41±5.03; $p<0.01$, 8.36±3.78 vs 13.96±2.02; $p<0.05$, 14.75±3.56 vs 26.73±7.45; $p<0.01$, 50.58±5.46 vs 90.77±31.95; $p<0.05$, 1.68±0.64 vs 5.75±3.45; $p<0.01$). G-CSF, IFN-g, IL-5 and IL-10 levels were decreased in the spexin and/or adropine groups ($p<0.01$).

CONCLUSION: In our study, therapeutic effects of adropin and spexin on some chemokines and cytokines in CRF-induced cardiac inflammation were demonstrated.

Keywords: Adropin, spexin, chronic kidney disease, cardiovascular, inflammation

OC13

The Effect of Different Doses Apelin 13 on Erythrocyte Deformability in Rats

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AIM: Apelin and apelin receptor (APJ) form a signaling pathway and are widely expressed in a variety of tissues including the heart, kidney and vessels. Apelin and APJ have various effects in many systems such as regulation of blood pressure and vascular tone, cardiac contractility, nociception, heart rate, apoptosis, inflammation. The fact that apelin can be used as a protective and therapeutic agent in the future will make important contributions both for human health and economically. Therefore, we aimed to investigate the effects of apelin-13 administration on erythrocyte deformability in rats.

METHODS: Thirty male Wistar Albino rats were randomly divided into 5 groups. Rats were identified as control, Apelin-25, Apelin-50, Apelin-100 and Apelin-200 groups. Apelin-13 was administered intraperitoneally at 25, 50, 100 and 200µg/kg. The same volume of saline was administered intraperitoneally to the control group. After the administration, intraperitoneal ketamine 100 mg / kg was administered to all rats and euthanasia was performed. Erythrocytes were obtained from heparinized whole blood samples. Deformability measurements were performed on erythrocyte suspensions in phosphate buffered saline. For the measurement of erythrocyte deformability, a constant flow filtrometer system was used and the relative resistance was calculated.

RESULTS: The erythrocyte deformability index was significantly different between the groups ($p=0.043$). Apelin application of 200 µg/kg was found to increase the relative resistance. The erythrocyte deformability index was significantly higher in the 200 µg/kg Apelin group compared to the control and 50 and 100 µg/kg Apelin groups ($p=0.030$, $p=0.027$, $p=0.011$, respectively). The deformability index of the control group and Apelin 25, 50 and 100 µg/kg groups were similar.

CONCLUSIONS: We did not find any studies about the effects of apelin on erythrocyte deformability in different doses in the literature. We found that high-dose apelin-13 administration adversely affected erythrocyte deformability. However, these findings should be supported by clinical and experimental studies in more detailed and large series.

Keywords: Apelin 13, erythrocyte deformability, rat

OC14

Determination of Hemorheological Parameters in Patients with Major Depression

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AIM: Cardiovascular disease (CVD) incidence is high in patients with major depression. CVD have been related to high blood viscosity. This study aimed to evaluate the determinants of blood viscosity, in patients with major depression.

METHODS: Patients diagnosed to have major depression (n=25) according to DSM-V criteria. The level of depression was determined by Beck Depression Inventory Hamilton Depression Scale. Depression duration was not determined. Recurrence rates of major depression episodes were recorded. Control group (n=30) received a psychiatric interview excluding major depression. All participants were between 18-65 years old. Individuals with CVD, hypertension, diabetes mellitus and smokers were excluded from both groups. Blood viscosity was evaluated through hemorheological parameters. Plasma viscosity was determined by cone-plate viscometer at 900 sec^{-1} (120rpm) shear rate. Erythrocyte deformability and aggregation were determined by LORCA (laser-assisted optical rotational cell analyzer). Measurements were made at 37°C. "t test" and "Mann Whitney U test" were used as statistical methods.

RESULTS: Compared with the controls, plasma viscosity of the patient group was higher (1.33±0.09 and 1.39±0.02 mPa.sec respectively) and erythrocyte deformability index at 0.53Pa shear stress was lower (0.065±0.002 and 0.059±0.002 respectively) ($p<0.05$). Erythrocyte aggregation parameters: AMP, AI, t½ and γIscmax revealed no statistically significant difference between groups. Complete Blood Count revealed no difference in erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, red cell distribution width and leukocyte count between groups. Mean corpuscular hemoglobin concentration was lower in the patient group ($p<0.05$).

CONCLUSION: High plasma viscosity and low erythrocyte deformability in patients with major depression may contribute to the high risk for cardiovascular diseases. Further studies carrying out long-term follow-up of patients with major depression and relating the initial hemorheological findings to emerging cardiovascular problems are needed to clarify the link between depression and cardiovascular diseases.

Keywords: Erythrocyte Aggregation, Erythrocyte Deformability, Hematocrit, Hemorheology, Major Depression, Plasma Viscosity

OC15

Effects of Estrogen and Estrogen Receptor Agonists on Acetaminophen-Induced Hepatorenal Toxicity in Rats

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AIM: Acetaminophen (APAP) is the most widely used analgesic, and APAP-induced intoxication is most common among voluntarily taken drugs. When taken at above-treatment doses, APAP becomes toxic on liver and kidneys. Estrogen receptor (ER) subtypes have been reported to have antioxidant and anti-inflammatory effects. The aim was to investigate the role of sex in APAP toxicity and therapeutic effects of treatment with selective estrogen receptor agonists on this toxicity.

METHODS: Wistar albino female (n=56) and male (n=16) rats were used. Female rats underwent overiectomy (OVX) or sham-OVX under ketamine anesthesia. Forty days after OVX, rats were injected subcutaneously (each, 1mg/kg/day) with 17β-estradiol, ERα agonist propyl-pyrazol-triol (PPT), ERβ agonist diarylpropionitrile (DPN) or vehicle (oil), while male and sham-OVX rats were injected with vehicle for 10 days. On 49th day, rats were orogastrically given APAP (3g/kg) or saline (control) and decapitated 24 hours later. Renal and hepatic myeloperoxidase activity, antioxidant glutathione levels and luminol/lucigenin chemiluminescence levels, and serum alanine aminotransferase (ALT), aspartate aminotransferase (AST), blood urea nitrogen (BUN) and creatinine levels were measured. Histopathological examinations were performed. ANOVA and Mann Whitney-U tests were used for data analysis.

RESULTS: Compared to control group, serum AST, ALT, BUN and creatinine levels in the APAP-given male, OVX and sham-OVX groups were elevated, while hepatic histological damage scores, renal myeloperoxidase activity were increased, hepatic glutathione levels were depleted ($p<0.001$). However, hepatic MPO activity was increased only in male rats ($p<0.05$). PPT treatment reversed changes in both kidney and liver ($p<0.05$-0.001), while DPN and 17β-estradiol replenished glutathione levels in the liver and reduced renal MPO activity and creatinine levels ($p<0.05$-0.01).

CONCLUSIONS: Except an additional increase in hepatic neutrophil infiltration in males, acetaminophen-induced acute hepatorenal toxicity was similar in female/male sex or in menopause, while pretreatment with ER agonists provided protection by decreasing toxicity-induced oxidative damage.

Keywords: Acetaminophen, estrogen receptors, hepatorenal toxicity, antioxidant

OC16

Assessment of the Blood and Salivary Level of Oxidative Stress and Insulin Resistance Factors in Gestational Diabetes Mellitus

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AIM: Gestational diabetes mellitus (GDM) is a medical complication of pregnancy mirroring the prevalence of type 2 Diabates Mellitus (DM). Present study is aimed to investigate the plasma and salivary levels of malondialdehyde (MDA) and nitric oxide (NO) which are biomarkers of oxidative stress, sulfhydryl compounds (RSH) and thioredoxin reductase (TrxR) that have been implicated in antioxidant defense, and chemerin which plays a role in insulin sensitivity in normal pregnancy and GDM.

METHODS: Study group (n=51) which are systemically healthy, mean of ages Control=30,2±4,1, GDM=32,1±4,3 (p>0,05), and body mass index Control=24,2±2,9 and GDM=25,7±2,5 (p>0,05) were divided into two groups as control (n=29) and GDM groups (n=22) diagnosed by administering oral glucose tolerance test (50-100g). Saliva samples were collected without stimulation between 08.30-10.00 am. Then salivary and blood TrxR and chemerin levels were measured by Elisa method using commercial kits whereas saliva and plasma MDA, RSH and NO levels were determined by spectrophotometric analysis. The Ethical approval accession number:10.02.2014/78. Statistical analysis was performed by Shapiro Wilk, Mann Whitney U, Student's t test. Statistical significance was assumed when $p<0.05$. Since the data hasn't show normal distribution, non-parametric tests were used and the median values were compared.

RESULTS: High density lipoprotein levels were significantly lower in GDM ($p<0.05$). The plasma and salivary levels of chemerin, NO, RSH showed no significant difference in GDM ($p>0.05$). GDM groups had significantly lower median plasma TrxR ($p<0.05$) whereas salivary TrxR level was significantly higher ($p<0.001$). The median plasma levels of MDA showed no significant difference between control and GDM ($p>0.05$) whereas salivary MDA levels were found to be statistically significant higher in GDM ($p<0.001$).

CONCLUSION: A good glycemic control with diet in GDM may explain that insulin resistance and oxidative stress parameters are not different from control.

Keywords: Gestational diabetes mellitus, insulin resistance, oxidative stress

OC17

Intracerebroventricular MOTS-C Infusion Suppresses Thyroid Hormone Secretion in Rats

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AIM: Discovered in 2015, Mitochondrial-derived peptide (MOTS-c) is a peptide with 16 amino acids encoded by mitochondrial DNA. Studies have shown that MOTS-c decreases obesity and insulin resistance and plays an active role in cell metabolism. In our previous study, we reported that intracerebroventricular (ICV) MOTS-c infusion increases feed intake in rats but does not cause changes in body weight. All these findings suggest that peptide may play a role in metabolic rate and energy balance. This study was conducted to investigate the effects of ICV MOTS-c infusion on thyroid hormone secretion in rats.

METHODS: Forty male Wistar-Albino rats were used in the study. The rats were divided into 4 groups (n = 10) each with approximately body weights. Osmotic mini-pumps were attached to the brain infusion kits placed in the lateral ventricles of rats other than the control group and a volume of 5µl/h infusion were applied (yBOS in the sham group, 10 and 100 µM MOTS-c in the treatment groups) for 14 days. At the end of the infusion after the decapitation of rats, brain (hypothalamus) and blood samples were collected. TRH mRNA level was determined by using RT-PCR method from the hypothalamus tissue and serum TSH, T3 and T4 hormone levels were determined from blood samples by ELISA method.

RESULTS: In rats, MOTS-c infusion partially reduced TRH mRNA levels, but significantly decreased serum TSH, T3 and T4 hormone levels ($p <0.05$).

CONCLUSION: The results of the study show that MOTS-c can play important physiological roles in the hypothalamus-pituitary-thyroid axis. If the effect of MOTS-c on the HPT axis can be explained in more detail, a different approach will be obtained for the treatment of these axis-based diseases. This study was supported by TUBITAK (Project:116S744).

Keywords: MOTS-c, TRH, TSH, T3, T4

OC18

Vitamin D, Parathormone, Bone Weight and the Amount of Mineral in Pre- and Post-Menopausal Obese Women

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AIM: The fact that vitamin D is lower in obese compared to normal weight individuals suggests that vitamin D may play a role in obesity. Therefore, we aimed to determine the relationship between vitamin D, Parathormone (PTH), bone weight and the amount of mineral in pre- and post-menopausal obese women.

METHODS: 200 pre-menopausal and 200 post-menopausal obese women were included in our study (Ethics Committee Number: 2019/0212). Body composition was measured with bioelectrical impedance analyzer (TANITA-48M) and blood parameters were determined by biochemical tests. Student's t, Mann-Whitney U, Shapiro-Wilk, Spearman's rho and Pearson correlation tests were used and $p<0.05$ was considered statistically significant.

RESULTS: According to the obesity classification, 71 pre-menopausal women and 68 post-menopausal women were class I obese, 77 pre-menopausal women and 61 post-menopausal women were class II obese, 52 pre-menopausal women and 71 post-menopausal women were class III obese. The mean vitamin D levels were 16.91±13.17 in pre-menopausal women and 22.59±16.49 in post-menopausal women ($p<0.05$). While 83.75% of 400 obese women had vitamin D deficiency or insufficient, 16.25% (65) of obese women had normal vitamin D values (>30 ng/mL-150 ng/mL). Age, weight, height, vitamin D, calcium and phosphorus levels, bone density, muscle mass, lean mass, the amount of mineral and basal metabolic rate were significantly different in pre- and post-menopausal women, ($p<0.05$). PTH and mineral amounts were negatively correlated with vitamin D in pre-menopausal women, while there was a negative correlation between body mass index, weight, fat and PTH with vitamin D in post-menopausal women ($p<0.05$).

CONCLUSIONS: The prevalence of low vitamin D in obese women was found 83.75%. As vitamin D levels decreased both body weight and PTH increased in obese women while only mineral amount increased in pre-menopausal women. Our findings suggest that obesity may be related to vitamin D levels.

Keywords: Obese women, vitamin D, pre-menopausal, post-menopausal

OC19

The Effect of Ileal Interposition in Rats With Metabolic Syndrome

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AIM: Metabolic syndrome (MetS) is a cluster of metabolic abnormalities that includes hypertension, central obesity, insulin resistance, and atherogenic dyslipidemia. It includes abdominal obesity, insülin resistance, elevations of serum triglyceride, glucose, blood pressure, and reduced HDL cholesterol. The presence of three or more of these constitutes a clinical diagnosis. Our aim is to prevent the evolution of the parameters that define the MetS, with ileal interposition (IT) technique.

METHODS: IT is a surgical procedure involving the transposition of a distal ileum segment to the proximal jejunum in a properistaltic direction. MetS was induced in male Wistar rats by neonatal administration of monosodium glutamate (4g/mg body weight, BW) during the 0, 2, 4, 6, 8, 10^{th} days. Control group received saline (0,01ml/g BW) during the 0, 2, 4, 6, 8, 10 days. At the 5 month, Mets rats were submitted to ileal interposition or sham surgery. A 15cm segment was transected from 25 to 10cm proximal to the ileocecal valve. The jejunum was transected 5cm distal to Ligament of Treitz. The previously transected 15cm ileum segment was then interposed in an isoperistaltic fashion. After 2 months; lipid levels (HDL, LDL, TG, T-chol), abdominal obesity (perigonadal-retroperitoneal fad pad weighing), oral glucose tolerance test (OGTT), Lee index (by dividing the cubed root of body weight, by the nose-to-anus length), insulin resistance (HOMA-IR scor) and secretion were evaluated. Continuous variables were expressed as mean ± standard deviation and categorical variables as number and percentage.

RESULTS: In IT rats; retroperitoneal (Mets: 6,708 ± 0,523, IT: 2,396 ± 0,768, $p<0,05$), perigonadal (Mets: 6,104 ± 0,787, IT: 2,381 ± 0,629, $p<0,05$) fat content and Lee index (Mets: 0,321±0,003, IT: 0,306±0,002, $p<0,05$) statistically significant decrease was observed. It was also observed that IT caused improvement in insulin resistance (Mets: 12,935 ± 2,763, IT: 6,314 ± 1,115, $p> 0.05$) and impaired lipid profile (TG: 1,86±0,189, IT: 0,874±0,125, $p<0,05$) in the Mets group.

CONCLUSION: The primary effect of GLP-1 is that it stimulates insulin secretion. The observed results in our study may be due to the increase in GLP-1 level after metabolic surgery.

Keywords: Ileal interposition, metabolic syndrome, rat

OC20

Salivary Cortisol Levels Were Higher in Women Than Men at the Noon and in the Mid-Night

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AIM: Cortisol, the end product of the hypothalamopituitary (HPA) axis, is secreted into the bloodstream from the adrenal gland. In blood, cortisol is either in free or protein bound form. As a small steroid hormone, free cortisol easily passes into the saliva and therefore salivary cortisol represents the free or effective cortisol. Nowadays, measurement of salivary cortisol is widely used to assess the activity of HPA axis non-invasively. Aim of the current study was to measure salivary cortisol levels in women and men throughout a day.

METHODS: Women (n=54) and men (n=62), 18-to-32-year-old, were participated to the current study following ethical consent from Malatya Clinical Research Ethics Committee, Turkey. Saliva was collected at the 30th min of awakening, at noon and in the mid-night before sleeping. They were stored frozen until analyses by ELISA. Data did not have a normal distribution and Kruskal Wallis test was used for statistical analyses. Data were presented as median (min-max) and p less than 0.05 were denoted as significant.

RESULTS: Awakening salivary cortisol levels did not differ between the women and men (11.4 vs.14.7 ng/ml, respectively, P=0.499). However, salivary cortisol levels were higher in women than men at noon (13.3 vs 10.3 ng/ml, respectively, P=0.016) and at mid-night (6.5 vs. 5.5 ng/ml, respectively, P=0.042). Mean salivary cortisol was not different between the women and men (12.3 vs. 11.2 ng/ml, respectively, P=0.228).

CONCLUSIONS: The results suggest that men and women have different diurnal stress reactivity. Moreover, it seems that this reactivity is stronger in women than man from noon till mid-night. The significance of this difference remains to be elucidated but suggests a sexually dimorphic HPA axis observed in rodents (Oyola and Handa, 2017). Oyola MG and Handa RJ (2017). Stress, 20:476-494. Supported by the Scientific Research Unit (BAP, TDK-2017-812), İnönü University, Malatya.

Keywords: Salivary cortisol, woman and men stress level, hypothalamo-pituitary (HPA) axis

OC21

mTOR Inhibition and Melatonin Treatment Reduces Glioblastoma Cell Viability in Vitro

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AIM: Glioblastoma multiforme (GBM), grade IV astrocytoma, is the most common primary brain tumor with high malignancy and poor prognosis. The standard therapy includes the resection of the tumor followed by the radiotherapy or radiotherapy and chemotherapy combination. The phosphatidylinositol 3-kinase (PI3K)/AKT/mechanistic target of rapamycin (mTOR) pathway is indicated to be frequently deregulated in GBM. Melatonin is an indolic hormone and its anticancer activity has extensively been studied in vitro and in vivo. However, studies investigating effects of melatonin on GBM are limited. Therefore, in this study, effect of melatonin and mTOR inhibition with rapamycin on GBM viability was investigated in vitro.

METHODS: The human GBM cell lines A172 and U87-MG were maintained in DMEM containing 10% FBS and 1% PSN at 37 °C under 5% CO2 humidified atmosphere. Cytotoxicity of Rapamycin and melatonin were determined by WST-1 colorimetric proliferation assay following treating the cells with rapamycin and melatonin alone or in combination for 24 and 48h in 96-well culture plates. Cell viability was measured. Statistical analysis was done by Two-way ANOVA.

RESULTS: Rapamycin and melatonin differentially decreases GBM cell viability as at 24 h, melatonin significantly decreased the cell viability at 100 and 400μM doses in U87-MG, but not A172 (U87-MG: $p<0.001$ vs. Control and U87-MG vs. A172: $p<0.001$), while rapamycin was more effective in A172 cells at 48h at 20 nM ($p<0.001$). On the other hand, 100 nM rapamycin + 400 μM melatonin treatment were found to be more effective in U87-MG compared to A172 cell line ($p<0.001$) at both time points.

CONCLUSIONS: Our in vitro findings suggest that combinatorial treatment with melatonin and rapamycin may be an option for treatment in GBM. However, one should note the importance of genetic background differences in GBM. In vivo studies are needed to elucidate effectiveness of rapamycin and melatonin on GBM.

Keywords: mTOR, Glioblastoma, melatonin, cell viability

OC22

Green Synthesis of Mgs Nanoparticles and Their Effects on Neuroblastoma Cells

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AIM: Magnesium Sulphur nanoparticles (MgS NPs) is one of the important nano metals that are being used effectively in drug delivery systems. Neuroblastoma, which is the most common extracranial tumor of childhood, is a cancer which is extremely difficult to treat. This study was conducted to determine the anticancer activity and oxidant-antioxidant properties of MgS NPs.

METHODS: Magnesium Sulphur nanoparticles have been synthesized by green synthesis, a cleaner method for toxic effects. Na_2S and Punica granatum plant extracts were used in green synthesis method. In cell culture, aseptic conditions SH-SY5Y was developed in suitable nutrient medium. Five different (10, 25, 50, 75 and 100 µg/mL) doses of MgS NPs were applied on the cell line for 24 hours. The analysis of the study, which was conducted in a positive and negative controlled manner, was performed with MTT cell viability test and total oxidant and total antioxidant tests.

RESULTS: As a result, application of 75 µg/mL MgS NP dose was found to reduce cancer cell viability by 51.56% compared with the control. It has been determined that the effects of MgS nanoparticles increase especially with increasing doses. In light of the data obtained, it was noted that the oxidant effects of MgS nanoparticles increased in cancer cells in a correlation with MTT analysis.

CONCLUSIONS: The efficacy of MgS nanoparticles on cancer cells was clearly demonstrated by the tests performed. It is clear that nanoparticles synthesized by green synthesis have antiproliferative effect on SH-SY5Y cells.

Keywords: MgS NPs, SH-SY5Y, cancer cell lines, green synthesis, neuroblastoma (NBL)

OC23

Mir663 Prevents Erythropoietin Inhibition Caused By TNF-Alpha in Normoxia and Hypoxia

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AIM: In chronic inflammatory diseases, pro-inflammatory cytokines such as Tumor necrosis factor-alpha (TNF-α) are present in high amounts in the circulation. Experimental studies have shown that TNF-α inhibits the synthesis of Erythropoietin (Epo), the main stimulant of hematopoiesis. Our aim was to figure out which micro-RNAs are involved in the Epo repression by TNF-α.

METHODS: First we determined the dose of TNF-α in HepG2 cells that has no cytotoxic effect by MTT and that inhibits Epo synthesis by qRT-PCR and ELISA. Then we performed the micro-RNA array study with TNF-α (20 ng/ml) treated cells and array results were confirmed by qRT-PCR. We transfected miR663 group with the miR663 mimics (30 pmol) for 24 hrs, other groups treated with transfection reagent, followed by treatment of TNF-α and miR663 groups with TNF-α for 24 hrs, control group incubated with normal medium. We analyzed Epo mRNA level by qRT-PCR. If miR663 mimic prevents the Epo-repression by TNF-α more Epo dependent UT-7 cells would survive. So, we co-cultured HepG2 cells with UT-7 cells. Percentage of apoptotic UT-7 cells were determined by TUNEL assays.

RESULTS: According to our array study, TNF-α significantly decreases miR663 expression. After transfection of miR663 mimics into HepG2 cells, TNF-alpha was unable to decrease Epo mRNA amounts. Furthermore, miR663 mimics transfection resulted in a lower apoptosis rate of UT-7 cells in co-culture experiments.

CONCLUSIONS: miR663 is involved in Epo mRNA production and that is able to prevent or reverse the inhibitory effect of TNF-α. In our co-culture study, transfecting HepG2 cells with miR663 mimics decreased apoptosis of UT-7 cells. This study is supported by The Scientific and Technological Research Council of Turkey (TUBITAK, no: 216S729), by the Eskisehir Osmangazi University Scientific Research Projects Committee (no: 2017-1635), Turkey and by Erwin-Riesch-Stiftung, Germany.

Keywords: Array, erythropoietin, inflammation, miRNA, TNF-α

OC24

Investigation of the Effect of Melatonin Administration on Calpain-1 Expression and Atrophic Morphology in Atrophy of Mouse Myoblast Cell Line Exposed to Hydrogen Peroxide

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It is known that oxidative stress is the main factor in the formation of disuse muscle atrophy, the most common type of muscle atrophy. The first important damage which is exerted by oxidative stress on proteases such as calpain-1 has been demonstrated in several studies. Treatment options include antioxidants, and in these groups mitochondrial targeting antioxidants such as melatonin have been shown to be more effective.

AIM: In this study, we aimed to determine the effect of melatonin treatment on oxidative stress-induced atrophy morphological change, calpain-1 expression and redox balance in C2C12 muscle cells.

METHOD: We have used H_2O_2 to generate oxidative stress. Four groups of C2C12 cells were created as K(Control), M(Melatonin), H(H_2O_2), M+H (Melatonin+ H_2O_2) groups. For morphological evaluation, measurement of myotube diameter with Image J Program was performed. In the second step, the amount of calpain-1 protein from total protein lysates was measured by western blot method. TAS and TOS kits were used to find out the antioxidant/oxidant statuses of the cells. Statistical analyzes were performed in SPSS program. The level of significance was set at $p < 0.05$.

RESULTS: There was a statistically significant decrease in the mean myotube diameters of the H group compared to the other groups (K, M, M+H) and statistically significant increase in mean myotube diameter of M group compared to K and H groups. The expression level of calpain-1 protein was increased in H, M and M+H groups compared with K group. TOS was higher in the H group than other groups. The highest mean TAS value was seen in the H group (rebound effect).

CONCLUSION: These results suggest that H_2O_2 produces muscle atrophy in C2C12 cells and that melatonin prevents morphological change and in addition to calpain-1 protein, other mechanisms can also take part in the prevention of disuse muscle atrophy. Functional studies need to be carried out to better explain this effect.

Keywords: Muscle atrophy, calpain 1, melatonin, mitochondria targeted antioxidants, redox balance

OC25

Acute Effects of Intermittent Exercise Performed at Anaerobic Threshold Level on Vascular Function in Healthy Young Men

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AIM: Although the effect of different intensity exercise is known, the intermittent exercise effects on vascular endothelial function is unknown. Vascular endothelial function of intermittent exercise which interspersed by short resting intervals performed at the anaerobic threshold levels were compared with continuous exercise.
METHODS: Peak oxygen consumption (VO_2 peak) was determined by analysis at breath by breath in physically active 18-24 years old healthy men (n=12). Intermittent exercise consisting of 1 minute long 8 loads and 75 second rest periods is described on the bicycle ergometer and the duration of the continuous exercise at the same workload was determined. After 2 exercise bouts with 1-week break in between, venous blood lactate levels were measured immediately. Brachial artery flow-mediated dilation (FMD) was measured at baseline and at 30 minutes after exercises. Endothelial nitric oxide synthase (eNOS), endothelin-1, adiponectin levels were measured by ELISA in serum obtained at 5 and 60 minutes after each exercise. Sample size was calculated according to differences of adiponectin in moderate intensity, intermittent and continuous exercise, with power analysis ($d=0.8$ and $\alpha=0.05$). Wilcoxon Signed Ranks Test was used for statistical comparisons.

RESULTS: Mean VO2peak (33.42 ± 5.9ml/min/kg) and anaerobic threshold levels (47.33±5.85%) of the participants were determined. Blood lactate levels of continuous exercise were found to be higher than intermittent exercise (27.76 ± 7.43mg/dl, 18.54 ± 4.87mg/dl; $p<0.05$, respectively). There was no difference in FMD response after both exercises (7.05±15.11%; 2.49±16.24%). Endothelin-1, eNOS activity, and adiponectin levels were not different before and after in intermittent and continuous exercises.

CONCLUSION: Considering the increase in blood lactate levels in continuous exercise, resting periods can be factor that facilitates adaptation for individuals who feel difficulty in exercising. However, we suggest that intermittent or continuous exercise at the anaerobic threshold level in healthy men does not produce a significant acute change in endothelial function.
The study was supported by TUBAP (2018/100). Ethical approval (05/22).

Keywords: Anaerobic threshold, intermittent exercise, FMD, vascular function

OC26

The Protective Effect of Weekend Warrior and Continuous Exercise Models on Depression Induced Cognitive Impairment

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AİM: Depression is an important physiopathological process that goes on with cognitive decline. Exercise improves depressive mood. Our aim was to show the role of weekend warrior and continuous exercise models on cognitive impairment in depression, to exhibit the possible underlying mechanisms.
METHODS: Male rats (n=36) were separated as; Sedentary (SED), weekend warrior (WW: moderate intensity swimming 75 min/day, 2 days/week) continuous exercise (CE: moderate intensity swimming 30 min/day, 5 days/week) groups. The groups were then divided into subgroups according to depression induction with chronic mild stress (CMS) procedure (n=6/group). CMS and exercise protocols continued for 6 weeks. Cognitive functions were evaluated by object recognition and fear conditioning, anhedonia by sucrose preference, anxiety like behavior by Porsolt, open field and elevated plus maze. Following decapitation, brain tissue glutathione (GSH) levels, superoxide dismutase (SOD), catalase (CAT), as an indicator of inflammatory response myeloperoxidase (MPO) activities, malondialdehyde (MDA) level were measured, tissue damage was evaluated. Data was analyzed by ANOVA, student's t tests, $p<0.05$ was significant.
RESULTS: Cognitive function, sucrose preference was decreased with CMS, increased in both CMS-induced exercise groups ($p<0.05$). Increased freezing time with CMS was decreased in CMS+WW group ($p<0.05$). Suppressed SOD, CAT activities in SED+CMS group and also GSH content were improved via both exercises ($p<0.05$). MPO activity, MDA levels was increased with CMS and reinstated back with both exercises ($p<0.05$). Latency in Fear Conditioning Test decreased with CMS ($p<0.05$) and increased with CE ($p<0.05$). The rearing number was decreased with CMS and improved with CE ($p<0.05$). Histopathological grade changes of damage in neurons was alleviated with both exercises. CMS-induced memory decline was improved by both exercise protocols via suppressing inflammatory process, anxiety level, by improving antioxidants.
CONCLUSION: WW had similar effect with CE on CMS-induced depression model by improving cognitive function, decreasing anxiety like behavior, anhedonia, repressing inflammatory process and improving antioxidant system.
Keywords: Cognitive function, depression, exercise, weekend warrior,

OC27

Comparative Evaluation of Effective Exercise Intensity Using Metabolic Equivalent and Anaerobic Threshold

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AIM: Metabolic Equivalent (MET) and anaerobic threshold (AT) are commonly used methods to determine exercise intensity levels. We aimed to evaluate effectiveness of MET and AT comparatively on determination of exercise intensity in young male subjects.

METHODS: Total of 31 male participated to this study (20.7±2.0 years, 72.1±9.6 kg, 179±8 cm). Each subject performed an incremental exercise test (15 W/min) to their maximal levels using a cycle ergometer. Ventilatory and pulmonary gas exchange parameters were measured by using metabolic gas analyzer and turbine volume transducer and evaluated breath-by-breath. AT was estimated using V-slope method. One MET is equal of 3.5 millilitres of O2 consumed per kilogram of body weight per minute (mL/kg/min). Pearson correlation analysis and paired-t test were used for statistical analyses ($p<0.05$).

RESULTS: The work rates (mean ± SD) at the AT and maximal exercise were found to be 135±19 W and 220±26 W, respectively. O2 uptakes at the AT and at maximal exercise were found to be 1.89±0.26 L/min and 3.02±0.35 L/min. MET at the AT was varied from 5.71 to 9.98 and averaged 7.59±1.2. AT occurred 62% of maximal oxygen uptake (minimum 53% and maximum72%). There was a low but significant correlation between percent of AT and MET values ($R=0.43497$, $p=0.01$).

CONCLUSION: Moderate exercise intensity based on MET parameter is generally varies between 3 to 6. In addition, AT that reflects the onset of metabolic acidosis, also indicates moderate exercise intensity. However, MET <6 observed in only 4 subjects (12%) at the AT reflecting moderate intensity and >6 observed in 27 subjects (88%) reflecting higher exercise intensity. Consequently, AT is a more accurate tool for determining exercise intensity compared with MET due to the variations in fitness status of each individual.

Keywords: Anaerobic threshold, metabolic equivalent, oxygen uptake

OC28

Determination of Time-Related Muscle Damage/ Regeneration and the Pathways Involved in Response to Swimming Exercise in Mice

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AIM: Maintaining muscle mass is important in quality of life. Although exercise is known to have beneficial effects on muscles, pathways involved and time-dependent muscle damage and regeneration processes in response to swimming exercise have not been elucidated. The aim of this study was to investigate early, late skeletal muscle damage, regeneration as well the pathways involved in response to acute, prolonged swimming exercises.

METHODS: 8-12 weeks old male mice were divided as control and swimming. After exercise groups were divided into acute and chronic, each group was further divided in terms of time (3, 24 hours) passed from the last exercise session till the end of the experiment. Acute exercise was applied as 30 min, one session, chronic group swam 5 days/week, 6 weeks, 30 min/day. Plasma creatine kinase (CK) activity was measured by a kit. Muscle damage, percentage of muscle damage, histological damage score (H-score) and leukocyte infiltration were determined using gastrocnemius-soleus muscles. Real-time PCR was used to validate whole-transcriptome results. Data were evaluated with Kruskal Wallis Analysis of Variance, Mann Whitney U test with Bonferroni Correction. $p<0.05$ was considered statistically significant. The study was approved by the ethics committee (PAUHADYEK-2017-17).

RESULTS: The percentage of muscle damage, H-score and leukocyte infiltration were higher in exercise groups compared to control. Increases in acute 3 hour, acute 24 hour, chronic 3 hours groups were statistically significant ($p<0.05$, $p<0.001$, respectively). No significant difference was observed in CK activity. Expression changes of skeletal muscle actin alpha-1 *acta1*, somatic cytochrome c *cycS*, skeletal fast 2 troponin I *tnni2* genes which demonstrated most dramatic expression changes in whole-transcriptome analysis were confirmed by real-time quantitative PCR.

CONCLUSION: Based on the findings and literature, the pathways involved in skeletal muscle damage and regeneration in response to swimming exercise were drawn. This study was supported by PAUBAP (2017SABE014).

Keywords: Swimming exercise, skeletal muscle regeneration, muscle damage, creatine kinase, real-time PCR

OC29

Effects of Nicotine Administration on Anxiety Tests in Nicotine Preferred Rat Lines

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AIM: Studies show that nicotine reduces anxiety and stress. This effect may contribute to development of addiction. In our laboratory, nicotine-preferring (NP) rat line is generated using selective breeding. This study aimed to reveal the regulatory effect of genetic background, which increases tendency to addiction, and chronic nicotine treatment on anxiety. Accordingly, we studied the changes in anxiety-like behavior observed before (basal) and after nicotine exposure in NP rat lines and their controls.

METHOD: This study involved 4 groups (n=12): Control-Males (CM), Control-Females (CF), NP-Males (NPM), NP-Females (NPF). In all groups, anxiety tests [open-field (OF), marbel-burying (MB), forced-swim (FS)] were performed during basal state. Anxiety tests were repeated during the last two weeks of forced oral nicotine (50 μg/ml) administration (seven-weeks).

RESULTS: In OF-test, nicotine decreased total distance traveled and speed (indices of locomotor activity) in all groups ($p\leq0.001$); NP-groups traveled less than controls. Number of line crosses in outer zones decreased in NP-groups ($p\leq0.001$), males ($p=0.029$) and with nicotine ($p<\neg0.002$). In NP-groups, time spent in outer zones was less than controls ($p=0.016$) which is reduced further by nicotine. There was a main effect of line on the number of line crosses (increased in NP-groups, $p=0.005$) and time spent in inner zones; NPM spent more time than controls ($p=0.001$).
In MB-test, burying behavior decreased in NP-groups ($p=0.005$) and females ($p=0.012$); nicotine exposure reduced marble burying in all groups ($p=0.002$). In FS-test, nicotine had no effect on immobility time. Diving ($p<0.001$) and struggling ($p<0.001$) were decreased with nicotine exposure, whereas swimming was increased ($p<0.001$).

CONCLUSION: All tests demonstrated that nicotine reduced anxiety in all groups. OF and MB tests showed that basal anxiety in NP-groups was lower than controls. However, OF-test showed that nicotine decreased anxiety-like behavior more in NP-groups. These findings indicate that the genetic background that plays a role in nicotine dependence is associated with anxiety.

(Research Fund Grant TYL-2018-20417 EÜHADYEK 2019-001).
Keywords: Nicotine, anxiety, nicotine preferred rat line

OC30

Effect of Oral Nicotine Administration on Expression of Neuropeptide Y and Neuropeptide Y2 Receptor in Rat Brain

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AIM: Neuropeptide-Y (NPY), one of the most common neuropeptides in brain, plays crucial role in many physiological processes including addiction. Nicotine is a compound causes addiction. It has been reported that withdrawal-induced stress and negative affect may be associated with NPY. Studies report anxiogenic effects of NPY through NPY-Y2 receptors. However, this subject is not studied comprehensively. The aim of our study is to investigate expressions of NPY and NPY-Y2 receptor in different brain regions after oral nicotine exposure and withdrawal.

METHODS: Forty adult, male Wistar rats were used for study. Rats were divided into four groups as Control (n=10), Nicotine (n=10), 24-hour withdrawal (24-W, n=10) and 48-hour withdrawal (48-W, n=10). Tap water was given to controls, while three other groups received forced oral nicotine (50µg/ml in tap water) for 12 weeks. After nicotine treatment, Control and Nicotine groups were decapitated 60 minutes, whereas 24-W and 48-W groups were decapitated 24 and 48 hours after removal of drinking bottles, respectively. Prefrontal cortex (PFC), hippocampus, nucleus accumbens, dorsal striatum, ventral tegmental area, medial hypothalamus, septum and amygdala were dissected. NPY/NPY-Y2 expressions were analyzed using qRT-PCR. SPSS v25 was used for statistical analyses.

RESULTS: NPY expressions were increased in PFC of 48-W compared with other groups ($p<0.001$) and in hippocampus of Nicotine group compared with control ($p=0.007$) and 24-W ($p=0.048$). There was an upregulation of NPY in amygdala of 24-W compared with control ($p=0.027$) and 48-W ($p=0.036$). NPY-Y2 expression was increased in PFC of 48-Y compared to control and Nicotine group ($p<0.001$).

CONCLUSION: We can suggest that regulation of NPY/NPY-Y2 receptor expression by nicotine withdrawal may be related to withdrawal-induced negative affect and contribute to development of addiction. This study was supported by Ege University Scientific Research Projects Commission (project numbers: 18-BAUM-001 and TYL-2019-20469) and approved by Institutional Animal Ethics Committee of Ege University (approval number:2017-101).

Keywords: Amygdala, hippocampus, neuropeptide Y, nicotine, NPY-Y2, prefrontal cortex

OC31

The Effect of CDP-Choline on Hippocampal tCAMKII, pCaMKII and pCREB Levels in REM-Sleep Deprived Rats

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AIM: The aim of this study was to investigate the effects of cytidine 5-diphosphocholine (CDP-choline) on learning, memory and long term potentiation (LTP) in REM sleep-deprived (SD) rats.

METHODS: Male Wistar albino rats (n=72, 200-300 g, 8-12 weeks old) were randomized to 12 groups and placed in appropriate cages. Sleep deprivation or environmental control was induced by placing rats on a platform with 6.5cm or 13cm diameter, respectively, for 4 days according to Flower pot method. Learning parameters were tested for 4 consecutive days and on the 5th day memory parameters were tested in Morris Water Maze (MWM). 30 minutes before the MWM, saline (S) or 100 µmol/kg (C100), 300 µmol/kg (C300), 600 µmol/kg (C600) doses of CDP-choline were administered intraperitoneally. After behavioral tests rats were decapitated and pCREB, tCaMKII and pCaMKII proteins were analyzed in hippocampus homogenates using Western-blot (WB) technique. The groups were compared using One-Way ANOVA and Student's t test.

RESULTS: Escape latencies decreased significantly in all groups ($p<0.001$). REM sleep deprivation impaired memory parameters ($p<0,001$) and latency of the first occurrence in platform area was significantly ($p<0,001$) shorter in rats receiving CDP-choline ($p<0.05$). WB analysis revealed that, tCaMKII ratio was unchanged while the pCaMKII ($p<0,05$) and pCREB ($p<0,01$) ratios were decreased as a result of sleep deprivation. Also, pCaMKII levels were greater in SD+C600 group compared to those receiving saline ($p<0,05$).

CONCLUSION: We observed that REMSD has no effect on learning but may impair memory and CDP-choline can reduce the impairment in memory parameters. We determined that the model used to generate REMSD may cause stress and escape latencies of REMSD rats were shorter on the first two days of the MWM, which is probably associated with exploratory behavior due to enhanced stress. Therefore, stress affects the learning, memory and CDP-choline may have positive effects on stress. We observed that sleep deprivation diminishes important proteins in LTP pathway.

Keywords: REM sleep deprivation, Morris water maze, learning, memory, CDP-choline

OC32

The Role of Sex in Maternal High Fat Diet Induced Changes in Autonomic Signaling

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AIM: Exposure to high fat diet (HFD) during perinatal age has been shown to induce neuroplastic changes in autonomic circuitry. Using rats exposed to maternal HFD, this study was designed to investigate the short and the long term changes in autonomic outputs and the role of sex in these changes.

METHODS: Pregnant rats were fed with HFD from prenatal day-14 to postnatal day-21. ECG was recorded and HRV was analyzed in 10- and 20-week age male and female offsprings. In anesthetized rats, (ketamine 60 mg/kg; xylazine 6 mg/kg, ip) muscarinic receptor blocker atropine (2 mg/kg, ip) or beta adrenergic receptor blocker propranolol (4 mg/kg, ip) was administered following a baseline recording, then drug-induced changes were recorded. Differences among the groups were analyzed by Mann Whitney-U test. Experimental protocols were approved by the Animal Ethical Committee of Akdeniz University (2017.09.005).

RESULTS: Compared to control rats, high frequency component (HF) was found to be lower in 10-week old male rats exposed to maternal HFD; low frequency component (LF) and LF:HF, an indicator of sympatho-vagal balance was found to be significantly ($p<0.05$) higher. These changes were restored in 20-week old male rats. In 20-week old female HFD rats, HF component was recovered, in contrast, LF component and LF: HF were measured significantly higher ($p<0.05$) compared to the control rats. Moreover, a desensitization of atropine- and propranolol-induced responses in heart rate and HRV components was detected in 20-week old female rats exposed to maternal HFD.

CONCLUSIONS: The present data indicate that perinatal HFD-induced alterations in autonomic signaling were restored in male rats, while, increased sympathetic tone exhibited a sustained pattern in female rats.

Keywords: Heart rate variability, high fat diet, sex, sympathetic tone

OC33

Effects of Angiotensin IV on Learning-Memory and Hippocampal Oxidative Stress in Diabetic Rats

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AIM: The angiotensin IV molecule and its receptors are one of the leading molecules in the brain renin-angiotensin system and have been associated with the regulation of cognitive functions. In this study, we aimed to investigate whether angiotensin IV has a protective effect on cognitive functions and oxidative stress in streptozotocin-induced diabetic rats.

METHODS: 32 male Wistar albino rats, 250-300 g, were used and divided into four groups of control, diabetes, angiotensin IV (5 µg/kg, sc, 21 days) and diabetes+angiotensin IV. Diabetes was induced by intraperitoneal administration of Streptozotocin (60 mg / kg) and blood glucose were measured. The Morris water maze test performed to determine the learning and memory levels of rats at 21st day. In addition, hippocampi were taken for biochemical analysis. Statistical analyzes were performed with the Instat Statistical Package Program at $p<0.05$ significance level. Comparison between groups performed with One-Way ANOVA or Kruskal Wallis tests. Post-hoc comparisons were performed with Bonferroni and Dunn tests.

RESULTS: Time spent in platform area in diabetes group was lower than the control group ($p<0.05$) and the Ang IV group was higher than the diabetes group ($p<0.001$). There was no significant difference between control and D+Ang IV group. Superoxide dismutase, glutathione peroxidase and malondialdehyde levels increased in diabetic group compared with control group ($p<0,01$) and decreased in Ang IV group compared with diabetes group ($p<0.001$). Brain-derived neurotrophic factor levels were lower in the diabetes group compared with the control group ($p<0.01$), but increased in the Ang IV and D+Ang IV groups compared with the diabetes group ($p<0.001$, $p<0,05$).

CONCLUSIONS: It is suggested that exogenous administration of angiotensin IV has a positive effect on impaired spatial learning and memory and hippocampal oxidative stress in diabetic rats. This project was supported by Istanbul University-Cerrahpasa Scientific Research Projects Unit.

Keywords: Diabetes mellitus, hippocampus, angiotensin IV, cognitive functions, oxidative damage

OC34

N-(P-Amylcinnamoyl) Anthranilic Acid Attenuates Remedial Effects of Memantine on Memory Deficits Following Intracerebroventricular Streptozotocin Administration in Rats

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AIM: Alzheimer's disease (AD), a neurodegenerative disease, accounts for great majority of dementias. Current drugs are not capable of halting the progression of AD. So, more effective novel agents are urgently needed. N–(p–amylcinnamoyl) anthranilic acid (ACA) is an antagonist of transient receptor potential melastatin–2 (TRPM2) which is a non–selective, Ca^{2+} –permeable cation channel. Oxidative stress is a substantial etiologic entity for AD pathogenesis. Cellular stress leads to ischemia and Ca^{2+} accumulation by activating TRPM2. Effect of ACA on memory impairment associated with AD has not been known. The aim of the study is to relief oxidative stress and improve spatial memory by administering ACA treatment.

METHODS: A total of 60 Wistar rats randomly divided into six groups; (1) control, (2) sham–operated, (3) intracerebroventricular (ICV)–STZ, (4) ICV–STZ + memantine (5 mg/kg ip), (5) ICV–STZ + ACA (25 mg/kg ip) and (6) ICV–STZ + ACA + memantine.

RESULTS: Only memantine (5 mg/kg) treatment exhibited a therapeutic efficacy in Morris water maze test. Western blot analyses in hippocampal tissues showed that TRPM2 protein expression was markedly suppressed in 3rd group ($p<0.001$). ACA, memantine or memantine + ACA treatments ameliorated that suppression ($p<0.05$, $p<0.01$, $p<0.01$).

CONCLUSION: Our findings showed for the first time that TRPM2 protein expression was significantly suppressed in the rat model of STZ–induced memory impairment while each of the ACA, memantine and ACA + memantine treatments reversed this suppression. However, ACA did not provide any improvement in spatial memory, instead it worsened the spatial memory.

Gaziantep Experimental Animals Local Ethics Committee Decision No: 2017/32

Keywords: Memantine, N–(p–amylcinnamoyl) anthranilic acid, TRPM2

OC35

Effect of Neurokinin 3 Receptor on Cognitive Behavior and Catecholaminergic System in a Rat Experimental Alzheimer Model

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AIM: Alzheimer's disease is considered to be a form of progressive/ irreversible dementia that creates serious health problems with increase of aging population. Cognitive impairment usually begins nearly with memory damage, progresses to loss of daily living activities. It is known that catecholaminergic systems are commonly affected in AD. Neurokinin B is tachykinins family hormone. Neurokinin 3, NKB receptor, is involved in learning/memory related processes. Activation of NK3R facilitate releasing of many neurotransmitters like dopamine and noradrenaline. Aim of project is to investigate role of NK3R agonism in cognitive functions and its effects on catecholaminergic system in AD.

METHODS: Experiment was performed on 50 adult male Wistar albino rats:1) Control 2) AH, 3) Control+NK3R agonist, 4) AH+NK3R agonist, 5) AH+NK3R agonist+antagonist groups. Experimental Alzheimer's model was established by applying amyloid beta 1-42 intracerebroventricularly. Following NK3R agonist/antagonist injections, Morris water maze test was performed for learning/memory assessment. At the end, animals were decapitated, tissues were collected. Catecholamine analysis was performed from brainstem tissue by HPLC method. SAS University Edition 9.4 was used for statistical analysis.

RESULTS: Distance moved on test stage of MWM was compared between groups and statistically significant difference was found ($p<0.05$). AH group had greatest distance between all groups. Distance covered by AHS group was significant when compared with AHSO/ KS groups ($p<0.05$). There was no significant difference in NA concentration between groups ($p>0.05$). NA was lower in AH group compared with other groups. It was found to be increased in AHS group compared to AH group. DA concentration was significantly different between groups ($p<0.0001$). DA was lower in AH group compared with other groups. In AHS group, DA level was increased.

CONCLUSION: Impaired learning/memory parameters were recovered with NK3R agonism in AD group. Activation of NK3R increased NA/DA in brainstem. Positive effects of NK3R on learning are likely to be catecholamine mediated. Further studies are needed to clarify action of NK3R on learning and memory in AD.

Keywords: Neurokinin 3, Alzheimer, behavior

OC37

The Effect of Hippocampal Replay-Induced During Wakefulness on Learning and Memory in Rats

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AIM: Hippocampus is essential for long-term memory. Daily experiences are reactivated in the hippocampus during slow wave sleep. We aimed to reveal the effects of hippocampal replay induction during wakefulness on learning and memory in rats.

METHODS: Spraque Dawley male rats weighing 300-350 g were used. Groups were designed as control group (n=12), sound-matched swimming group (SMS; n=12) and sound-matched swimming+replay group (SMSR; n=12). Morris water tank test was used to assess learning and memory. Control group had acquisition trials for four days, followed by probe trials on the 5th and 10th days. SMS rats received a 50-80 dB sound with ups and downs in 5-10 kHz frequency range during acquisition trials and SMSR received additionally two times a day for 4x90 s during wakefulness. Rats in the SMS and SMSR groups were randomly divided into two subgroups on the 5th day. The first subgroup received the sound for 4x90 s during wakefulness between days 5-10, to evaluate the effect of persistent reactivation on memory. The second subgroup received no sound and got the probe trial on the 10th day. One-way ANOVA test was used for statistical analysis.

RESULTS: Escape latency significantly shortened on the fourth day compared with the first day in all groups ($p<0,001$). Escape latencies of SMS group and SMSR groups were significantly shorter than that of control group on the second day ($p<0.05$). This difference disappeared in the following days. In the probe trial applied on the 5th day, the time spent in target quadrant in the SMSR group was significantly longer than that of the control group ($p<0.05$). None of the parameters assessed in the probe trials on the 5th and 10th days revealed any difference.

CONCLUSION: Our results suggest that exposure to sound during learning accelerates the learning process and replay induction increases the memory performance.

Keywords: Learning, memory, replay, hippocampus

OC38

Neuroprotective and Antioxidant Role of Astaxanthin Against Brain and Hippocampal Damage Caused by Methotrexate

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AIM: Methotrexate (MTX) is a chemotherapeutic agent widely used in the treatment of certain types of cancer. Chemotherapeutic agents may have toxic effects on different organs. In this study, we aimed to investigate the neuroprotective and antioxidant effects of astaxanthin (AST) against brain cortex and hippocampal injury caused by MTX.

METHODS: After approval of the Ethics Committee (12.12.2018/475), Twenty-four female Wistar Albino rats were randomly divided into three groups; Group I (control), Group II (study group - 20 mg/kg MTX, i.p, single dose, 2th day), Group III (treatment group – MTX+AST, 20 mg/kg MTX, i.p, single dose, 2th day + 100 mg/kg AST, by gavage, 7 days). The rats were sacrificed under anesthesia after the last AST application. The brain and hippocampus tissue samples were collected for biochemical, pathological and immunohistochemical analyzes. Total antioxidant capacity (TAS) and total oxidant capacity (TOS) were measured in brain cortex and hippocampus. Also, iNOS, caspase-3, G-CSF, growth regulated oncogene (GRO), and myelin basic protein (MBP) immune reactions were analyzed. One-Way ANOVA and post-hoc Tukey test were used for data analysis. $p<0.05$ was considered significant.

RESULTS: MTX; increased TOS levels in brain cortex and hippocampus ($p=0.001$), and decreased TAS levels. AST treatment brought these values closer to the control group. Histopathological examination revealed marked hyperemia and degeneration in some cells in the MTX group. Also, edema was observed in the brain. Hyperemia and edema decreased in AXA treated group. In MTX group, caspase-3, iNOS, GCSF and GRO immune reactions increased while MBP expression decreased in brain and hippocampus tissue samples ($p<0.001$). AST treatment reversed the MTX induced reactions in brain and hippocampus ($p<0.001$).

CONCLUSION: Results of the present study revealed that MTX induced both brain cortex and hippocampus cells damage. AST has ameliorative effects both biochemical and pathological findings in rats.

Keywords: Methotrexate, astaxanthin, brain, hippocampus, neurodegeneration.

OC39

Investigation of Ventilatory Long Term Facilitation Exposed to Intermittent and Sustained Hypoxia and Comparison of Its Effects on Brain Stem and Spinal Cord in Rats

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AIM: Exposing to intermittent hypoxia (IH) causes a permanent increase in amplitude of respiratory motor output which is known as long-term facilitation (LTF). Increased hypoxic ventilatory response during sustained hypoxia causes ventilatory acclimatization to hypoxia (VAH) and both give rise to ventilatory neural plasticity. The pathways that induce LTF activate serotonin (5-HT2A) and adenosine (A2A) receptor activation-dependent metabotropic receptors (Gq and Gs). Although LTF is mainly serotonin-dependent, it is thought that the adenosine-dependent pathway suppresses the serotonin pathway due to increased severity and/or duration of hypoxia. In our study, we hypothesized that A2A receptor activation, which causes acute intermittent isocapnic hypoxia (AAIH) induced ventilatory LTF (vLTF) plays a major role on VAH.

METHODS: Three experimental groups were used in the study. Normaxic group (n=10; FIO2=0.21) was kept in normaxia. For AIIH group (n=11) was performed 5 times 5 minutes hypercapnic hypoxic (FIO2=0.10 and FICO2=0.04) bursts interrupted normoxic gas fraction for 4 times 5 minutes. Whole body plethysmography (WBP) was used to measure V, fR and TV. CSH group (n=10; FIO2=0.10) was exposed to hypobaric hypoxia for one week. After tissues were perfused 5-HT2A, A2A receptors and BDNF pERK and pAkt proteins in 30µ thick transverse brainstem (NTS) and spinal cord (phrenic nerve) sections were labeled with immunofluorescence staining method. Statistical significance was accepted as $p<0.05$ for WBP measurements and immunoreactivity.

RESULTS: In this study interactions between signaling pathways and pathways causing LTF were investigated for VAH. For results, the Gq pathway that was activated after moderate AIIH caused LTF formation on NTS and phrenic motor neurons, but no evidence of vLTF formation was found according to WBP measurements. VAH was similar to that of plasticity due to A2AR activation.

CONCLUSION: It is thought that understanding these interactions specific to Gs and Gq proteins through defined cross-talk inhibition mechanisms within other systems including respiration will contribute to explaining the mechanisms of neural plasticity occurring in sensory and motor neurons.
Keywords: Adenosine, hypoxia, long term facilitation, serotonin, ventilatory acclimatization to hypoxia, ventilatory neural plasticity

OC40

The Roles of mTOR Pathway Substrates on the Regulation of Muscle Mass and Force Production in Skeletal Muscle Hypertrophy

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AIM: Although the protein synthesis and hypertrophy in skeletal muscle are known to be mediated by mammalian target of rapamycin (mTOR) pathway, recent studies have reported that the roles of different substrates of mTOR in muscle hypertrophy may vary due to differences in their sensitivity to rapamycin. The aim of this study was to investigate the roles of rapamycin-sensitive and insensitive components of mTOR on muscle mass and force production during exercise induced muscle hypertrophy.

METHODS: Skeletal muscle hypertrophy was induced by applying chronic resistance exercise. mTOR inhibitor rapamycin (1.5 mg/kg) or carrier was administered by intraperitoneal injection 3 days/week for 8 weeks. Muscle strength was recorded weekly. Hind leg wet muscles were weighed. Muscle cross-sectional area was determined by Hematoxylin-Eosin staining. Akt and S6K1 levels were measured by western-blot. One-way or two-way ANOVA was performed between the groups followed by Tukey-Kramer multiple comparison test.

RESULTS: Wet muscle weight and cross-sectional area decreased in the groups receiving rapamycin compared with control exercise group although resistance exercise has elevated muscle mass and fiber size values ($p<0.05$). Muscle strength was increased at the end of the exercise program in all groups receiving rapamycin or its carrier ($p <0.05$). S6K1 expression levels were not different among the groups. Akt expression level in exercise+rapamycin group decreased comparing to the other groups ($p<0.05$).

CONCLUSION: The results of our study showed that while rapamycin-sensitive mTOR pathway regulates muscle mass increase during skeletal muscle hypertrophy induced by resistance exercise, rapamycin-insensitive mTOR pathway could be necessary to provide force production. Since the main problem in skeletal muscle pathologies is the decrease in muscle strength, besides the alterations in muscle mass the mechanisms that regulates the force production needs to be better understood as well.

Keywords: Hypertrophy, mTOR, rapamycin, resistance exercise

OC41

The Effect of Adenosine 2A Receptor Agonist and Antagonist Administration on Hypoxic Ventilatory Response

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AIM: Changes in hypoxic ventilatory response (HVR) due to the intensity and severity of hypoxic stimulation are shown as examples of neuroplasticity, resulting in short-term effects that alter transient synaptic activity, such as increased neurotransmitter release. Increased severity and / or duration of hypoxia is known to increase adenosine release from central nervous system (CNS) neurons. The aim of this study was to show the effects of adenosine 2A receptor (A2AR) activation/inhibition due to increased amount of adenosine with hypoxia on HVR.

METHODS: In our study, there are four groups and each groups have 12 Sparaque-Dawley rats weighing 250-300 grams were used. Each group was kept in normoxic conditions for one week. Except for control group (Sham_CON), dimethyl sulfoxide (DMSO; Sham_DMSO), adenosine 2A receptor agonist (CGS21680; Sham_AG) and adenosine 2A receptor antagonist (MSX-3; Sham_ANT) groups were administered 1 mg/kg daily. Ventilation (V), respiratory frequency (f) and tidal volume (TV) measurements were measured by whole body plethysmography (WBP) to demonstrate the change of HVR at the end of one week. V, f and TV parameters were analyzed and $p<0.05$ significance level was accepted for statistical analysis.

RESULTS: According to the WBP measurement results, V, f and TV values were significantly increased in the Sham AG group HVR measurement compared with the other groups. When reoxygenation was achieved after HVR, there was no significant difference between V, f and TV values between the groups.

CONCLUSION: In this study, we aimed to determine the role of adenosine release which is considered necessary for plasticity in respiratory centers. Short-term continuous hypoxia exposure with A2AR agonist administration increased adenosine release. With this ongoing study, we think that the release of adenosine in plasticity is essential for the maintenance of the mechanism of ventilatory acclimatization to hypoxia (VAH) and for development of AH through chronic sustained hypoxia (CSH).

Keywords: Adenosine, hypoxic ventilatory response, neuroplasticity

OC42

Omega 3 (DHA) Treatment of Collagenase-Induced Achilles Tendinopathy in Rats: Analyses of Histopathological and Biomechanical Aspects

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AIM: Achilles tendon is the strongest tendon with the heaviest load carrying capacity in human body but is the most frequently traumatized and ruptured. Achilles tendinopathy (AT) is more frequent pathology in athletes. Docosahexaenoic acid (DHA, Omega-3) has anti-inflammatory, anti-nociceptive and analgesic effects and is emphasized to increase collagen synthesis. In this study, we aimed to investigate histopathological and biomechanical effects of DHA in induced AT model in rats and compare with collagen effectiveness.
METHODS: This study was approved by Ataturk University Local Ethics Committee for Experimental Animals. AT model was induced with application of type I collagenase to the left peritendinous area on rats. Groups are randomly divided into 4 groups (Group1: diseased control, Group2: DHA (150mg/kg), Group3: DHA (300mg/kg), and Group 4: collagen (7.2mg/kg). Duration oral treatment was 8 weeks. Right tendons of first group rats were used as healthy control. At the end of the experiment, rats were sacrificed under general anesthesia and Achilles tendons (with calceneus bones) were removed for biomechanical and histopathological testing.
RESULTS: Biomechanically, it was observed that maximum rupture strength and maximum strength values caused permanent damage on tendons are decreased statistically in first group ($p<0.05$) and increased in 2nd, 3rd and 4th groups ($p>0.05$) when compared with healthy controls. Histopathologically, in the first group, normal structure of tendon was disrupted, tendon cells were degenerated and inflammation cells were present, whereas no lesion was observed in healthy control group. In groups 2, 3, and 4, decreased degeneration and increased proliferation of dense connective tissue cells (fibrocytes and fibroblasts) with new capillary vascular formation was noted.
CONCLUSION: It was determined that DHA increased formation of fibroblasts and collagen synthesis histopathologically and tendon elasticity and breaking strength biomechanically. In this context, it was concluded that DHA may be an alternative compound that can be used easily in AT treatment. (Ataturk University Scientific Research Project No: THD-2019-7060).
Keywords: Omega 3, collagen, Achilles tendinopathy

OC43

Effect of Moderate Swimming Exercise on Learning-Memory and Investigation of Role of Sirtuin-1 on Elderly Rats

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AIM: The aim of this study is to investigate the effect of physical exercise on the essential protein of long-term potentiation (LTP) in the hippocampus, cyclic AMP-Responder Element Binding Protein (CREB) and Brain-Derived Neurotrophic Factor (BDNF) which were important in neuronal survival, growth, and synapse stabilization and their relations with Sirtuin-1(SIRT1) which is one of the important family of proteins in regulation of gene expressions related to aging.

METHODS: In the study 32 male Sprague-Dawley rats (300-500g) aged between 11-12 months and 15-16 months old were used. The study was randomly separated into four groups and 8 rats in each group. Groups; Control-1 (C1/11-12 months), Exercise-1 (E1/11-12 months), Control-2 (C2/15-16 months), Exercise-2 (E2/15-16 months). Exercise protocol was 30 minutes/per day, 5 days/week training period 8 weeks of moderate swimming. The animal was subjected to Morris Water Maze test 5 days before sacrifice. After sacrifice, the hippocampus was removed for histological analysis. One-way analysis of variance (One Way ANOVA) was used to compare the characteristics of the groups examined over time. Statistical significance was taken as $p<0.05$.

RESULTS: There was no statistical difference between the groups according to time in the platform finding parameter ($p>0.05$). There was a statistically significant difference between Exercise 1 and Exercise 2 in the platform zone input parameter and the number of entries increased ($p=0.026$). In the hippocampus tissue, it was found that each of SIRT1, BNDF, CREB immunoreactions increased in E1, K1 groups ($p=0.001$). In comparison with E2, K2 group, each of CREB and BDNF immunoreactions were increased ($p=0.001$). CONCLUSION: We foresee that SIRT1 is a signaling pathway activating BDNF that activates CREB and activates neuroplasticity. We think that this pathway activated by SIRT1 is an alternative route for enhancing effect of mild exercise on the plasticity on elderly rats and may be a new therapeutic target for dementia.

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Keywords: BDNF, CREB, learning-memory, LTP, SIRT1

OC44

Investigation of the Role of Asprosin in Physiopathology of Experimental Hypertension Model

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AIM: Hypertension is one of the most common cardiovascular diseases and in more tahna 95% of cases its cause is unknown. Asprosin is a newly discovered hormone which white adipose tissue secretes. It is known that asprosin might be related to obesity and cardiovascular diseases due to its effects on glucose metabolism. The aim of our currently study was to evaluate the relationship between asprosin and blood pressure and renal functions.

METHODS: Ethics committee approval was received. 16 male Spraque Dawley rats weighing 260-310 grams were separated into two groups as Control (C) and Hypertension (HT). In terms of group HT, L-NAME at a dose of 400 mg/L was put in the rats' drinking water for 6 weeks. Blood pressure was measured each week by tail-cuff plethysmography. At the end of the sixth week, 24-hour urine was collected from the rats. Then, blood and kidneys were taken under anesthesia and euthanasia was performed. Mann-Whitney U test was used for statistical comparisons. $p<0.05$ was considered significant.

RESULTS: In the HT group, there was a significant increase in systolic, diastolic and mean blood pressure levels after 2 weeks ($p<0.05$). Serum urea, creatinine, calcium and magnesium levels were increased and serum asprosin levels were significantly decreased ($p<0.05$). Although the increase in urine asprosin levels and decrease in creatinine clearance were not significant, there was a significant increase in fractional $Na+$, $K+$, $Ca2+$ and $Mg2+$excretion ($p<0.05$).

CONCLUSION: Our results showed that asprosin is associated with renal glomerular and tubular dysfunction and may play a role in the pathogenesis of hypertension. We suggest that asprosin has a role in the pathophysiology of hypertension and its relationship with glomerular and tubular dysfunction should be further investigated.

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Keywords: Asprosin, kidney, hypertension, glomeruler function, tubuler function

OC45

Asymmetric Change of Some Memory-Related Mediators in Hippocampus in Spatial Memory Improvement Induced by Enriched Environment in Adolescent Rats

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AIM: Hippocampus, which is the critical brain region for learning/memory function, has been reported to be associated with optimal function of lateralization and right hippocampus is predominant in spatial memory. However, asymmetry of mediators which are critical for memory in hippocampus is unclear and effects of external factors have not been studied. In this study the effects of enriched environment (EE) in right and left hippocampus to neurotrophic factors (BDNF) and oxidative stress markers (postulated act as signal molecules) were investigated.

METHODS: Male adolescent rats were divided into two groups: Control and EE (n=11/group). EE group was placed in enriched cages 1h/day as differently than control. Four-weeks later, spatial memory was tested in Morris water maze. The right and left hippocampus were separated. BDNF, lipid-peroxidation product-malondialdehyde (MDA), protein-oxidation product-protein carbonyl (PCO) and antioxidant enzyme superoxide dismutase (SOD) were measured by ELISA. Results were compared with Two-Way ANOVA test.

RESULTS: EE improved spatial memory ($p<0.05$). The control group had left>right asymmetry for BDNF ($p<0.001$). BDNF in right and left hippocampus in EE group were higher compared to control ($p<0.001$) and although there was left>right asymmetry, similar to controls, level of asymmetry was lower ($p<0.05$). There was no right-left asymmetry for oxidative stress markers in control group. In EE group, PCO and SOD values were similar with control. Interestingly, MDA level in right hippocampus of EE group was higher than the right of control group ($p<0.01$) and right>left asymmetry ($p<0.001$) was seen.

CONCLUSION: Our findings suggest that BDNF is responsible for enhanced spatial memory in both halves of hippocampus (although left-dominance is maintained). Our original finding that spatial memory improvement with increased MDA in right hippocampus, supports the suggestion that oxidative stress products may act as signal molecule in spatial memory formation. Moreover, we suggest that this occurs predominantly in the right hippocampus.

Keywords: Enriched environment, hippocampal asymmetry, spatial memory, BDNF, malondialdehyde

OC46

Effects of Ginkgo Biloba Components and Calcium Channel Blockers on Cortical Neuron Excitability in WAG/Rij Rats with Absence Epilepsy: In Vitro Calcium Imaging Study

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AIM: There are clinical and experimental studies showing that Ginkgo biloba extract (EGb 761) causes epileptic seizures. Determining the proconvulsant mechanism of action of EGb 761 is important for clinical applications of this drug. The aim of the present study was to investigate the effects of EGb 761 active components and calcium channel blockers on the neuronal excitability in cortical neuron culture of WAG/Rij rats with genetically absence epilepsy by using calcium-imaging technique.
METHODS: Ethical committee permission was obtained, and cortical neuron culture obtained from WAG/Rij rats (P1-P4) was used in the study. Measurement of intracellular calcium levels were performed under confocal microscope using Fluo-4 calcium indicator dye. Neuronal excitability was induced by 30 mM KCl. The cultured cells were treated with the active ingredients of EGb 761, ginkgolide A, B, C and bilobalide concentrations of 1, 10 and 100 µM. Calcium channel blockers nicardipine (10 µM), mibefradil (10 µM) or dantrolene (10 µM) were administered together with the most effective component of EGb 761 to determine the ion channel responsible for calcium exchange. Calcium imaging values were expressed as relative fluorescence change ($\Delta F/F0$) after normalizing in percent. Experimental groups were compared using Mann-Whitney U test after Kruskal-Wallis analysis of variance. $p<0.05$ was considered statistically significant.
RESULTS: It was determined that 10 and 100 µM doses of Ginkgolide B caused a significant increase in intracellular calcium level ($p<0,001$). However, it was found that intracellular calcium increase due to ginkgolide B was inhibited by all three of calcium channel blockers nicardipine, mibefradil and dantrolene ($p<0,001$).
CONCLUSION: Ginkgolide B has been shown to increase the cortical neuron excitability in WAG/Rij rats. It was concluded that T-and L-type voltage-gated calcium channels and ryanodine receptors may be responsible for the increase of neuronal excitability due to ginkgolide B.
This study was supported by TUBITAK (Project No: 115S348)
Keywords: Ginkgo biloba, WAG/Rij, calcium imaging, absence epilepsy, neuronal excitability

OC47

The Role of 5-Hydroxytryptophan and 7-Nitroindazole on Absence Epilepsy

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AIM: Serotonergic and nitric oxide systems are known to be involved in neurological diseases including epilepsy. The aim of this study was to investigate the effect of serotonin precursor, 5-Hydroxytryptophan (5-HTP) and specific neuronal nitric oxide synthase inhibitor 7-Nitroindazole (7-NI) on absence epilepsy.

METHODS: Six-eight months aged male WAG/Rij rats weighting 200-300gr were used in this study. The experiments consisted of control group, 5-HTP group (50 mg / kg i.p), 7-NI group (40 mg / kg i.p) and 5-HTP + 7NI groups. Baseline ECG recordings taken for 3 hours at 10 am daily and 3hour ECO recordings after drug administration were analyzed and compared statistically. The OMU Animal Experiments Local Ethics Committee approved this study (OMU HADYEK).

RESULTS: Compared with baseline ECG recordings, 5HTP (50mg / kg) significantly increased the number and duration of spike waves ($p < 0.05$). The 7-NI (40 mg / kg) and 5-HTP + 7-NI groups did not significantly alter in terms of the number and duration of spike waves ($p > 0.05$).

CONCLUSION: 5-HTP increased epileptic activity in WAG / Rij rats and 7NI inhibited this effect. The role of antioxidants in this effect need to be clarified with further studies by using biochemical analyzing methods.

Keywords: 5-HTP, 7-NI, absence epilepsy, WAG/Rij

OC48

Investigation of the Interaction of Exenatide and Cannabinoid Receptors in Penicillin-Induced Epilepsy Model

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AIM: This study aims to investigate the interaction between exenatide, a glucagon-like peptide-1 receptor agonist, and cannabinoids on epileptiform activity in penicillin-induced cute epilepsy model.

METHODS: Our study is approved by ethics committee. Male Wistar rats (180-240 g) were divided into 11 groups (n=8). Intracortical penicillin-G (500 IU) injection was used to induce epileptic seizures (Control group). Intracerebroventricular (i.c.v.) exenatide (0.5, 1 and 5 μg/kg) was injected 30-min after penicillin to determine its effective dose. Other groups received i.c.v. injection of CB1 receptor agonist ACEA (7.5 μg/rat) or CB1 receptor antagonist AM-251 (0.25 μg/rat) with or without effective exenatide dose, 0.5 μg/kg exenatide (ineffective dose) and 2.5 μg/rat ACEA (ineffective dose) together or 1 μl dimethyl sulfoxide (solvent for ACEA and AM-251,) 30-min after penicillin injection. In addition, 2,5 μl physiological saline (solvent for penicillin) was injected into the somatomotor cortex. Three-hour electrocorticography recordings were obtained. One-way ANOVA test was used for statistical analysis.

RESULTS: Effective exenatide dose was 1 μg/kg and significantly reduced spike frequency between 60-180 minutes ($p<0.05$). ACEA (7.5 μg/rat) significantly decreased the spike frequency while AM-251 (0.25 μg/rat) increased ($p<0.05$). When exenatide (1 μg/kg) and ACEA (7.5 μg/rat) was given together, spike frequency significantly decreased but this effect was not different from their effects when applied alone. There was no significant change in spike frequency when exenatide (1 μg/kg) and AM-251 or the ineffective doses of exenatide and ACEA were given together, compared with the control group.

CONCLUSION: The finding that ACEA did not potentiate the effect of exenatide and no change in the frequency of epileptiform activity by co-administration of ineffective doses of exenatide and ACEA, shows that antiepileptic effects of exenatide and cannabinoids may involve different pathways. This study was supported by OMU (PYO.TIP.1904.18.007).

Keywords: Epilepsy, GLP-1, exenatide, rat, cannabinoid, penicillin

OC49

Investigation of Rumination and Distraction Emotion Regulation Strategies from a Neuro-Cognitive Point of View

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AIM: "Emotion regulation" term describes the ability to unconsciously manage the emotions in daily life. Since, this term can be considered as a sub-type of emotion-cognition interaction, researchers discuss how the neural systems underlying the particular emotion regulation strategy exist. The aim of this study is to show the relations between neuro-cortical spontaneous activities and emotion regulation strategies in terms of principal components extracted from EEG epochs in both eyes-opened (EO) and eyes-closed (EC) states.

METHODS: 64-channel surface EEG series, downloaded from publicly available dataset so called LEMON, were collected from females aged between 20-65 years old in EO and EC states. Principal Components (PCs) of EEG epochs of 2 s were estimated from both EC and EO recordings. Then, two groups who use two emotional strategies so named rumination and distraction with high scores and low scores were compared to each other in both statistical tests and deep learning classifications in terms of PCs.

RESULTS: Significant statistical differences ($p<0.5$) were obtained between two groups in both EO and EC states mostly at occipito-parietal regions. In particular, frontal (Fp2, F2, F6, FT8, AF8), central (C1, C3, C4, C6), parietal (CP2, CP5, P7, P8, PO9) differences were obtained in EO state ($p<0.5$), while both frontal (F3, F4, F5, F6, F7, AF3, AF4, AF7, FC4, FT7) and occipito-parietal (O2, O7, Oz, CP1, CP2, CP6, Pz, P2, P5, P6, PO4, PO7) differences were obtained for EC state ($p<0.5$) in groups. When the PCs estimated from EEG epochs in both EO and EC states were combined in a single feature set, the groups were classified by using deep learning algorithms with high accuracy of 96.84%.

CONCLUSION: Findings reveal that the regulation of emotion is controlled by interactions between regions within the amygdala–frontal neuronal circuitry. Probably, emotion regulation strategies can be determined by analysing EEG measurements in adults.

Keywords: Emotion regulation, EEG, rumination, distraction

OC50

Artificial Intelligence Assisted Tactile-Visual Substitution System

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AIM: In this study, we aimed to design a high yield-low cost artificial vision system, which will enable the sense of touch to be used as a sense of sight in blind individuals.

METHODS: The project consists of two parts as mechanical and electronic ones. In the mechanical part, a vest model is designed in three dimensions in computer environment and then the appropriate servo motors are mounted on the vest and connected to the electronic system. In the electronic part, a video camera was connected to a minicomputer (Raspberry Pi) and the image was processed using Python programming language and Tensorflow library. In this way, a device is designed to instantly process the image and to touch the appropriate places on the person's back at appropriate times. It was examined whether the appropriate pattern could be transferred to the model by showing the letters, objects and numbers to the designed device and the correct estimation rate hypothesis was examined by Pearson chi-square test.

RESULTS: The medical device was tested on a model and its success in recognizing snapshots was recorded. Before testing, the question was asked whether the accuracy of our device was 90% and attempts were made to investigate the accuracy of this hypothesis. Twenty random numbers and letters were determined, and they were shown to the machine provided and the correct pattern was drawn on the model. The accuracy of artificial vision device was 90% ($p<0.05$).

CONCLUSION: A system is designed to minimize the error and transfer letters, numbers and objects to the sense of touch by making image improvements with the help of artificial intelligence algorithms. We have got very accurate results in the model stage, and we have started the necessary studies to test this system in humans.

Keywords: Artificial intelligence, vision substitution, artificial vision, robophysiology

OC51

Effects of Ionotropic GABA Receptor Blockade in Septic Encephalopathy

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AIM: Sepsis induced encephalopathy which affects the central nervous system and the tissues coordinated with the CNS, has a higher mortality and morbidity rate. We aimed to investigate the effects of the ionotropic GABAA receptor antagonist Bicuculline on encephalopathy on brain tissue of rats with sepsis induced by lipopolysaccharides in the present study.

METHODS: The adult male Sprague Dawley rats were divided into 4 groups as the control (n.6), LPS (10 mg/kg i.p.) (n:8), Bicuculline (1.5 mg/kg s.c.) (n:8), and LPS+Bicuculline (n:8) (Ethics number: 2016/08) in the study. LPS were aDMİN applied 10 mg / kg i.p. as a single dose. Rats were decapitated 24 hours after injection. Rectal body temperatures were measured for monitoring the hemodynamic changes, and neurophysiologic changes were noninvasively recorded using the electroencephalography (EEG). The pro-inflammatory cytokine TNF-α, anti-inflammatory cytokine IL-10 and GABA levels in brain tissue were determined using ELISA, and MDA levels were determined using the spectrophotometric method for the lipid peroxidation analysis. The morphological analysis was performed by immunofluorescence staining method using Neun, S100-ß and synaptophysin antibodies. One-way variant analysis, and Tukey test were used for statistical analysis.

RESULTS: We found that the inflammation in the LPS group increased the inflammatory parameters and increased MDA and GABA levels in the brain tissue compared with the levels in the control group, and caused damage in tissue level ($p<0.05$). There was no significant difference between control, Bicuculline and LPS+Bicuculline groups ($p> 0.05$). In the electrophysiological recordings, activity compatible with acute non-focal seizures was observed in the LPS group, however, activity compatible with resting was detected in other experimental groups ($p<0.01$).

CONCLUSION: In conclusion, we suggest that a GABAA receptor antagonist-Bicuculline may be effective in treatment in septic encephalopathy.

Keywords: Sepsis, GABA, bicuculline, encephalopathy

OC52

The Role of Peroxisomes in the In Vivo Alzheimer's Disease Model Induced by Administration of Aβ 1-42 and the Effect of Taurine

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AIM: Oxidative stress is one of the major causes of Alzheimer's disease, a multifactorial disease that results in neurodegenerative dementia. In this study, we investigated the role of peroxisomes and taurine, a powerful antioxidant, in the Alzheimer's disease model induced by amyloid beta 1-42 (Aβ 1-42) neurotoxicity.

METHODS: In our study, old (28±4 months) Wistar albino male rats; were divided into 5 groups (n=6) as control, sham, Aβ 1-42, taurine, Aβ 1-42+taurine. Taurine was given to animals at dose of 1000 mg/kg/day for 6 weeks with drinking water. Following taurine administration, animals were injected intracerebroventricular (icv) Aβ 1-42 (into the lateral ventricles, 5 µl) by stereotaxic surgery. After 14 days, cerebral cortex and hippocampus tissues were isolated from the brain. MDA and GSH levels were measured spectrophotometrically. The expressions of peroxisomal PEX14 and PMP70 membrane proteins with CAT enzyme were demonstrated by Western blotting. Kruskal Wallis and Mann Whitney U test and Bonferroni correction were used for statistical analysis. $p<0.01$ was considered significant.

RESULTS: It was found that Aβ 1-42 injection decreased CAT expression in the cortex, PEX14 and PMP70 expressions and GSH levels in the hippocampus, and increased MDA levels in the cortex and hippocampus ($p<0.01$). Although taurine administration partially improved the adverse effects of Aβ 1-42 injection, a significant increase was found only in the hippocampus GSH level ($p<0.01$).

CONCLUSION: The decrease in peroxisomal proteins and antioxidant capacity in the brain with icv Aβ 1-42 injection in old rats showed that peroxisomes may play a role in the neurodegenerative and oxidative processes related to Alzheimer's disease. Taurine supplementation may have positive effects especially on increasing antioxidant capacity, but it did not have a significant effect on peroxisomal functions in the dose and duration used in our study.
This work was supported by the project GU-BAP-01/2017-30. Ethical approval: (G.Ü.ET-17.058).

Keywords: Alzheimer's disease, neurodegeneration, oxidative stress, peroxisome, taurine

OC53

The Role of Phosphatidylinositol-3 Kinase/Akt and ERK-1/2 Pathways in The Neuroprotective Activity of Lithium

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AIM: Lithium is commonly used as a mood stabilizer in bipolar disorders. Current studies show that lithium treatment results in neuroprotective effects on neurodegenerative diseases even its mechanism is not clearly understood. This study focuses on intracellular mechanism mediated by lithium after cerebral ischemic injury.

METHODS: Experiments were conducted with the approval of the local ethics committee (2019/28). 8-10 weeks old male Balb/c mice were divided in three sets. In the first set, mice were exposed 90 minutes middle cerebral artery occlusion model (MCAO) than 24 hours reperfusion. At the onset of reperfusion, animals were subjected to intraperitoneal lithium injection. The brains were sliced to evaluate infarct volume, oedema and blood-brain barrier impairment. 30 minutes MCAO followed by 72 hours reperfusion performed for the other set of experiment to assess apoptosis and apoptosis-related proteins by TUNEL staining and Western blot (WB) analyzes.

RESULTS: In the first set of experiments, the lithium treatment significantly decreased infarct volume and brain oedema compared with the control group after 90 minutes MCAO ($p=0.03$, $p=0.014$). In the second set, the lithium treatment significantly decreased the apoptotic cell number compared with the control group after 30 minutes MCAO ($p=0.238$). The effects of lithium on apoptosis related pathways after cerebral ischemia were assessed and the results showed that lithium increased the Akt and Erk1/2 protein levels after MCAO ($p=0.02$, $p=0.000$). Akt and ERK1/2 phosphorylations were suppressed with the use of inhibitors Wortmannin and PD98059 respectively. SPSS was used for statistical analysis. Statical significance was analyzed by one–way analysis of variance (ANOVA) followed LSD tests ($p<0.05$)

CONCLUSION: The increase of Akt phosphorylation with lithium treatment after MCAO were reversed with Wortmannin injection, besides any alteration with inhibition of ERK1/2. It was shown the neuroprotective mechanism of lithium mediated by Akt phosphorylation after ischemic injury.

Keywords: Ischemia, lithium, Akt, Erk

OC55

The Effect of Electromagnetic Field Exposure in The Prenatal Period on Behavior and Synaptic Proteins and The Role of Zinc Support

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AIM: We aimed to investigate the relationship between autism-like behaviors and EMF exposure as an environmental factor during the prenatal and postnatal periods, the role of synaptic proteins such as NLGN3 and SHANK3, gender differences and the effects of zinc supplementation.

METHODS: Rat pups born from four groups of pregnant rats were used: Control group (n=4), EMF group (n=6), Control+Zinc group (n=3), EMF+Zinc group (n=5). Zinc was administered orally to pregnant rats (5 mg/kg/day, 5 days/wk). Pregnant and pup rats were exposed to EMF using Helmholtz coil system (50 Hz, 3 mT, 5 days/wk, 4 h/day). EMF exposure of rat pups was initiated on the first day of pregnancy and continued until the 28th postnatal day. Social approach, open field, elevated plus maze and forced swim tests were performed on days 28 and 42. Blood and brain tissue samples were taken after the tests. Zinc levels in blood, NLGN3 and SHANK3 levels in prefrontal cortex, hippocampus, and amygdala tissues were measured by ELISA. Synaptic structures in amygdala were examined by electron microscopy. Differences between groups were evaluated by One-way ANOVA Post-hoc Bonferroni, and paired group comparisons by T-test. $p<0.05$ was considered significant.

RESULTS: Behavioral tests showed that EMF exposure had no effect on social behavior in offspring, but adversely affected activity and exploratory behavior and increased anxiety, while zinc supplementation had a partially positive effect on female offspring, but not on male offspring. SHANK3 and NLGN3 proteins were significantly lower in EMF groups and zinc supplementation was not found to have a positive effect.

CONCLUSION: Exposure to EMF may alter the levels of synaptic proteins in the developing brain, leading to behavioral changes with gender differences. Zinc supplementation, which can be used in different doses, might be useful for ameliorating EMF-related behavioral and structural effects.

Keywords: Behaviour, electromagnetic field, neuroligin3, SHANK3, synapsis, zinc

OC56

Investigation of the Effect of Different Intensity of Acute Stress on GLP-1, IGF-1 and MMP2 Levels of Hypothalamus and Intestine in Rats

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AIM: Glucagon-like peptid-1 (GLP-1) is a new important hormone for insulin metabolism, food intake and control of body weight. GLP-1 is also closely related with insulin-like growth factor-1 (IGF-1) and matrix metalloproteinase2 (MMP2) that are important for tissue homeostasis and health. The aim of this study was to investigate the effects of different intensity of acute stress on intestine and hypothalamus GLP-1, GLP-1 receptor levels, as well as IGF-1, MMP2 levels.

METHODS: After approval of Dokuz Eylul University School of Medicine Animal Care Committee, thirty adult outbred male Sprague Dawley rats were divided into three groups: 1-Control, 2-0.2mA foot-shock (low-intensity), 3-1.6mA foot-shock (high-intensity). Stress groups were exposed to electric foot-shocks for 160 ms duration with 20 min intervals. One hour later, blood sampling was completed under carbondioxide anesthesia. Hypothalamus and terminal ileum tissues were extracted. Serum corticosterone and tissue GLP-1, GLP-1 receptor, IGF-1, MMP2 levels were measured by ELISA protocol. Significant differences between groups were analyzed by one-way ANOVA and post-hoc Bonferroni test.

RESULTS: Both of low and high-intensity acute stress decreased intestinal GLP-1, IGF-1 and MMP2 levels (both stress groups compared with control, $p<0.0001$). Only high intensity stress decreased intestinal GLP-1 receptor levels (compared with control, $p<0.05$; compared with low-intensity stress, $p<0.002$). However, low-intensity acute stress increased GLP-1 levels ($p<0.0001$), high-intensity stress increased GLP-1 receptor levels ($p<0.05$) in hypothalamus. Stress did not change IGF-1 and MMP2 levels in the hypothalamus. Strong positive correlations were found between intestinal GLP-1 levels and IGF-1 levels ($r=0.757$, $p<0.0001$) and also between intestinal IGF-1 levels and MMP2 levels ($r=0.806$, $p<0.0001$).

CONCLUSION: Our results indicate that acute stress mainly affected intestinal GLP-1, IGF-1, and MMP2 levels; all of which were found to be decreased with differences in CNS and periphery. Further researches are needed to investigate the mechanisms of acute stress in different intensities; the role of dopaminergic system and other stress related pathways in acute stress.

Keywords: GLP-1, gut-brain-axis, hypothalamus, IGF-1, intestine, MMP2

OC57

Effects of Western Diet and Short-Chain Fatty Acids on Colonic Inflammation

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AIM: Western diet (WD) worsens inflammatory and metabolic events, which are improved by short-chain fatty acids (SCFA). Therapeutic effects of SCFA were studied in combination with WD in colonic inflammation induced by dextran sulfate sodium (DSS).
METHODS: Wistar-albino rats (n=40) were divided into five groups. Both control and DSS groups were fed with either normal diet (ND) or WD for 31 days or last 10 days by adding DSS (0.05%) to water. In half of ND- or WD-fed groups, SCFA (150mM/L-acetate, 50mL/L-propionate, 50mM/L-butyrate) was added to water. Body weight, serum glucose levels were measured. Hepatic functions and lipid profile were evaluated. IL-6, IL-10, TNF-alpha were measured in colon, while myeloperoxidase (MPO) activity, lipid peroxidation (MDA), glutathione, chemiluminescence levels were measured in colon and liver. Macroscopic scoring, histopathologic evaluation of colon tissue was performed. ANOVA and t-test were used for statistical analyses.
RESULTS: In ND-fed rats, DSS induced colonic inflammation (increased colon-MPO, $p<0.01$). Inflammation also observed histopathologically. In contrast to feeding with ND, WD reduced inflammatory parameters; colon MPO ($p<0.05$) and macroscopic scoring ($p<0.01$), while adding SCFA had no significant effect. Increased serum triglycerides ($p<0.01$), VLDL ($p<0.01$) and hepatic injury (elevated AST-ALT, $p<0.01$) were observed in WD groups, which were reversed by SCFA ($p<0.05$). Despite that DSS-alone did not affect hepatic functions significantly when given with WD, hepatic MPO ($p<0.05$) and luminol ($p<0.05$) levels were increased. Addition of SCFA in both ND and WD had no further effect on these parameters. DSS increased proinflammatory cytokines (IL-6, TNF-α) and reduced anti-inflammatory cytokine (IL-10) levels ($p<0.01$), while SCFA improved these alterations. However, adding WD had no significant impact on these cytokines.
CONCLUSION: Despite its beneficial effect against DSS-induced colonic inflammation, WD worsened serum lipid profile. Consumption of SCFA improved WD-induced lipid profile alteration but had no impact on colonic inflammation.

Keywords: Colonic inflammation, short chain fatty acids, western diet

OC58

P-Coumaric Acid Ameliorates Colitis by Means of Preventing Neutrophil Infiltration and Endogen Anti-Oxidant Depletion

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AIM: P-Coumaric acid (CA) is a hydroxycinnamic acid that is found in wide variety of edible plants. It has been reported to exhibit antioxidant, antimicrobial, anti-inflammatory effects. Crohn's disease is a chronic inflammatory disease involving any part of gut. Aim of the study is to investigate anti-inflammatory effects of CA on trinitro-benzene-sulfonic acid (TNBS) induced colitis model.

METHODS: Following 24-h of starvation, Spraque Dawley rats (female=male, 200-300gr) were divided into 5 groups. Rats were given 1ml TNBS (30 mg/ml dissolved in 40% ethanol) or 1ml saline intrarectally. Groups were treated with either p-coumaric acid (250-500-1000 mg/kg suspended in 1ml tween-80) or tween-80 (Colitis and control groups) by oral gavage for 5 days and were euthanized. Colon samples were collected for macroscopic evaluation, tissue wet weight index (WI), myeloperoxidase (MPO) activity as the indicator of neutrophil infiltration, malondialdehyde (MDA) which is the end-product of lipid peroxidation and endogen anti-oxidant glutathione (GSH) levels. Values were compared by ANOVA and Tukey-Kramer test.

RESULTS: The macroscopic score and WI of colitis group (6.86±0.63 and 0.66±0.33); respectively) is significantly higher compared with the control group (0.43±0.43 and 0.27±0.20; respectively) ($p<0.001$ for both MS and WI) and 500 mg/kg CA treatment (3.86±0.72) reduced both parameters significantly ($p<0.05$ for both MS and WI). Both 500 mg/kg (10.22±2.08 nmol/g) and 1000 mg/kg (12.31±2.68 nmol/g) CA treatment attenuated increased MDA levels (21.91±2.47 nmol/g-colitis group) ($p<0.01$ and $p<0.05$; respectively) and MPO activity (142.4±19.17 U/g, $p<0.05$ and 111.5±31.89 U/g, $p<0.05$; respectively) in rats with colitis (211.6±19.6 U/g). The GSH depletion in colitis group (0.84±0.09 µmol/g) is prevented by only 500 mg/kg CA treatment (1.35±0.12 $p<0.05$ µmol/g).

CONCLUSION: The results of the study indicated that CA ameliorates the inflammation induced by TNBS. As most effective dose 500 mg/kg, CA ameliorates colitis by protecting endogen anti-oxidant content and preventing neutrophil infiltration.

Keywords: Colitis, coumaric acid, inflammation, TNBS, inflammatory bowel diseases

OC59

The Role of Asprosin in the Physiopathology of Renal Ischemia/Reperfusion Injury in Rats

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AIM: Secreted by white adipose tissue, Asprosin,is a novel protein hormone that is involved in glucose metabolism. We aimed to investigate the relationship between asprosin and glomerular and tubular functions in ischemia-reperfusion (I/R) injury and its role in the pathophysiology of I/R kidney injury.

METHODS: Ethics committee approval was received. Male Spraque Dawley rats weighing 300-350 grams were divided into three groups (n = 7). Under anesthesia; Except for the rats in the control group, the blood flow in the renal vessels of rats in the IR48 and IR168 groups was clamped and 60 min ischemia was performed. IR48 group rats were reperfused for 48 hours and IR168 group rats for 168 hours. After 24 hours urine collection of rats in all groups; Blood and both kidneys were taken under anesthesia and euthanasia was performed. Mann-Whitney U test was used for statistical comparisons, $p<0.05$ was considered significant.

RESULTS: Serum urea, creatinine, Mg^{2+} levels and fractional Na^+, K^+, Ca^{2+}, Mg^{2+} and phosphate excretion were increased in IR48 group compared with control group; creatine clearance decreased and urine asprosin level increased ($p<0.05$). Serum urea, creatinine and Ca^{2+} levels increased in IR168 group; serum asprosin levels and creatine clearance decreased ($p<0.05$). Fractional Na^+, K^+, Ca^{2+} and Mg^{2+} excretion and urine asprosin levels were increased. When IR48 and IR168 groups were compared; decrease in serum asprosin, urea, creatinine, Na^+, Mg^{2+} and phosphate levels; increased creatine clearance and fractional Mg^{2+} excretion; fractional Na^+, K^+ and phosphate excretion were decreased ($p<0.05$).

CONCLUSION: In the period of severe damage (IR48), impaired functions improved towards the late reperfusion period (IR168). Urine asprosin levels correlated with glomerular and tubular functions. Further research is needed to determine the role and effect of asprosin in renal ischemia reperfusion injury.

This project was funded by TÜBİTAK (1919B011800680).

Keywords: Asprosin, acute kidney Injury, ischemia/ reperfusion, glomerular function, tubular function

OC60

Administration of Acute Agomelatine Reduces Increased Oxidative Stress Due to Experimental Renal Ischemia / Reperfusion Damage in Rats

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AIM: Sepsis, shock, hypotension, some renal surgeries, renal stone-related surgical procedures, renal transplantation and partial nephrectomy may cause renal ischemia. As these conditions endanger the supply of continuous oxygen needed by the tissue and organ, the process of tissue damage begins. Clinical and experimental studies reported that ischemia/reperfusion injury occurs through Reactive Oxygen Species (ROS). Agomelatine, a melatonin (MT1/MT2) receptor agonist and serotonin antagonist, has been reported to have antioxidant effects. The aim of this study was to investigate the effects of agomelatine on oxidative damage due to ischemia.

METHODS: Forty male Sprague Dawley rats were used in the study. The rats were divided into 4 groups as control, sham, 20 and 40 mg/kg agomelatine group (n = 10). The control group did not receive any treatment, while the sham group exposed to 1hour ischemia and 24 hours reperfusion in both kidneys. In agomelatine groups, agomelatine 20 and 40 mg/kg concentrations were given orally 1 hour before the surgical procedures applied to the sham group. The rats were decapitated after 24 hours and renal tissues were collected. MDA and GSH levels and SOD, CAT, GPx enzyme activity were measured in the collected kidney tissues.

RESULTS: Renal ischemia/reperfusion caused an increase in MDA level ($p < 0.05$), and decreased SOD, CAT, GPx enzyme activity and GSH levels ($p < 0.05$). However, it was determined that 20 and 40 mg/kg oral agomelatine decreased MDA levels in rats in the ischemia/reperfusion groups ($p < 0.05$), and increased SOD, CAT, GPx activity and GSH levels ($p < 0.05$).

CONCLUSION: These results show that agomelatine has protective effect against ischemia / reperfusion induced kidney damage with its antioxidant and free radical scavenging effect. This study was supported by Inonu University BAP (Project no: TYL-2019-1762).

Keywords: Agomelatine, ischemia, reperfusion, Reactive oxygen species, antioxidant

OC61

The Protective Effects of Carvedilol on Diabetic Nephropathy in A Streptozotocin-Induced Diabetic Rat Model

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AIM: Diabetic nephropathy (DN) is a common, severe complication of diabetes, developing in 20–40% of diabetic patients. Hyperglycemia, hypertension, dyslipidemia, oxidative stress and inflammation have been proposed to account for the development of nephropathy in diabetic subjects. Carvedilol, an antihypertensive drug, exhibits additional effects on ameliorating oxidative stress and inflammation, making it an attractive candidate for diabetic nephropathy. Moreover, diabetes and hypertension frequently coexist and patients are at high risk for DN. Thus, the aim of the present study was to evaluate the protective and therapeutic effect of carvedilol on streptozotocin (STZ)-induced DN in rats.

METHODS: Twenty-one adult male rats were included in the study. This study was approved by the Institutional Animal Care and Ethical Committee of Ege University. Fourteen rats were administered a single dose of 60mg/kg intraperitoneal (i.p.) streptozotocin (STZ) to induce diabetes. Seven rats served as control group (Group 1). Diabetic rats were randomly divided into two groups: Group 2 (n=7) and Group 3 (n=7) were treated with 4 ml tap water/day and Carvedilol 25 mg/kg/day (in 4 ml water) by oral gavage for 4 weeks, respectively. Then, the animals were euthanized, blood and urine samples were collected, and nephrectomy were performed for histopathological examination. Statistical analyses were performed using non-parametric (Mann-Whitney U) and Student's t-test.

RESULTS: In diabetic Group 2, all biochemical and histopathological parameters were increased significantly compared with control group (Group 1) ($p<0.0001$). Administration of Carvedilol (Group 3) caused a significant decrease in glomerular area, severity of sclerosis, fibronectin immunoexpression, VEGF, TGF-beta, BUN, creatinine, proteinuria levels ($p<0.05$). Blood glucose levels were significantly increased in Group 2, but there was no significant difference between Group 2 and 3.

CONCLUSION: Results of the present study demonstrate the anti-inflammatory, anti-oxidant and beneficial effects of Carvedilol on the functional properties of the kidney in STZ-induced diabetic nephropathy model in rats.

Keywords: Carvedilol, diabetic nephropathy, inflammation, oxidative stress, streptozotocin

OC62

The Effects of Agomelatine, Fluoxetine and Sertraline on Overactive Bladder

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AIM: We aim to determine the possible effects of selective serotonin reuptake inhibitor group of antidepressants; agomelatine, fluoxetine and sertraline's contraction responses in rat bladder tissues and to compare the effects of three popular antidepressant agents in overactive bladder syndrome.

METHODS: Adult (300-350 g) male Wistar Albino rats were used. Animals were undergone cervical dislocation under ether anesthesia. Bladder was rapidly separated and taken into Krebs solution. After removal of tissue and blood debris, strips of 3-4 millimeters were cut from bladder, placed into isolated organ bath with 37°C, continuously gassed (95% O2 and 5% CO2) in Krebs solution and tension was adjusted to 1 g. Tissues were washed for 1 hour with 15 minutes periods. Isometric contractions were induced with 10^{-5} M Ach and agomelatine (10^{-9} M and 10^{-4} M), fluoxetine (10^{-8} M and 10^{-3} M), sertraline (10^{-8} M and 10^{-3} M), were added separately. Contractions were recorded as frequency and amplitude parameters.

RESULTS: Inhibition observed with agomelatine at 10^{-8} M and 10^{-7} M. Statistically significant inhibitions were noticed at 10^{-4} M and 10^{-3} M doses ($p<0.001$). Although significant inhibitions were observed in fluoxetine from 10^{-7} M, statistically significant responses were recorded at 10^{-5} M, 10^{-3} M ($p<0.001$). Sertraline responses were similar, statistically significant results were obtained at 10^{-4} M and 10^{-3} M doses ($p<0.001$).

CONCLUSION: Different doses of agomelatine, fluoxetine and sertraline showed markedly inhibitory effect on bladder smooth muscle. Selective serotonin reuptake inhibitor antidepressants slowed down the re-uptake of neurotransmitter molecules (specifically serotonin) by presynaptic neurons. Since serotonin reuptake was inhibited, serotonin molecules remained in synaptic range longer and had a greater chance of activating postsynaptic neurons.

Keywords: Overactive bladder, bladder, agomelatine, fluoxetine, sertraline

Poster Communications

PC001

Regular Exercise, Overweight/Obesity and Sedentary Lifestyle Cause Adaptive Changes in Thiol-Disulfide Homeostasis

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AIM: Thiols contribute to the maintenance of homeostasis by participating in synthesis or structure of the proteins, performing some specific tasks in intracellular signaling pathways, having some regulatory roles in some parts of the cell cycle, acting as a catalyst in chemical reactions and forming compounds with metalic elements. Also, they occupy an important place in antioxidant defense system. We aimed at revealing whether there is any specific aberration in thiol-disulfide homeostasis according to lifestyle in three distinct categories.

METHODS: A total of 72 male individuals, including 1) 21 of whom exercise regularly (fitness group), 2) 23 of whom have a sedentary lifestyle (sedentary group) and 3) 28 of whom are overweight or obese (overweight/obese group). Prior to the study, individuals in overweight/obese and sedentary groups were selected among those who had not exercised regularly for years by face-to-face interviews. As for individuals in the fitness group were selected among those who have been exercising regularly with 3 or 4 sessions a week each of which lasts at least 40 min with a heart rate exceeding 120 beats/min. Plasma native thiol (-SH) and total thiol [(-SH) + (-S-S-)] levels were quantitatively determined.

RESULTS: Total thiol levels in sedentary group were significantly lower than those in overweight/obese ($p<0.05$) and fitness groups ($p<0.001$). Also, disulfide values in fitness group were significantly higher than those in sedentary and overweight/obese groups ($p<0.005$, $p<0.05$). On the other hand, disulfide level, reduced and oxidized thiol ratios and oxidation/reduction ratio in fitness group differed significantly from the other groups ($p<0.05$).

CONCLUSION: The results of our study strongly indicates that high total thiol and disulfide levels are conspicuously distinctive features of individuals exercising regularly. Total thiol pool and its components exhibit adaptive changes according to the lifestyle.

Gaziantep University Clinical Ethics Committee Decision No: 2017/313.

Keywords: Exercise, Obesity, Thiol-disulfide homeostasis

PC002

Regular Exercise Affects the Relationship Between Autonomic Nervous System Activity and Anaerobic Power

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AIM: Heart rate variability (HRV) is preferred as a noninvasive method to evaluate autonomic nervous system modulation under various physiological conditions. The aim of this study was to investigate the relationship between HRV and anaerobic power in handball players.

METHODS: 20 healthy sedentary male (mean age: 24.83 ± 4.42 years; mean height: 176 ± 6.4 cm; BMI: 24.96 ± 3.46 kg / m2) and 20 active male handball players (mean age: 21.3±3.48 years; mean height: 181±7.4 cm; BMI: 24.13 ± 3.62 kg/m2), total of 40 people was participated in this study voluntarily (Power analysis=0.925). The participants were subjected to Wingate anaerobic power test (WAnT). HRV data were examined by using Electrocardiogram recordings obtained as pre and post test. Data were analyzed by using Pearson and Spearman correlation and alpha value $p<0.05$ considered as significant. The study protocol was approved by the ethics committee of Ondokuz Mayıs University (no:2018/26)

RESULTS: A significant correlation was obtained between HRV and WAnT parameters in both groups ($p<0.05$). However, it was observed that the parameters having this correlation were more in the athlete group than the sedentary group. In the sedentary group, it was seen that statistical significance was more intensive in the post WAnT measurements. In the athlete group, significant correlations were obtained from pre and post WAnT. It has been observed that mean R-R and PNN50 (The proportion of NN50 divided by the total number of NN (R-R) intervals) were the best reflecting parameters of HRV.

CONCLUSION: In the present study, the relationship between anaerobic capacity and autonomic nervous system was examined for the first time; it was found that regular exercise significantly affected HRV structures. HRV parameters measured at rest could be used as a marker reflecting anaerobic power in athletes rather than sedentaries.

Keywords: HRV, autonomic nervous system, anaerobic power, handball

PC003

Damage Markers Caused By Exhausting Exercise at Different Time Intervals in Rat Heart Muscle and Skeletal Muscle

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AIM: The temporal differences in rat heart and skeletal muscle of exhausting exercise-induced damage markers have been investigated.

METHODS: Rats were divided into groups as sedantary controls (Con, n=6), acute–immediate (Ai, n=6), sacrificed immediately after exhaustion, acute-1 (A1, n=6), sacrificed 1-day after exhaustion. Exhausting exercise was performed on treadmill (0° inclination), with a speed starting at 15m/min, increasing by 5m/min every 3 minutes to 35m/min. Blood, gastrocnemius, left ventricular tissues were taken from rats sacrificed by cardiac blood collection under anesthesia. Plasma cortisol and cardiac-troponin-I (cTnI), and muscular myeloperoxidase (MPO) activity were measured; histomorphological examinations were performed in muscle and left ventricle. ANOVA, post-hocTukey test was used to examine the differences between the groups ($p<0.05$).

RESULTS: In plasma, compared to control, in Ai group; cTnI ($p=0.041$) and cortisol ($p=0.04$) levels increased; in A1 group, cortisol ($p=0.004$) level was decreased. According to Ai, MPO activity ($p=0.037$) was increased in A1 group. Histologically, inflammatory and damage findings such as leukocyte infiltration, increase in interfibrillary distance, number of picnotic nuclei, started in Ai group and continued on the following day in the heart, but was more prominent 1-day after exhaustion than Ai group in skeletal muscle.

CONCLUSION: The level of cTnI, is accepted as a marker of heart injury, increased in the Ai group; MPO activity, is a marker of neutrophil infiltration in muscle, was increased in A1 group. In histomorphologic imaging, inflammatory findings were more prominent immediately after exhaustion in heart, whereas inflammation was more prominent in gastrocnemius 1-day after exhaustion than in control and Ai group. According to these results, it is thought that cortisol, which increases blood levels during exhausting exercise, can suppress the inflammatory process in muscle, but it cannot create such a protective effect on the heart.
This study was approved by the ethics committee of Gazi University, ET-18.001 on 05/01/2018, was supported by Gazi University BAP Unit (01/2018-24).

Keywords: Exhaustive exercise, Skeletal muscle damage, Myocardial damage, Cortisol

PC004

Improved Pinch Force Sense in Adolescent Female Weightlifters

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AIM: Force sense is an aspect of proprioception, which is most commonly assessed by reproducing a percentage of maximal voluntary isometric contraction. Exercise improves joint position sense and kinesthesia, but there are contradictory findings regarding the effects of exercise on force sense. It is aimed to assess the effects of long-term elite-level weightlifting training on pinch force sense in adolescents.

METHODS: Twenty-five elite female adolescent weightlifters, who have been training regularly for at least 4 years and competed at national and/or international level (mean age: 16.4±1.63) and 22 sedentary adolescents (mean age: 15.7±0.45) were recruited for the research. Maximum key and tip pinch strength of participants were measured. Later, participants were asked to press the pinchmeter with 50% of their maximal strength 3 times while looking at the scale. Participants then tried to reproduce 50% of their maximum key and tip pinch strength without any visual feedback 3 times. Absolute error, constant error, root mean square error and coefficient of variation were calculated and these values were normalized by diving to the target values. Accuracy was evaluated by absolute error and root mean square error; directionality of errors by constant error and the precision by coefficient of variation. This study was approved by Local Ethics Committee (2018/1584).

RESULTS: Weightlifter adolescents had higher key (6.8±1.02 kg) and tip pinch strength (4.3±1.24 kg) values compared to sedentary (key: 6.0±1.02 kg, tip: 3.6±0.75 kg), ($p=.03$ and $p=.02$, respectively). Normalized absolute error was lower in weightlifters than in sedentary in both key and tip pinch force sense ($p<0.01$, both.).

CONCLUSION: These results demonstrate that regular weightlifting training improves accuracy in pinch force sense without affecting precision or directionality of error. In future studies, it would be appropriate to investigate whether higher accuracy in force sense would also be evident in adult weightlifters.

Keywords: Adolescence, weightlifting, force sense, pinch strength, proprioception

PC005

Effect of Voluntary Exercise on Water Intake and Blood Pressure in Male Rats

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AIM: Few studies have been examined the role of water consumption during voluntary physical activity on blood pressure. The aim of this study was to investigate the effect of eight weeks of voluntary exercise on water consumption and blood pressure in male rats.

METHODS: Sprague-Dawley male rats (264.6±4.2 g) were divided into control (C; n=7) in standard cage and activity (A; n=7) in cages with running wheel groups after ethical approval (TÜHADYEK-2018/25). The rats, each placed in separate cages, were provided with free access to standard laboratory chow and drinking water through the reverse osmosis system for eight weeks. Daily fluid intake, activities and weekly body weights were measured. Blood pressure was measured by *tail-cuff* plethysmography before and at the end of the 8th week. Weight change was determined by Lee index, and cardiac hypertrophy by cardiac weight/tibia length ratio. Heart, liver and kidney weights were determined. Mann-Whitney U test was used for statistical comparisons.

RESULTS: The mean daily physical activity of group A rats was found to be 2.61±2.0 km/day. Basal weight and blood pressure were similar before exercise in both groups. When difference between weekly water intake was compared, it was seen that fluid consumption of group A rats was higher than group C ($p<0.05$). Systolic blood pressure was lower in group A (125.3±4.6 mmHg) than group C (130.3±2.2 mmHg) ($p=0.02$). The last weight gain was lower in group A (355.2±14.8 g) than group C (387.1±12.2 g) ($p<0.05$). Heart, liver, kidney weights and heart weight/tibia length ratio did not differ between groups ($p>0.05$).

CONCLUSION: The findings of this study suggest that decreased blood pressure and weight gain associated with voluntary physical exercise may result from increased water consumption.

Keywords: Exercise, voluntary physical activity, water consumption, blood pressure

PC006

Effect of Acute Exhausting Exercise on Oxidative Process and PON-1 Enzyme Activity in Rats' Right and Left Ventricles

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AIM: Exhausting exercise increases oxygen consumption in cardiomyocytes, causes an imbalance between reactive oxygen species and antioxidant system. Paraoxonase-1 (PON-1), an antioxidant enzyme, is thought to be cardioprotective. Inflammatory responses of right and left ventricle to exhausting exercise, differ in developmental, biochemical and functional aspects, were examined histologically. The role of oxidant system and PON-1 activity in these responses were evaluated.

METHOD: A total of 18 rats were used as; non-exercising controls (C, n=6), acute–immediate (Ai, n=6), sacrificed immediately after exhaustion. Acute-1 (A1, n=6), sacrificed 1-day after exhaustion. Exercise was performed on treadmill with increasing intensity, reaching the speed of 40 m/min, a slope of 0°. Total Antioxidant Status (TAS), Total Oxidant Status (TOS) levels and PON-1 activity were measured in right and left ventricle. ANOVA, post hoc Tukey and paired-sample t test were used to examine differences in groups, between two ventricles ($p<0.05$).

RESULTS: Relative to control, in Ai group; decrease in TAS level and PON-1 activity in left, decrease in TAS level in right, in A1 group; decrease in PON-1 activity in left, decrease in TAS and TOS levels in right ventricle were found. In left ventricle compared to right, TAS was lower and TOS was higher in the control; TAS level and PON-1 activity were low in Ai group, TAS was low and TOS was high in A1 group. Histologic findings show that left ventricle has more pronounced inflammation findings than the right, especially in the Ai group.

CONCLUSION: It was concluded that exhausting exercise significantly decreased antioxidant capacity, especially in left compared to right ventricle. PON-1 did not show cardioprotective effect against oxidative damage after exhausting exercise. The adaptation responses of right and left ventricle to exercise may have caused these differences. This study, approved by the ethics committee of Gazi University, ET-17.040, was supported by Gazi University BAP Unit (01/2017-29).

Keywords: Left ventricle, Paraoxonase, Right ventricle

PC007

Effects of Acetaminophen on Liver Oxidant-Antioxidant Balance in Acute Exercised Rat

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AIM: Regular physical exercise is beneficial to the body. Acute exercise causes oxidant stress by creating an unbalanced status between oxidant and antioxidant levels. Reactive oxygen species also occur in the liver during exercise. Analgesic drugs are commonly consumed to reduce the pain after exercise. Acetaminophen, which is a widely used over-the-counter analgesic, is hepatotoxic. This damage, which is believed to be initially caused by oxidation, occurs only after depletion of liver glutathione. The aim of this study was to investigate the effect of subtoxic acetaminophen which is given after the acute and exhaustive exercise on oxidative injury, glutathione status and antioxidant enzyme systems.

METHODS: All experiments were performed in accordance with the guidelines provided by the Experimental Animal Laboratory and approved by the Animal Care and Use Committee of the Dokuz Eylul University, School of Medicine. The experiments were carried out with 63 male Wistar rats (4-6 month-old, weighing 200-250 g). 9 Trial groups were formed. Rats were exercised at moderate intensity and exhaustive and then received subtoxic dose of acetaminophen (100mg/kg and 250mg/kg) intraperitonelly. Results are presented as mean± S.E.M. Kruskal–Wallis test was used for statistical analyses. Statistical analysis was performed using Mann–WhitneyU-test to detect differences among groups.

RESULTS: Administration of acetaminophen and/or exercise did not affect hepatic glutathione status and plasma alanine aminotransferase activity. It was observed that there were vacuolization in hepatocytes, sinusoidal dilatation and accumulation of eosinophilic material in the liver sections stained with hematoxylin-eosin in all groups compared with the control group. It was recorded that the group which received 250mg/kg acetaminophen has more severe morphological changes.

CONCLUSION: As a result, although histopathological changes occurred by acute exercise and/or acetaminophen, oxidant-antioxidant balance in liver and plasma enzyme activity were not affected.

Keywords: Exercise, acetaminophen, oxidative stress

PC008

Probiotics Attenuates Exercise-Induced Oxidative Stress in Wistar Rats

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AIM: The aim of this study was to investigate the effect of probiotic and exercise on thiol disulfide balance, which is a marker of oxidative stress.

METHODS: Male albino Wistar rats (n = 32) were randomly divided into four groups as follows: control (C), exercise group (EX), probiotic group (PRB), and probiotic + exercise group (PRBex). A pool of probiotics that included L. rhamnosus, L. acidophilus and B. bifidum (Solgar, USA) was given for 4 weeks daily (1×109 CFU of bacteria). Prior of gavage, the probiotics were diluted in 300 µl of sterile water. Exercise and probiotics administration were performed 5 days per week for 4 weeks. Following completion of the experimental protocol, to determine oxidative stress parameters, serum total thiol and native thiol concentrations were measured. Dynamic disulfide status (DD), reduced thiol (RT), oxidized thiol (OT), and thiol oxidation reduction (TOR) percentage ratios were compared between the groups. The difference between the groups was analyzed by SPSS v.21 ANOVA test and the alpha value was assumed to be $p<0.05$.

RESULTS: In comparison with the control group, serum DD levels were significantly lower in the PRBex group and highest in the EX group. The lowest OT and the highest RT rates were determined to be in the PRBex group. The highest OT value was observed in the EX group. TOR values were found to be highest in the PRBex.

CONCLUSION: As a result, it was found that exercise increased oxidative stress and probiotic application together with exercise decreased dynamic disulfide value and significantly reduced oxidative damage. In addition, the new oxidative stress measurement method used in this study is a promising practical and useful method to evaluate and improve the performance of athletes.

Keywords: Exercise, probiotics, oxidative stress, thiol disulphide homeostasis

PC009

The Short-Term Effects of Acute Supramaximal Exercise on Olfactory Function

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AIM: The effects of exercise on olfactory performance were established with the development of the objective methods for measuring the sense of smell. There is increasing evidence about the acute and/or chronic effects of aerobic exercise. Yet, the effects of short-term and high-intensity anaerobic exercise on the olfactory performance are not well understood. The aim of this study was to investigate the acute effects of supramaximal exercise on olfactory performance.

METHODS: Fifteen healthy male athletes (mean age 22.4 years) participated to the study. Participants were randomly assigned to two groups and underwent to the Sniffin' Sticks Test (SST), which was applied to determine the odor threshold, discrimination and identification performances. Participants who had normal olfactory performance included in the study. After the SST, Wingate test protocol (WAnT) was applied to the study group. During WAnT, a load which was 90 gr/kg of body weight was applied for 30 seconds. The participants in the control group were passively rested within same time period as WAnT was performed. Both groups underwent to a SST-Discrimination test after the sessions. A 5x2 ANOVA was employed for the statistical analysis.

RESULTS: There was no significant difference between the groups according to the results of ANOVA. On the other hand, pairwise comparisons revealed that the odor discrimination scores increased significantly ($p = 0.012$) in after exercise session. Additionally, it was observed that the discrimination scores increased in each participant in the exercise group.

CONCLUSION: It was that supramaximal exercise improves the olfactory performance. The study is a preliminary study and the number of participants should be extended for the more generalized results. Further studies are needed to determine the physiological mechanisms which are responsible from the increase of the discrimination scores.

Keywords: Olfactory performance, exercise effect, anaerobic exercise, smell, Sniffin Sticks

PC010

Effects of Docosahexaenoic Acid (DHA, Omega 3) with Exercise on Experimental Achilles Tendinopathy in Rats

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AIM: Achilles tendinopathy (AT) is common pathology in athletes due to overuse of tendon. Docosahexaenoic-acid (DHA, Omega-3) is unsaturated fatty acid that increases collagen synthesis and has various biological effects. Exercise to work out for specific muscle groups is known to increase tendon volume and tensile strength. We aimed to evaluate efficiency of DHA with exercise in AT induced with type-1 collagenase enzyme in rats.
METHODS: This study was approved by Ataturk University Local Ethics Committee for Experimental Animals. AT model was formed with injection of type-1 collagenase to left peritendinous area of rats and groups were formed by randomly. (Group1: Diseased control, Group2: Exercise, Group3: DHA (150 mg/kg/day) and Group4: DHA (150 mg/kg/day + Exercise). DHA were given orally for 4 weeks to adaptation and 8 weeks (5days/week) for treatment to rats. Exercise were performed on rodent treadmill for 8 weeks (5days/week, 20 m/min, 30 min/day) after 1week adaptation (10 m/min, 30 min/day). Right tendons of Group1 rats were used as healthy control. At the end of experiment, rats were sacrificed under general anesthesia and Achilles tendons (with calceneus bones) were removed for histopathological testing. Blood samples were taken for analysis of IL1-β by ELISA.
RESULTS: Histopathologically, in Group1, tendon cells were degenerated, normal structure of tendon was disrupted whereas no lesion was observed in healthy control. In groups 2, 3 and 4 increased density of fibrocyte and fibroblast cells of connective tissue with new capillary vascularization and tendon fibers were formed regularly, the most apparent healing was seen in 4th group. There was statistically significant decrease in serum IL1-β levels in Group3 and Group4 compared to Group1 ($p<0.05$).
CONCLUSION: The importance of DHA in the elimination/ reduction/amelioration of inflammation which plays an important role in the pathogenesis of AT was determined. It was concluded that DHA usage with exercise may be recommended in AT patients.
This study was supported by Şeymanur Yılmaz Tascı's OYP grant.
Keywords: Achilles tendinopathy, Exercise, Omega 3

PC011

Investigation of the Effect of Curcumin Treatment on Total Oxidant and Total Antioxidant Status in The Gastrocnemius Muscle in Aged Rats

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AIM: Curcumin is a natural polyphenol with strong antioxidant properties as well as anti-inflammatory and anti-tumor effects. With these properties, curcumin appears to be protective in aging and age-related disease models. Aging is known to increase the level of oxidative stress at most organ and tissue levels. In this context, we aimed to show whether curcumin application has an effect on reducing oxidative damage in skeletal muscle which is one of the tissues with high aerobic metabolism.

METHODS: A total of 18 Wistar male rats (young: 3 months old, aged: 22 months old) were divided into 3 groups; 1) Young-Control (n=6), 2) Aged-Control (n=6), 3) Aged-Curcumin (n=6). Young and aged control groups were treated with PBS (phosphate buffered saline) containing 4% DMSO (dimethyl sulfoxide) and curcumin, which was prepared by dissolving with 4% DMSO-PBS, was administered intraperitoneally at 30 mg/kg/day for 21 days. Total oxidant status (TOS; µmol H2O2 Equiv./L) and total antioxidant status (TAS; mmol Trolox Equiv./L) were measured by spectrophotometric method using appropriate commercial kits in the gastrocnemius muscles of all rats. The ratio of total oxidant status to total antioxidant status, i.e. the oxidative stress index (OSI), was also calculated. ANOVA, LSD were used for statistical analysis and $p<0.05$ was considered statistically significant.

RESULTS: Compared with the young control group, TAS significantly decreased in the gastrocnemius muscles of aged rats ($p=0.001$) and TOS increased significantly ($p=0.01$). Curcumin treatment significantly increased TAS in aging ($p=0.01$). OSI, which is accepted as an indicator of oxidative stress level, increased significantly with aging ($p=0.001$), while curcumin treatment decreased OSI ($p=0.033$).

CONCLUSION: Curcumin administration in aging seems to be effective in reducing oxidative stress in the gastrocnemius muscle.

This study was supported by TÜBİTAK 2209A project (1919B011802351).

Keywords: Aging, oxidative stress, gastrocnemius, curcumin

PC012

The Effect of Hypnosis on Respiratory Function in Addicted to Cigarette Smoking

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AIM: Most notably chronic obstructive pulmonary disease (COPD) and smoking brings about a variety of diseases contributing to lung cancer. Our aim is to investigate the effect of hypnosis on pulmonary functions in case smoker with spirometry.

METHOD: Our research was done on a 53-year old patient with COPD who has been smoking a pack of cigarettes a day for 30 years and suffering from exertional dyspnea for last 5 years. Spirometry was applied on the male patient consulted for smoking cessation by taking advantage of hypnotherapy. Using fast hypnosis technique, the patient was put into trance. Positive imaginations and breathing techniques were exerted during hypnosis. Spirometric measurements were recorded before and during hypnosis. The man was woken up by using count down method. These sessions were repeated once a week for three weeks. Teaching autohypnosis and breathing techniques, this method was done in home in intervals between sessions.

RESULTS: In our study, FEV1: %41, FCV: %69, FEV1/FVC: %49.7, FEF25-75: % 10.9 were recorded before hypnosis. In the first session, the measurements during hypnosis were FEV1: %45, FVC: % 70, FEV1/FVC: % 50.6, FEF25-75: %11.5, in the second session FEV1: %49, FCV: %72, FEV1/FVC: % 53, FEF25-75: %12, and in the third session FEV1: %50, FVC: %75, FEV1/FVC: %55, FEF25-75: %14 were found. At the end of the third week the number of daily smoking fell by half.

CONCLUSION: Improve in respiratory functions was recorded once the patient went under hypnosis process. Exerting positive imaginations on patient by hypnotherapist leads to an elevation in the blood circulation in limbic region there by the endorphins level goes up and unrest feelings reduce. Relaxation occurs in pulmonary muscles. Our research can be the first to show the impacts of hypnosis on dyspnea rehabilitation in smoker patient suffering from COPD.

Keywords: Hypnosis, Respiratory Function Test, Cigarette, COPD, Asthma

PC013

Cannabinoid Type 2 Receptor Activation Reduces Inflammation and Apoptosis in the Lung in Model of Sepsis Induced by Cecal Ligation Puncture

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AIM: Sepsis, which can cause multiple organ failure, is an important health problem with high mortality rate. Increased immune response due to inflammatory mediators causes organ damage in sepsis. Cannabinoid type 2 (CB2) receptors, which are widely expressed in immune cells, have been shown to have an effect on the immune response. In this study, we investigated the effect of CB2 receptor agonist JWH-133 on inflammation and apoptosis in lung in cecal ligation and puncture (CLP) induced sepsis model.

METHODS: In our study, sprague-Dawley male rats were divided into 5 groups (Sham, CLP, CLP+JWH-133 0.2 mg/kg, CLP+JWH-133 1 mg/kg and CLP+JWH-133 5 mg/kg). The cecum of the rats was reached through the abdominal incision. The cecum was ligated with surgical suture thread. The cecum was punctured from the distal region with a needle. Then the cecum was inserted into the abdomen and the incision site was sutured. Three different doses of JWH-133 were administered intraperitoneally to the treatment groups. After 24 hours, the animals sacrificed and their organs were placed in formaldehyde solution for immunohistochemical analysis. Phosphorylated Nuclear factor κB (p-NF-κB), Caspase-3, tumor necrosis factor alpha (TNF-α), interleukin 1-beta (IL-1β), interleukin-6 (IL-6) levels were measured by immunoistochemical method in lung tissue.

RESULTS: In our study, p-NF-κB, Caspase-3, TNF-α, IL-1β and IL-6 levels in lung tissue of CLP group increased compared with sham group ($P<0.05$). While the levels of caspase-3 and IL-6 decreased at 1 and 5 mg/kg doses of JWH-133 compared with CLP group ($P<0.05$); p-NF-kB, TNF-α and IL-1β levels decreased significantly in all doses administered JWH-133 compared to the CLP group ($P<0.05$).

CONCLUSIONS: We found that CB2 receptor agonist JWH-133, has protective properties by preventing inflammation and apoptosis in lung tissue in sepsis model induced by CLP. This study was supported by Yozgat Bozok University (BAP-6602c-TF/18-229).

Keywords: cecal ligation puncture, Sepsis, Cannabinoid type 2 receptors, JWH-133

PC015

Cardiovascular Effects of Melatonin, Hormone Replacement Therapy and Exercise in Postmenopausal Rats

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AIM: Postmenopausal estrogen deprivation paves the way for development of cardiovascular diseases. Hormone replacement therapy (HRT) or exercise ameliorates postmenopausal symptoms. Since HRT has side effects, new alternative treatments are required. In order to ameliorate oxidative damage that can be caused by HRT and/or exercise in postmenopausal rats, protective effects of antioxidant melatonin as an adjunctive treatment were elucidated.
METHODS: Following ovariectomy under anesthesia, Sprague-Dawley rats (n=8, 8 groups) were given tap-water, HRT (1 mg/kg/day), melatonin (4mg/kg/day) or HRT + melatonin in drinking water. On 14th day, they were divided as sedentary (SED, SED-HRT, SED-melatonin, SED-HRT-melatonin) or exercise (30 min/day, 5 days/week, 8 weeks swimming; E, E-HRT, E-melatonin, E-HRT-melatonin). Rats were weekly weighed. Heart rates were determined using ECG. After decapitation on seventieth day, cardiac malondialdehyde levels, antioxidant glutathione and myeloperoxidase activity (MPO) were evaluated. 8-hydroxydoxyguanosine (8OHdG) levels (ELISA) and TNF-alpha, IL-10 and SIRT1 levels (western-blot) indicating DNA damage in heart and abdominal aorta were measured. Hematoxylin-Eosin staining was performed. ANOVA and Student's t-test were used for statistical analyses.
RESULTS: All HRT groups lost weight ($p<0.05$). All treatment modalities decreased TNF-alpha levels and increased IL-10 levels ($p<0.05$). Heart rates were not different among groups. Cardiac glutathione levels in HRT groups were decreased ($p<0.05$), but malondialdehyde and MPO levels were unchanged. Although 8OHdG levels in abdominal aorta were decreased with all treatments ($p<0.05$), elevated cardiac 8OHdG level in HRT was suppressed by melatonin ($p<0.05$). The highest SIRT1 levels were observed in HRT-E and HRT-E-melatonin ($p<0.05$). Thinner aortic wall, endothelial detachment and irregular cardiomyocytes were observed in sedentary groups; but nearly normal tissue organization was evident in groups with HRT, exercise, melatonin or their combination.
CONCLUSION: Usage of HRT alone or combined with exercise disrupted oxidant/antioxidant balance, while addition of melatonin alleviated HRT-induced cardiovascular inflammation. Our findings support postmenopausal use of melatonin.

Keywords: Cardiovascular effects, exercise, hormone replacement therapy, melatonin, menopause

PC016

The Effect of Systemic Adropin Treatment on Levels of Oxidant and Antioxidant of Cardiac Muscle in Diabetic Rats

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AIM: In Type 1 diabetes mellitus (T1DM), hyperglycemia is considered a primary cause of diabetic cardiomyopathy and is associated with oxidative stress. Adropin is a recently identified protein that has been implicated in the maintenance of energy homeostasis, insulin sensitivity and act as a novel regulator of endothelial cells. Low adropin level may be used for early diagnosis of various heart diseases. The aim of our study to examine the effects of systemic administration of adropin on levels of oxidant and antioxidant of cardiac muscle in rat model of T1DM.

METHODS: This study was approved by the local ethics committee of the Gazi University. 28 male Wistar-Albino rats were divided into 4 groups. 1. Control 2. Control + Adropin. Diabetes 4. Diabetes+Adropin. Diabetes were established using streptozotocin (65 mg/kg/ip). After 72 hours rats with blood glucose levels of 250mg/dL and above were accepted as diabetic. 10 weeks after STZ induction, diabetic rats treated with adropin 450 nmol/kg/ i.p. twice daily for 10 days, 1 day after the last adropin administration, the animals were sacrificed by intracardiac blood collection under Ketamine-Xylazine (45-5 mg/kg) anesthesia. Oxidative damage to heart tissue; TOS and MDA levels were evaluated. Antioxidant Glutathione levels were measured. Results were evaluated by ANOVA and Tukey tests. $p < 0.05$ was considered significant.

RESULTS: Total oxidant and MDA levels increased significantly in diabetic group compared with control group ($p < 0.05$). Adropin administration caused a decrease in raised oxidative damage. There was no significant difference between control and control adropin groups. Adropin administration increased glutathione levels compared with diabetic group.

CONCLUSION: Systemic adropin administration increased antioxidant levels in diabetes-induced oxidant damage on heart tissue. That suggest systemic adropin may have effect on cardiac complications of diabetes. We think that our study will shed light on other studies in this field.

Keywords: Adropin, Diabetes Mellitus, Heart Tissue, Oxidant Stress, Antioxidant

PC017

Investigation of the Effect of Sertraline on Contraction Strength of the Heart; In Vitro Model

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AIM: The aim of this study was to determine the synergistic effects of Mg combined with sertraline, in the treatment or prevention of major depression in early postoperative period and in regulation of contraction strength of the heart.

METHODS: The study was conducted in Necmettin Erbakan University Department of Physiology. Wistar Albino rats were used. There were 6 groups including 40 animals. Their distribution was randomly determined.1.,5. and 6. groups, blood plasma taken from the heart tissues of rats under mild ether anesthesia was separated and stored at -20°C. The 3-4 mm long strips cut from rat atriums were placed in hooks of isolated organ bath. Isometric contractions were induced with 10-3M adrenaline and only observed in group 1 (control). The second group was cumulative (cum.) sertraline (10-9-10-4M), the third group was cum. Magnesium Sulphate ($MgSO_4$) (0.1,1,2,4,8,10 mmol/L), the fourth group was cum. sertraline and $MgSO_4$. Changes in contractions were recorded. The fifth group received 10 mg/kg/day sertraline injection for 29 days before decapitation and the sixth group received 20 mg/kg/day $MgSO_4$ injection for 14 days, during which time changes in weights were recorded. The 5th and 6th groups were subjected to same procedures as the group after decapitation. Statistical analyzes were performed using SAS University Edition 9.4.

RESULTS: There was no significant difference between the control and cum. sertraline groups in the relationship between strains. Strain relationship between cum. sertraline and cum. $MgSO_4$. A rapid inhibition of strain was observed in isolated organ bath, where cum. sertraline and cum. $MgSO_4$ were given consecutively. After 29 days of sertraline and 14 days of magnesium injection, it was statistically significant. While some plasma enzymes increased, Nt-BNP and CRP didn't change significantly.

CONCLUSION: The use of $MgSO_4$ in combination with antidepressants in the treatment of depression after coronary bypass may help sertraline to inhibit vasospasm in grafts, but may cause fatal risks as it shortens the clotting time.

Keywords: Atrium, Magnesium, Sulfate, Sertraline

PC018

Investigation of the Effect of Bronchoscopic Volume-reducing Surgical Procedure "Coil" on Hemorheological Parameters in COPD Patients

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AIM: Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable, curable disease characterized by persistent airflow limitation, respiratory symptoms due to airway and/or alveolar abnormalities caused by severe exposure to harmful particles and gases. During the bronchoscopic volume reduction process, which is a smart spiral wire treatment (coil), the volume of the lung parenchyma is reduced by shrinking the elastic recoil. Although there are studies showing worsening of hemorheological parameters in COPD exacerbations, no study investigated whether hemorheological parameters are improved after coil. The aim of this study was to assess the effects of coil therapy on erythrocyte deformability, whole blood viscosity (WBV) measured in autologous, standard (40%) hematocrit and plasma viscosity (PV) in COPD patients.

METHODS: 11 patients who had been indicated for coil according to Turkish Thoracic Society and GOLD guidelines were included. Venous blood samples were obtained before and 1 month after treatment. Erythrocyte deformability was determined at 0.3-30 Pa shear stresses by an ectacytometer (LORCA), while WBV, PV were measured using a rotational viscometer. Data were expressed as mean±standard deviation, median (smallest-maximum values). Pre, post-coil differences were evaluated by paired samples t test and Wilcoxon paired sample tests. $p < 0.05$ was considered statistically significant. Study was approved by Pamukkale University non-invasive clinical research ethics committee (number 11 on 11.06.2019).

RESULTS: Erythrocyte deformability measured at shear stresses of 0.3-0.95 Pa were found to be higher following treatment ($p=0.009$, $p=0.034$ and $p=0.046$, respectively) compared to pre-coil values. Treatment did not have a statistically significant effect on WBV measured in autologous, 40% hematocrit, PV and hematocrit.

CONCLUSION: Increased erythrocyte deformability determined following the coil procedure is a favorable finding, showing that the procedure can positively affect the hemodynamics of patients as well as causing clinical improvement.

Keywords: Chronic obstructive pulmonary disease (COPD), coil, erythrocyte deformability, viscosity

PC019

The Comparison of Sympatho-Vagal Tonus According to Gender in Health Personnel Working in Shift System

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AIM: Heart rate variability (HRV) is a noninvasive method used to evaluate autonomic nervous system (OSS) status and its effect on the heart. HRV is largely dependent on age and sex and may vary depending on these factors. The aim of the present study was to compare the heart rate variability in terms of gender with time and frequency dependent measurement methods in health care personnel working in shifts.

METHODS: After obtaining approval from the Malatya Clinical Research Ethics Committee (No: 2019/20), the study was conducted on men and women working at Turgut Özal Medical Center (TÖTM) at Malatya İnönü University. The inclusion criteria were; being healthy, being in the 18-45 age range, not smoking and not being in menstruation period. In women (group1, n=40) and men (group2, n=40), HRV was performed twice a day and night shift and blood pressure was measured. In this study, statistical analysis was performed by using Minitab 19 package program. T-test was applied to the data showing normal distribution and values were presented as mean±standard error. Mann Whitney U test was applied to non-normal data and the values were presented as median (min-max). $p<0.05$ was considered statistically significant.

RESULTS: Systole (women: 100 ± 1.35, man: 115 ± 1.42, $p=0.000$), diastole (women: 71 ± 1.31, man: 77. ± 1.25, $p=0.001$), low frequency (LF) (women: 61.75 (23.00-93.50), men: 76.70 (31.50-90,40), $p=0.000$) and sympathetic/vagal balance (LF/HF) (women: 1.465 (0.300-4.660), men: 3.295 (0.460-9.460), $p=0.000$) were higher in men than women. However, standard deviation of NN intervals (SDNN) (women: 40.77 ± 1.37, man: 36.36±1.52, $p=0.036$), mean square of successive RR interval differences (RMSSD) (women: 30.43±1.55, man: 24.86±1.38, $p=0.005$), the percentage difference between consecutive percentage of successive RR intervals that differ by more than 50 ms (pNN50) (women: 6.85 (0.00-82.30), man: 3.00 (0.00-35.00,$p=0.000$) and high frequency power (HF) (women: 38.84±1.73, man: 29.82±1.75, $p=0.000$) were found to be low in man compared to women.

CONCLUSION: Sympatho-vagal tonus and blood pressure were found to be higher in men working in the shift system, while HRV findings were low. Therefore, men were found to be more stressful and more at risk for health.

Keywords: Shift work, health personnel, heart rate variability, gender

PC020

Sympatho-Vagal Tonus in Mothers of Children Hospitalized for Malignant or Non-Malignant Diseases

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AIM: Childhood diseases can affect children and their families psychosocially. The families of children with cancer may experience more trauma-related symptoms than the families of children with other chronic diseases. Parents may experience post-traumatic stress after this psychological trauma. One of the systems activated in response to stress is the autonomic nervous system (OSS). Heart rate variability (HRV) is a noninvasive method used to assess OSS status and its regulation on the heart. The aim of the present study was to evaluate sympatho-vagal tone in mothers of children with malignant disease.

METHODS: The study was conducted with the approval (No: 2019/43) from Malatya Clinical Research Ethics Committee. The study was conducted on mothers of healthy children (group1, n =25) and mothers of non-malignant (group2, n= 25) and malignant (group3, n=25) children who were hospitalized at Turgut Özal Medical Center of İnönü University. HRV and blood pressure were measured. Statistical analysis was performed using Minitab 19 package program. T-test was applied to the data and values were presented as mean±standard error. $p<0.05$ was considered statistically significant.

RESULTS: There was no significant difference between groups in terms of standard deviation of NN intervals (SDNN) (grup1 (37 ± 2.11), grup2 (35 ± 2.30), grup3 (35 ± 2.68)), mean square of successive RR interval differences (RMSSD) (grup1 (32.45 ± 2.46), grup2 (30.08 ± 2.97), sympathetic/vagal balance (LF/HF) (1.697 ± 0.214), grup2 (1.401 ± 0.165), grup3 (1.265 ± 0.164)) and other HRV findings. The systolic values were higher in group1 (115 ± 2.31) than in group2 (102 ± 1.88) and group3 (109 ± 1.8). Diastole values were higher in group1 (79 ± 1.71) compared to group2 (73 ± 1.86), whereas similar results were found in group3 (78 ± 1.66).

CONCLUSION: There was no significant difference between the groups in terms of HRV values. This shows that all three groups have similar stress responses. Although there was a difference between the groups in terms of blood pressure and pulse values, these values were within normal limits in all three groups.

Keywords: Malignant disease, acute illness, mother, sympatho-vagal tonus

PC021

Investigation of Treatment-Related Early Serum Potassium Levels in Adult Patients with Megaloblastic Anemia

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AIM: We evaluated serum potassium levels of patients with severe megaloblastic anemia undergoing parenteral vitamin B12 treatment during which hypokalemia may develop. The main effects of hypokalemia are cardiac. Increased P wave amplitude and wave width, PR prolongation, T wave flattening and inversion, ST depression, prolonged QT and U waves are the main ECG findings.

METHOD: 9 male and 11 female patients with median age 66.5 years were included in the study. Serum potassium levels were evaluated before and on the third day of the treatment and the difference between was evaluated by t-test in dependent groups.

RESULTS: There was no statistical difference between the mean values of serum potassium levels before treatment and after the 3rd day of the treatment: $p = 0.062$. This may have been due to insufficient number of subjects.

CONCLUSION: Hypokalemia arises from a marked increase in potassium use during production of new hematopoietic cells in early response to B12 treatment. In our study, although there was a partial decrease in mean potassium level in the early period of treatment, no clinical findings were observed in ECG evaluation. Such patients should be closely monitored during treatment. The study can be performed prospectively in a larger patient population.

Keywords: Megaloblastic anemia, parenteral treatment, hypokalemia.

PC022

mRNA Expression Levels of Some TRP Channels in Psoriasis Patients

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AIM: Psoriasis is a chronic inflammatory skin disorder with an underlying immune dysregulation that predisposes to inflammatory skin lesions. Interactions between keratinocytes and immune system cells such as neutrophils, dendritic cells, T-lymphocytes and mast cells have a role in the development of psoriasis. Transient receptor potential (TRP) channels contribute to sustenance of skin barrier and cutaneous immunological and inflammatory processes. The purpose of the study was to evaluate, on peripheral blood mononuclear cell (PBMC) of the patients with psoriasis, the Transient receptor potential melastatin 2 (TRPM2), TRPM4, TRPM7, transient receptor potential ankyrin 1 (TRPA1), transient receptor potential vanilloid 1 (TRPV1), TRPV2, TRPV3, TRPV4, and transient receptor potential canonical 6 (TRPC6) mRNA expression.

METHODS: 30 patients with plaque psoriasis and 30 healthy control were enrolled in this study. The expression levels of TRP channels in PBMCs were measured by quantitative reverse transcription PCR.

RESULTS: The results of our study indicate that, a decreased TRPM4, TRPM7, TRPV3, TRPV4, and TRPC6 genes expression levels were found in the patient group compared with controls ($p<0.05$), whereas, an increased expression level was found in TRPM2 and TRPV1 genes in the patient group compared with controls ($p<0.05$). There was no significant difference in TRPA1 and TRPV2 genes between the patient and control groups. Although it is not statistically significant, TRPA1 gene expression was increased while TRPV2 gene expression was decreased in the patient group.

CONCLUSION: This is the first study showing the mRNA levels of TRP channels in the peripheral blood of psoriatic patients. Our results suggest that changing mRNA expression levels of TRP channels may have a role in the pathophysiology of the disease.

Keywords: TRP channels, mRNA, expression, psoriasis

PC023

Determination of Serum Irisin Levels in Patients with Knee Osteoarthritis and Comparison with Healthy Individuals

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AIM: Osteoarthritis (OA) is a multifactorial disease characterized by joint degeneration where pain and loss of function are most common in adults. Inflammation is thought to play an important role in the mechanism of OA. Irisin is newly discovered a peptide hormone that has anti-inflammatory properties, osteoblastic activity and involved in energy homeostasis, has been shown to be effective in various metabolic, inflammatory and cardiovascular diseases. In this study, it was aimed to determine serum irisin levels in patients with knee OA (KOA) and to investigate the relationship between irisin and OA by comparing with healthy individuals.

METHOD: Ethical committee approval was obtained from the Medical Faculty of Atatürk University Erzurum, Turkey on 07.06.2018 with the number of 197. Eighty patients with KOA (except traumatic arthrosis with secondary arthrosis and patients with rheumatic diseases like rheumatoid arthritis and metabolic disease) and 30 healthy individuals admitted to the Orthopedics and Traumatology Clinic of Erzurum Regional Training and Research Hospital were included in the study. Blood samples of these individuals were taken and serum samples were separated. Knee radiographs were taken and clinical features, body mass index (BMI), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and hemogram parameters were recorded. Irisin levels in all serum samples were determined by enzyme-linked immunosorbent assay (ELISA).

RESULTS: Serum irisin levels were significantly lower in KOA patients compared with healthy individuals ($p<0.05$). In addition, serum irisin levels showed a significant negative correlation with BMI and CRP levels.

CONCLUSION: This study demonstrated the relationship between KOA and serum irisin level. If further extended studies are supported, serum irisin level may be revealed as a new biomarker candidate for patients with KOA.

Ataturk University Scientific Research Project No: TSA-2018-6796.

Keywords: Knee Osteoarthritis, Irisin, Inflammation

PC024

Determination of Serum Daidzein Level with HPLC Method in Rat Administered Oral / Intra-Articular Daidzeine in Experimental Knee Osteoarthritis Model

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AIM: Osteoarthritis (OA) is a common degenerative joint disease in world. Daidzein (DZ) is a natural isoflavone belong to the family of polyphenolic compounds. In this study; we aimed to develop and validate of HPLC method for analysis of DZ and determine the level of DZ administered orally/intraarticular (i.a) in the experimental knee OA (KOA) model in rat serum.
METHOD: Chromatographic separation of HPLC method for DZ was achieved on the reverse phase C18 column (250x4.6mm, 5µm) by using mobile phase containing acetonitrile 0.5% acetic acid and water (40:60 v/v) at 249 nm wavelength. DZ from rat serum was extracted with acetonitrile and the validation of the method were performed. Administration of DZ/hyaluronic acid (HA)/DZ + HA were conducted 50 µL i.a per day for 1st, 7th, 14th and 21st days or 0.5 mL orally and twice daily for 21 days on wistar albino male rats (12-16 weeks and 250-300 grams) (Group1: DZ (orally; 20mg/kg/mL), Group2: HA (i.a.;0.5mg/50µL) + DZ (orally; 20mg/kg/mL), Group3:DZ (i.a.;0.6mg/50µL), Group4: HA (i.a.;0.5mg/50µL) + DZ(i.a.; 0.6mg/50 µL)). At the end of the experiment, rats were sacrificed under general anesthesia. Blood samples were collected, centrifuged and serum were separated and analyzed.
RESULTS: DZ extracted from serum was linear in the concentration range of 10-2500ng/mL. The analysis with quality control samples (50, 250, 1000ng/mL) showed that the accuracy values (RSD%) were less than 4.7% and it was detected from the serum that the mean extraction recovery was 97.5±6.61%. The DZ level was determined in all groups by the developed and validated HPLC method and the highest DZ concentration was found in the first group (163.53±18.03 ng/mL), followed by the 2nd, 3rd and 4th groups.
CONCLUSION: In this study; HPLC method for the determination of DZ in rat serum was found to be sensitive, accurate and rapid method and information related to pharmacological properties of DZ in KOA was obtained.
Ataturk University Scientific Research Project No: TCD-2018-6146.

Keywords: Knee Osteoarthritis, Daidzein, HPLC

PC025

Investigation of the Effects of Shiga-Toxin on Some Rat Blood Enzymes

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AIM: Shiga toxin (Stx) found in Shigella dysenteriae 1 and in some serogroups of Escherichia coli is one of the most powerful bacterial toxins known. The aim of this study was to investigate the changes in alanine aminotransferase (ALT), (aspartate aminotransferase (AST), and alkaline phosphatase (ALP) liver enzyme levels in rats exposed to shiga-toxin in a routine routine (quercetin-3-O-routineozide).

METHODS: In this study, 32 adult male Sprague Dawley rats weighing 250-300 g were used. Four rats (Control, Shiga-Toxin (Stx; 100 ng / kg), R50 + Stx (50 mg / kg Routine + 100 ng / kg Stx) and R100 + Stx (100 mg / kg Routine + 100 ng / kg Stx) was formed. The activity values of ALT, AST and ALP enzymes in four different experimental groups were determined using the kit. Statistical analysis was performed using ANOVA test SPSS 21.0.

RESULTS: It was determined that ALP level decreased in Stx group and this decrease was significant compared to R100 + Stx group ($p < 0.05$). AST levels were the lowest in the R50 + Stx group but were not statistically significant. A significant decrease in ALT level was observed in R100 + Stx group.

CONCLUSION: As a result, it was determined that there was a significant difference between the activity values of ALT, AST and ALP enzymes. All enzymes decreased in the Stx group compared with the control group. In the other two groups, they gave values between control and Stx.

Keywords: Blood Enzymes, Rat, Shiga-Toxin.

PC026

Examination of Changes in Total Glutathione Levels in Cysteine-S-Sulfate Treated HT-22 Hippocampus Cell Line

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AIM: Sulfite is a toxic molecule formed as a result of sulfur metabolism. In cases of sulfide oxidase enzyme deficiency, the sulfide molecule cannot be degraded to sulfate. In these patients, Cystein-S-Sulfate (SSC) is measured at high levels in plasma and urine. SSC is structurally similar to the glutamate molecule and has likewise been shown in studies with excitotoxic effects. It is thought to be responsible for toxic effects attributed to sulfite. The purpose of this study was to evaluate the antioxidant response of the HT-22 cell line to SSC.

METHODS: The HT-22 cell line was cultured in a CO2 incubator at 37 ° C with DMEM containing 10% FBS, 1% L-glutamine, 100 IU / ml penicillin / 10mg / ml streptomycin and high glucose. Cells were grown in 6 wells and differentiated with Neurobasal medium for 24 hours. Control (K) Cysteine-S-Sulphate (SSC), Memantine (M), LY341495 (LY), SSC + M, SSC + LY, SSC + M + LY, LY + M groups were formed with these cells. After 24 hours of drug exposure, cells were removed and total glutathione and cytotoxicity was measured by commercial kits.

RESULTS: Cytotoxicity responses to increasing doses of SSC were measured and probit analysis was performed to determine the LD dose to be 125µM. There was a statistically significant increase in total glutathione levels in all groups except LY341495 compared to the control group.

CONCLUSION: Based on these data, it was evaluated that the cytotoxic effects of SSC may have caused increased oxidative stress and HT-22 cells may have responded to this stress with elevated total glutathione levels.

Keywords: Cysteine-s-sulfate, glutathione, HT-22 Cell line

PC027

The Effect of Deinoxanthine on the Susceptibility of Breast Cancer Cells to Tamoxifen

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AIM: Deinoxanthine is unique carotenoid with a pro-apoptotic effect isolated from the radioresistant bacterium Deinococcus radiodurans. Drug resistance develops over time against tamoxifen used in the treatment of breast cancer. In this study, how does deinoxanthine affect the efficiency of tamoxifen in breast cancer cells and how do the activities of carbonic anhydrase (CA), and some antioxidant enzymes change during this treatment were studied.

METHODS: Human breast cancer MCF-7 cells were grown. Deinoxanthine (400-6.25 µg/ml), tamoxifen (20-0.3125 µM) and deinoxanthine+tamoxifen combinations were applied to the cells and incubated for 12 and 24 h. The Combination Index (CI50) calculated by the CompuSyn program was used to evaluate synergistic effect. Activities of CA, and some antioxidant enzymes including catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), and superoxide dismutase (SOD) were also measured. One-way ANOVA with post-hoc LSD test was used to compare the group means. $P<0.05$ was accepted statistically significant.

RESULTS: A synergistic effect was observed after 24 hours incubation at 200 µg/ml deinoxanthine + 10 µM tamoxifen combination. CA activity was not affected by deinoxanthine. Tamoxifen decreased CA activity slightly. However, combination of deinoxanthine and tamoxifen increased CA activity. CAT activity was not affected by deinoxanthine. Tamoxifen increased CAT activity slightly. Anyhow, combination of deinoxanthine and tamoxifen increased CAT activity remarkably. Activities of GPx, GR and SOD were not affected by deinoxanthine. Tamoxifen decreased the activities of all these enzymes. However, combination of deinoxanthine and tamoxifen increased the activities of GPx, GR and SOD.

CONCLUSION: Deinoxanthine, which has a proapoptotic effect, increased the efficacy of tamoxifen in breast cancer cells. CA increases the acidity, while upregulation of the antioxidant enzymes may be a response to a possible increased oxidative stress in drug treated cells. Further studies are needed to elucidate the synergistic action mechanism(s) of this combination in cells.

Keywords: Antioxidant enzymes, breast cancer, carbonic anhydrase, deinoxanthine, synergism, tamoxifen

C028

In Vitro Cytotoxic and Genotoxic Properties of Hexa Substituted New Organophosphazene Compounds

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AIM: The aim of this study was to determine the in vitro cytotoxic effects of new obtained hexa-substituted organophosphazene compounds against A2780, PC-3 and LNCaP cell lines.

METHODS: Hexane-substituted organophosphazene compounds (HSP-1a and HSP-1b) were obtained from the interaction of 3- (3,5-difluorophenyl)-1-(4-hydroxyphenyl)-prop-2-en-1-one (1a) and 3-(4-chloro-2-fluorophenyl)-1-(4-hydroxyphenyl)-prop-2-en-1-on (1b) [1] with Hekzachlorocyclotriphosphazene (HCSP), respectively. Cell viability of the obtained HSP-1a and HSP-1b compounds against A2780, PC-3 and LNCaP cell lines at concentrations of (1, 5, 25, 50 and 100 µM) were determined by MTT assay. LogIC50 concentration was calculated using the Graphpad-6 program. DNA damage studies were performed by comet assay due to the highest dose effect of the compounds. TI, TL and taTM parameters were determined by the compounds on the cancer cells at a dose of 100 µM and the presence and rate of DNA damage were determined.

RESULTS: According to the results obtained, HSP-1a and HSP-1b compounds were found to cause significant reductions in cell viability especially at the highest concentrations ($p<0.05$). LogIC50 values for HSP-1a compound were calculated as 1.526 µM in A2780 cell lines, 1.978 µM in LNCaP cell lines and 1.665 µM in PC-3 cell lines. LogIC50 values for HSP-1b compound were calculated as 1.182 µM in A2780 cell lines, 1.174 µM in LNCaP cell lines and 1.835 µM in PC-3 cell lines. As a result of the comet experiments, it was determined that the substances added to the culture medium were partially effective on the TI, TL and TM values of the cells, but this effect did not produce a statistically significant difference ($p>0.05$).
CONCLUSION: The fact that the substances added to the culture medium for 24 hours causes significant reductions in cell viability while not damaging the DNA reveals that the cell death mechanism is independent of DNA.
This study was supported by TUBITAK (Project no:116Z758).

Keywords: Organophosphazene, A2780, LNCaP, PC-3, MTT Assay, Comet Assay

PC029

Cytotoxic Properties of Amino Acid Substituted Novel Cinnamic Acid Compounds

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AIM: The aim of this study was to determine the cytotoxic effects of newly synthesized amino acid substituted cinnamic acid compounds against three different cancer cell lines.

METHODS: The cinnamic acid derivative was obtained by the condensation reaction of aromatic aldehyde 1-naphthaldehyde with malonic acid in the presence of pyridine and piperidine according to the Doebner-Knoevenagel modification [1]. The carboxylic acid part of the resulting cinnamic acid was activated with benzotriazole 1-Napth-CA-Bt [2] to interact with the free amino acids in the final step to give the target compounds 1-Napth-CA-Gly-OH and 1-Napth-CA-Ala-OH. % cell viability against human breast (MCF-7), ovarian (A2780) and prostate cancer (PC-3) cell lines at 1, 5, 25, 50 and 100 µM doses of these compounds (1-Napth-CA-Bt, 1-Napth-CA-Gly-OH and 1-Napth-CA-Ala-OH) were investigated by MTT assay method. The effective dose (LogIC50/IC50) which reduced cell viability by 50% was calculated using the Graphpad-6 program.
RESULTS: Results showed that 1-Napth-CA-Bt, 1-Napth-CA-Gly-OH ve 1-Napth-CA-Ala-OH compounds caused significant reductions in cell viability, especially at high doses ($p <0.05$).
CONCLUSION: The determination of the cytotoxic effect of the compounds on cell lines will give a different perspective to the researches in this field.
This study was supported by Bingol University Scientific Research Projects Unit (Project no: BAP-FEF.2018.00.003).

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[1] Doebner O. European Journal of Inorganic Chemistry, 1900, 33(2), 2140-2142.
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Keywords: Amino acid, Cinnamic acid, A2780, MTT Assay, PC-3

PC030

Cytotoxic Effect of Capsanthin, a Carotenoid, on Human Prostate Cancer Cell Lines

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AIM: The importance of plant secondary metabolites for human health is increasing day by day. Studies have shown that these compounds have many physiological and pharmacological effects. Also derived from these compounds may be used as a new drug molecules. carotenoids, one of the plant secondary methanolites, have been shown to exhibit significant antioxidant effects and have therapeutic effects in some types of cancer. In this study, we aimed to determine the cytotoxic effect of capsanthin, which is a carotenoid that gives its color to red pepper, in human prostate cancer cell lines.

METHODS: In the study, different concentrations of capsanthin compound were treated with human prostate cancer cell lines (PC-3 and LNCaP) for 24 hours. The effects of the compound on cell viability were determined by MTT (3- (4,5-Dimethylthiazol-2-yl) -2,5-diphenyltetrazolium bromide) test. Changes in cell viability after administration were expressed as %. Statistical analyzes were performed using GraphPad Prism 5 package program. Homogeneity of the variances was evaluated by Bartlett tests test. All values are expressed as mean ± Sd. Continuous data between groups were compared by one-way ANOVA. ANOVA tests were followed by Tukey's test. Differences with a value of $P < 0.05$ were considered statistically significant.

RESULTS: It was found that capsanthin applied to PC-3 cells decreased cell viability significantly from 5 µM ($p < 0.05$). In LNCaP cells, the compound showed cytotoxic effect starting from 250 µM ($p < 0.05$).

CONCLUSION: The results of the study showed that capsanthin exhibits significant cytotoxicity, especially at high concentrations in PC-3 and LNCaP cancer cell lines.

Keywords: Carotenoid, Capsanthin, Prostate cancer, LNCaP, PC-3, Cytotoxicity

PC031

The Effect of D-Limonene-Rich Citrus Grandis Essential Oil on Proliferation of Colon Cancer Cell Line HCT116

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AIM: Essential oils are substances obtained from certain parts of the plant, which have the characteristic odor and which contain 90% natural terpene components. These natural components found in the essential oils of citrus fruits and other plants have antitumor activity and have potential uses in the treatment of many diseases including cancer. Citrus grandis essential oil, which is known to be d-limonene as its main component, was formulated as an emulsion and investigated for its effects on the viability of HCT 116 colon cancer cells.

METHODS: HCT116 colon cancer cell line was cultured in DMEM supplemented with 10% FBS, 1% penicillin / streptomycin. The cells were incubated at 37 °C under 5% CO_2 in incubator. The cells were cultured in 24 well plates with $4X10^4$ cells in each well. Citrus grandis essential oil was emulsified with ethanol and DMEM at different concentration (0,1%,0,2%,0,3%,0,4%,0,5%) were added in the media and investigated for the cell dynamics. The same concentration of ethanol as the experimental groups was added to the control wells to eliminate the independent effect of ethanol on the cells. The indicated concentrations of Citrus grandis essential oil were incubated with cancer cells for 24 hours and 48 hours. At the end of the period, the collected cells were counted under the microscope with Neubauer slide with Trypan blue.

RESULTS: After 24 hours of incubation, 0,4% and 0,5% concentrations of Citrus grandis essential oil at the end of 48 hours incubation, the number of live cells at all concentrations decreased significantly compared with the control group with ethanol ($p<0.05$). Citrus grandis essential oil was indicated an antiproliferative effect on colon cancer cells with a dose depending manner.

CONCLUSION: Our in vitro findings suggest that citrus grandis essential oil, rich in monoterpenes, has an antiproliferative potential in colon cancer cells.

Keywords: Essential oil, HCT116, colon cancer, d-limonene, cell culture

PC032

Cytotoxic Properties of Peptide Substituted Novel Cyclotriphosphazene Compound

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AIM: The aim of this study was to determine the cytotoxic effects of newly synthesized peptide substituted cyclotriphosphazene compound against three different cancer cell lines.

METHOD: Dipeptide (Boc-Tyr-Ala-OCH3) was obtained from the interaction of carboxyl group protected alanine and amino group protected tyrosine amino acid [1]. The novel peptide-substituted cyclotriphosphazene compound (BPP-O-Boc-Tyr-Ala-OCH3) was obtained from the reaction of dipeptide (Boc-Tyr-Ala-OCH3) with 2,2-dichloro-4,4,6,6-bis[spiro(2',2''-dioxy-1',1''-biphenylyl)] cyclotriphosphazene (BPP) [2,3]. % cell viability against human breast (MCF-7), ovarian (A2780) and prostate cancer (PC-3) cell lines at 1, 5, 25, 50 and 100 μM doses of these compounds (Boc-Tyr-Ala-OCH3 and BPP-O-Boc-Tyr-Ala-OCH3) were investigated by MTT assay method. The effective dose (LogIC50/IC50) which reduced cell viability by 50% was calculated using the Graphpad-6 program.

RESULTS: Results showed that Boc-Tyr-Ala-OCH3 and BPP-O-Boc-Tyr-Ala-OCH3 compounds caused significant reductions in cell viability, especially at high doses ($p < 0.05$).

CONCLUSION: The determination of the cytotoxic effect of the compounds on cell lines will give a different perspective to the researches in this field. However, the mechanisms by which it performs this cytotoxic effect are not known. Additional and comprehensive studies to clarify the mechanism are thought to provide a different perspective for obtaining new pharmacological agents.

This study was supported by TUBITAK (Project no: 118Z286).

Keywords: Dipeptide, Cyclotriphosphazene, A2780, MTT Assay, PC-3

PC033

The Antiproliferative Effects of Cisplatin and CoS Nanoparticles on Neuroblastoma Cell

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AIM: The neuroblastoma cell line is one of the most common childhood tumors seen in the adrenal medulla and sympathetic ganglia. It is known that neuroblastoma cell proliferation, which is a solid tumor feature, is inhibited by cisplatin, an antineoplastic drug from platinum compounds. Cobalt sulfide nanoparticules, which can act as a photocatalyst thanks to its band gap and adsorption properties, have potential uses in solar selective coatings, IR detectors and photoelectrochemical storage devices as a storage electrode.
The aim of the study is to assess the antiproliferative effect of known cisplatin, and CoS nanoparticles (NPs) synthesized by green synthesis using Punica granatum plant extract on the cell viability of the neuroblastoma cancer line.

METHODS: In this direction, the SH-SY5Y cell line was grown in the appropriate cell culture medium. Doses of Cisplatin (5 μg/mL), CoS NPs (10, 25, 50, 75, 100 μg/mL), Cisplatin + CoS NPs (5 + 10 μg/mL, 5 μg/mL + 25 μg/mL, 5 μg/mL + 50 μg/mL, 5 μg/mL + 75 μg/mL, 5 μg/mL + 100 μg/mL) was applied on SH-SY5Y cancer cell lines for 24 hours. MTT cell viability test, total oxidant and total antioxidant tests were performed 24 hours after the application.

RESULTS: As a result of MTT test, combinations of isplatin and CoS NP decreased neuroblastoma cell proliferation between 49-69% compared to control. The most effective combination groups were Cisplatin + CoS 5 μg / mL + 25 μg / mL, 5 μg / mL + 100 μg / mL.

CONCLUSION: CoS NPs have been shown to increase the potential effects of these agents in combination with chemotherapeutic agents in cancer treatment. This increase in antiproliferative efficacy is thought to be important data to shed light on new treatment approaches.

Keywords: CoS NPs, SY-SH5Y, Cancer Cell Lines, Green synthesis, Neuroblastoma (NBL)

PC034

The Effect of CdS Nanoparticles on Neuroblastoma Cell Viability

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AIM: The therapeutic applications of nanoparticles (NPs) are rapidly increasing their use in medicine, especially in cancer therapy. CdS nanoparticles belong to chalcogenides group and due to their high catalytic and optical properties, they can be used effectively in the diagnosis and treatment of cancer. Neuroblastoma (NBL) is the most common solid tumor in children and may be rapidly fatal due to its biological type. In our study, cadmium sulfide nanoparticles (CdS NPs) were synthesized by green synthesis method using Na2S containing plant extract as reducing agent. We also investigated the antiproliferative effect of CdS NPs on the SH-SY5Y cell line.

METHODS: CdS NPs were obtained by the green synthesis method using plant extract and Na2S. The characterization of CdS NPs was performed using the Fourier transform infrared spectroscopy (FTIR), Scanning electron microscope (SEM), and X-ray powder diffraction (XRD) methods. The SH-SY5Y cell line was grown in normal cell culture medium. Different dose of CdS NPs (10, 25, 50, 75 and 100 µg/mL) was applied on SH-SY5Y cancer cell lines for 24 hours. The viability, antioxidant and antioxidant level were determined by using MTT kit, TAC and TOS test.

RESULTS: As a result of the MTT test, it was found that 100 µg/mL CdS NP decreased cell proliferation compared to control ($p<0.05$).

CONCLUSION: The prepared CdS NPs demonstrated the potential benefit for their selective toxicity to cancer cells both as antioxidant prophylactic and chemotherapeutic agent in cancer treatment.

Keywords: CdS NPs, SY-SH5Y, Cancer Cell Lines, Green synthesis, Neuroblastoma (NBL)

PC035

Green Synthesis of CeS Nanoparticles Using Plant Extract and Their Effects on Neuroblastoma Cells

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AIM: Neuroblastoma (SH-SY5Y) is a type of cancer showing aggressive and resistant features. Nearly 40% of patients with SH-SY5Y did not respond to chemotherapeutic drugs. Furthermore, the long-term use of the drug leads to the development of resistance. Cerium sulphur nanoparticles (CeS-NPs) are new compounds currently being pursued in pre-clinical trials for their potential use in the treatment of cancer. The aim of the current study is to evaluate of CeS-NPs and Cisplatin combination antitumor effects on SH-SY5Y. We try to answer this question, do CeS-NPs increase Cisplatin antitumor effect on the neuroblastoma cancer cells or not?

METHOD: CeS-NPs were obtained by green synthesis using plant extract and Na2S.The SH-SY5Y cell line was grown in the culture medium. Combination of Cisplatin (5 µg/mL) + CeS-NPs (10, 25, 50, 75 and 100 µg/mL) were applied on SH-SY5Y cancer cell culture for 24 hours. For evaluation of cell viability, antioxidant and oxidant status, 3-(4,5-Dimethylthiazol-2-Yl)-2,5-Diphenyltetrazolium bromide (MTT), Total Antioxidant Capacity (TAC) and Total Oxidant Status (TOS) tests were done 24 hours after drug administration.

RESULTS: According to our results, it was found that the combination of 5 µg / ml cisplatin and 100 µg / ml CeS-NP decreased the cell viability compared to the negative control group (DMEM added group only) and the positive control group (cisplatin + DMEM). It was also observed that total oxidant level increased and total antioxidant level decreased ($P<0.05$).

CONCLUSION: Our studies have shown that CeS-NPs increase the anti-tumor effect of cisplatin. Based on these findings, we anticipate that the use of CeS-NPs will become widespread in the future in order to reduce the use of chemotherapeutics, commonly used in the treatment of cancer such as cisplatin, and to eliminate their side effects.

Keywords: Neuroblastoma (NBL), CeS-NPs, Cisplatin, SY-SH5Y, Cancer Cell Lines, TAC; TOS

PC036

Neuroprotective Effects of Umbelliferone on Glutamate Excitotoxicity: Cell Culture Study

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AIM: Glutamate is the main excitatory neurotransmitter of the central nervous system and causes excitotoxicity in excessive release to the extracellular matrix. Umbelliferone is a kind of coumarin derivative compound found in many plants and has antioxidant, anti-inflammatory and neuroprotective effects. A natural antioxidant umbelliferon can also cross the blood brain barrier and protect neuronal cells from death. The aim of this study was to evaluate neuroprotective effect of umbelliferone in primary cortical neuron cultures exposed to glutamate excitotoxicity.
METHODS: This study was approved by Ataturk University Local Animal Experiments Ethics Committee (93722986-000-E.1900094667). Primary cortical neurons were prepared from cerebral cortex of newborn Sprague Dawley rats (n=20). Cells were exposed to 6x10-5 M glutamate to induce glutamate excitotoxicity and then incubated for 24 and 72 hours after applying different concentrations (10 µM-1mM) of umbelliferone. Cell viability was determined by using MTT method. Reactive oxygen species in the cells were evaluated by Total Oxidant Status (TOS) and Total antioxidant status (TAS) commercial kits.

RESULTS: According to MTT analysis results, 25-250 µM umbelliferone had a significant protective effect against glutamate excitotoxicity at 72 hours ($p < 0.05$).According to TAS and TOS analysis, results showed that antioxidant level in cells was increased at low concentrations of umbelliferone.
CONCLUSION: It was concluded that umbelliferone has a protective effect against glutamate excitotoxicity in primary cortical neuron cells and can be used as a therapeutic agent against glutamate excitotoxicity.

Keywords: Glutamate, Umbelliferone, Primary Neuronal Culture

PC037

Roles of Calcium Channel Blockers in Cancer Physiology

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AIM: Neuroblastoma is a type of childhood cancer and mostly are seen in the sympathetic nervous system. Recently it was reported that many patients who suffer the neuroblastoma cancer show high "adrenocorticotropic hormone" ACTH serum levels. ACTH is a significant hormone derived from the pituitary gland. Amlodipine is Ca channel blocker. Recent studies suggest that Ca ++ channels in neuroblastoma membrane play an important role in migration. In this study, we aimed to assess whether amlodipine reduces the spread of ACTH-dependent neuroblastoma.

METHODS: Neuroblastoma cultures were obtained from the department of medical pharmacology department of Ataturk University (Erzurum, Turkey). The cells were seeded in 24 well plates by fresh medium (antibiotic 1%, FBS 15%, and DMEM) and an incubate in 5% CO2 and 37°C). Amlodipine (10 mM), ACTH (25, 50 and 75 µg) and combinations of both were added to the well plate and incubate for 24 hours. After 24 hours 3- (4,5-dimethylthiazol-2-yl) -2,5-diphenyl tetrazolium bromide (MTT) test, Total Antioxidant Capacity (TAC), Total Oxidant Status (TOS) and Annexin-V-FITC apoptosis tests were performed. Data were analyzed with SPE 22.0 program by ONE WAY ANOVA method.

RESULTS: When data were analyzed, cell death was more than only ACTH application when amlodipine alone was administered. However, doses of amlodipine and ACTH co-administered neuroblastoma deaths were much higher ($P<0.05$) than a control group. These and similar studies are promising in the treatment of cancer.

CONCLUSION: Panner and counterparts' studies showed intracellular $Ca^{+2'}$ is significant in controlling proliferation as provide by swinging, of intracellular $Ca^{+2'}$ that happen in a cell cycle-dependent behavior in many carcinoma cells. In our study, we stop the development of neuroblastoma by preventing Ca regulation.

Keywords: Calcium Channel Blokers, Neuroblastoma, ACTH

PC038

Antitumor Effect of Combination Momordica and Melatonin on Prostate Cancer Pc-3 Cell Line

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AIM: Prostate cancer (PC) is the second most common malignant tumor that begins in the outer part of the prostate. It is mostly seen in older men. Recently, many efforts have been made to search for low cytotoxic agents that may reduce the spread of malignant tumors. Accordingly, Momordica extracts and monomer components have shown strong anticancer activity against various tumors. Also, Melatonin (MLT) has been shown to help apoptosis in many studies due to its antioxidant properties and thus suppress tumor formation. In this study, we aimed to investigate the antitumor effect of MLT and Momordica charantia (MC) combination therapy on PC-3 cell line for the first time.

METHODS: The PC-3 cell line was grown in culture medium. The different dose of cisplatin (2 µg / ml), MC and MLT and their combination were applied for 72 hours. 3-(4,5-Dimethylthiazol-2-Yl)-2,5-Diphenyltetrazolium Bromide (MTT) cell viability, Total Antioxidant Capacity (TAC), Total Oxidant Status (TOS) and Migration (Wound Healing) tests were done 72 hours after drug administration.

RESULTS: As a result of the tests, MC (100 µg/ml) and MLT (40 µg/ml) + MC (100 µg/ml) reduced cell proliferation compared to both control group and cisplatin ($P<0.05$). CONCLUSION: According to our result, MLT increased MC effect and reduced viability of cancer cells more effective than MC alone.

Keywords: Momordica, PC-3, Melatonin, Total Antioxidant Capacity (TAC), Total Oxidant Status (TOS)

PC039

Does Picnogenol and Melatonin Combination Decrease Tumor Cells Viability in Comparison to Platin Base Anti-Cancer Drug?

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AIM: Pycnogenol (PYG) is known for its antioxidant, anti-inflammatory and antitumor promotional properties. Melatonin (MLT) has effects on regulation of a variety of physiological and pathological processes, including antioxidation, anti-aging, anti-inflammation, anti-angiogenesis, stimulation of cell differentiation, and activation of the immune system. The aim of the current study is the evaluation of Melatonin (MLT) and Pycnogenol (PYC) combination on HT-29 cancer line and to answer the question if MLT increase PYC antitumor effect on the HT-29 or not.

METHODS: For this purpose, we designed the present study in 13 different groups. After growing the HT-29 cell line in culture medium, cisplatin (2 µg / ml), a chemoteropic agent commonly used in the treatment of various cancers (2 µg/ml), MLT (40 µg/ml), different dose of PYC (10, 20, 40, 60, 80 and 100 µg/ml) and, combination of PYC (10, 40, 80 and 100 µg/ml) + MLT (40 µg/ml) were applied on HT-29 cell line for 72 hours. 3- (4,5-Dimethylthiazol -2-Yl) -2,5-Diphenyltetrazolium Bromide (MTT) cell viability, Total Antioxidant Capacity (TAC), Total Oxidant Status (TOS) and Migration (Wound Healing test) tests were done 72 hours after drug administration.

RESULTS: Combination group of MLT+ PYG 100µg/ml are induced cell damage and morphological changes more effective than Cisplatin and the other groups in cell line. It was also observed that total oxidant level increased and total antioxidant level decreased. MLT PYC (100 µg / ml) group was statistically significant when compared with the control group and other groups ($P<0.05$).

CONCLUSION: In conclusion, a combination of the MLT+PYG may inhibit the proliferation of HT-29 cancer cells. The combination of MLT + PYG show promise to be a new anticancer agent for treatment of HT-29 patients and adjuvant for reduction of the side effects of chemotherapeutics.

Keywords: Pycnogenol, HT-29, Melatonin, Total Antioxidant Capacity (TAC), Total Oxidant Status (TOS).

PC040

Bromelain Makes Glioblastoma Multiforme Cells Susceptible to the Temozolomide Cytotoxicity by Affecting the Activities of Carbonic Anhydrase and Some Antioxidant Enzymes

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AIM: Glioblastoma multiforme (GBM) is the most common central nervous system cancer among brain tumors. The difficulty to treat GBM successfully is the emergence of resistance to drugs. Activity of carbonic anhydrase (CA), a hypoxia marker, correlates with tumor progression in various cancers. Bromelain is a cysteine protease having anti-inflammatory, antioxidant and anticancer activities. This study was designed to determine whether bromelain could potentiate the antitumor activity of temozolomide (TMZ) in GBM cells by affecting the carbonic anhydrase and some antioxidant enzyme activities.
METHODS: Human GBM cell line T986 was used. Cells were treated with different concentrations of TMZ (50-350µM) and bromelain (5-320µg/ml) for 48 h to determine the IC50 value. Then, TMZ (200µM) and increasing concentrations of bromelain (20-160µg/ml) combinations were applied to the cells for 48 h to investigate the synergistic effects. MTT test was used for the cytotoxicity. CA enzyme activity was examined to determine acidic surroundings in the cells. Additionally, antioxidant enzymes, namely catalase (CAT), glutathione peroxidase (GPx), glutathione reductase (GR), and superoxide dismutase (SOD) activities were also measured. Bivariate (Pearson) correlation analysis and one-way ANOVA with post-hoc LSD test was used to analyze data.
RESULTS: IC50 of TMZ was found to be 196,3µM. CA and CAT activities increased, GR was not affected and GPx and SOD activities decreased in GBM cells exposed to TMZ and increasing bromelain combinations. CA and CAT activities positively correlated with bromelain concentrations in cells exposed to TMZ+bromelain, while GPx and SOD activities negatively correlated, however, there was no correlation in GR activity.
CONCLUSION: Bromelain potentiated the anti-tumor activity of TMZ in T986 cell by increasing the activities of CA, and CAT enzymes, while decreasing GPx and SOD activities. According to the results of this study, bromelain has the potential to be used in chemosensitization of GBM cells to TMZ. However, further studies are needed to clarify mechanisms of action of bromelain.
Keywords: Antioxidant enzymes, bromelain, carbonic anhydrase, Glioblastoma multiforme, temozolomide

PC041

Laminaria Japonica Decrease Toxicity Induced by DMSO on Fibroblast Cell Line: Migration and Cytotoxicity Test

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AIM: In recent years, many marine resources have attracted attention in the search for bioactive compounds to develop new drugs and healthy foods. Laminaria japonica, a member of brown algae (Phaeophyta), is a species that has been frequently used as a medicine since ancient times. Recent studies have demonstrated the antioxidant and anticoagulant effects of polysaccharides isolated from Laminaria japonica. In our study, we investigated the proliferation and migration properties of Lamaria japonica on dimethyl sulphoxide (DMSO) induced fibroblast toxicity model.

METHODS: Fibroblast cell lines were obtained from Atatürk University Medical Pharmacology Department. Aqueous extract of 40,80,160 and 320µg/mL of Laminaria japonica was tested. Toxicity model was achieved with 7%DMSO. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, a tetrazole (MTT) and migration test (picture was captured 6,12 and 24h) was done. The established 6 groups were applied to fibroblast cell culture and after 24 hours the reading was performed in at 570 nm wavelength. MTT results were analyzed by one-way ANOVA method in SPSS, IBM 21.00 program.

RESULTS: In the control group, viability was defined as 100% and the other groups were evaluated accordingly. The 7%DMSO group was the lowest with 63% viability compared with the control. The combination of 7%DMSO + 320µg/mL laminaria japonica is highest with 89% viability compared with the control group. When the combination groups were compared with the control group, it was observed that the viability rate increased depending on the dose.

CONCLUSION: In their study, Zhenfei Peng (2013 Aug) et al. examined the anti-tumor effects and cytotoxic properties of water-soluble polysaccharide (WPS) and WPS-2-1 polysaccharides isolated from laminaria japanica in A375 cell line and vascular smooth muscle cells. Their results showed that polysaccharides showed anti-tumor effects even a low dose of 0.031mg/mL. The same polysaccharides were also studied in vascular smooth muscle cells, and their proliferative effects were explored and no cytotoxic effects were observed on cells other than cancer cells.

Keywords: Laminaria japonica, cytotoxicity, migration, fibroblast, in vitro.

PC042

Aloe Barbadensis Miller Increase Migration and Activity Properties of Fibroblast Cells: Induced DMSO Toxicity Model

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AIM: Plants play an important role in health care worldwide. Recently, Aloe vera has been used for anti-cancer and anti-inflammatory properties as well as angiogenesis and wound healing. In our study, we investigated the proliferation and migration properties of Aloe vera barbadensis miller on fibroblast induced dimethyl sulphoxide (DMSO) toxicity model.

METHODS: Fibroblast cell lines were obtained from Atatürk University Medical Pharmacology Department. Aloe barbadensis miller plant extract was obtained from Nurbal, Istanbul. Extracts of 100, 150, 200 and 250µg / mL aloe barbadensis were tested. Toxicity was induced by 7%DMSO. 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide, a tetrazole (MTT) and migration test (picture was captured 6,12 and 24h) was done. The established 6 groups were applied to fibroblast cell culture and after 24 hours they were read at 570 nm wavelength. MTT results were analyzed by one-way ANOVA method in SPSS, IBM 21.00 program.

RESULTS: In our control group, viability was defined as 100% and the other groups were evaluated accordingly. The 7% DMSO group was the lowest with 68% viability compared to the control group. The combination of 7%DMSO + 250µg/mL aloe vera is highest with 92% viability compared to the control group. When the combination groups were compared with the control group, it was observed that the viability rate increased depending on the dose.

CONCLUSION: Aloe barbadensis extract showed a protective effect by preventing dose-induced toxicity due to dose-dependent anti-inflammatory and antioxidant effects. In their study, also Samira Negahdari (march, 2017) and colleagues used different doses of aloe vera (aloe barbadensis miller) on normal mouse skin fibroblast cell line (C147). They observed that aloe vera treatment group increased the migration of fibroblast cells more when compared with the control group and other plant groups. At the end of the study, they showed that aloe vera removes dead tissue and facilitates wound healing.

Keywords: Aloe Barbadensis, cytotoxicity, migration, fibroblast, in vitro

PC043

The Role of Neuronal Nitric Oxide Synthase Inhibition on the Effect of Resveratrol on Penicillin-Induced Epileptiform Activity

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AIM: Resveratrol is one of the strongest antioxidants and produced by the plants against environmental stress and diseases. 7-Nitroindazole is a selective antagonist of neuronal nitric oxide synthase (nNOS). The aim of this study was to investigate the role of nNOS inhibition on the effect of resveratrol on penicillin-induced epileptiform activity.

METHODS: In our study, totally twenty-four male Wistar albino rats were used. All rats were divided into four groups (n:6): I- Penicillin group (Control); II- Resveratrol (50 mg/kg, intraperitoneally (i.p)) group; III- 7-Nitroindazole (40 mg/kg, i.p) group; IV- Resveratrol (50 mg/kg, i.p) + 7-Nitroindazole (40 mg/kg, i.p) group. Epileptiform activity was induced by administering 500 IU of Penicillin-G into the cortex (intracortical). Drugs were administered 30 min after the injection of penicillin. Electrocorticogram (ECoG) recordings were conducted for 3 hours after 500 IU penicillin injection. The frequency and amplitude of epileptiform activity were analyzed offline. This study was approved by the Animal Experiments Local Ethics Committee (OMU HADYEK) and supported by OMU Project Office (PYO.TIP.1904.17.019). For statistical analysis, one-way variance analysis and Post Hoc Tukey tests were used.

RESULTS: Resveratrol (50 mg/kg), compared to the control group reduces significantly in spike frequency between 30-50 and 130-180 minutes ($p<0.05$). 7-Nitroindazole (40 mg/kg) decreased the spike frequency throughout the experiment ($p<0.05$). When Resveratrol + 7-Nitroindazole were given, spike frequency decreased significantly during the experiment ($p<0.05$). There was no statistically significant difference in amplitude values between groups ($p>0.05$).

CONCLUSION: Resveratrol has decreased penicillin-induced epileptiform activity. 7-Nitroindazole increased the antiepileptic activity of the resveratrol

Keywords: Resveratrol, Epilepsy, Penicillin, Rat, 7-Nitroindazole

PC044

The Role of Inducible Nitric Oxide Synthase Inhibition on the Effect of Resveratrol on Penicillin-Induced Epileptiform Activity

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AIM: Resveratrol (3,4,5-trihydroxy-stilbene) is a natural phytoalexin that exists in many different plants, especially grapes. Aminoguanidine (AG) is a compound that selectively inhibits inducible nitric oxide synthase (iNOS). The aim of this study was to investigate the role of aminoguanidine (inducible nitric oxide synthase) in the effect of antioxidant resveratrol on penicillin-induced epileptiform activity.

METHODS: Twenty-four male Wistar rats were used in our study (n: 6). Epileptiform activity was induced by administering 500 IU Penicillin-G into the cortex (intracortical) in a volume of 2.5 microliters with a Hamilton microinjector. 30 minutes after penicillin injection, Resveratrol (50 mg/kg); Aminoguanidine (100 mg/kg) and Resveratrol + Aminoguanidine were administered intraperitoneally. This study was approved by the Animal Experiments Local Ethics Committee (OMU HADYEK) and supported by OMU Project Office (PYO.TIP. 1904.17.019). One-way analysis of variance and Post Hoc Tukey tests were used for statistical analysis.

RESULTS: Resveratrol (50 mg/kg) significantly reduces spike frequency ($p<0.05$) between 30-50 and 130-180 minutes compared to the control group. Aminoguanidine (100 mg/kg) significantly increased the spike frequency between 80 to 100 minutes ($p<0.05$). When Resveratrol + Aminoguanidine were given, spike frequency decreased significantly between 30 and 50 minutes ($p<0.05$). No statistically significant difference was found between the groups in terms of amplitude values ($p>0.05$).

CONCLUSION: Resveratrol showed anticonvulsant effect on penicillin-induced epileptiform activity and blocked the proconvulsive effect of aminoguanidine. In order to elucidate the physiological mechanism of this result, it needs to be supported by biochemical and molecular studies.

Keywords: Resveratrol, Epilepsy, Penicillin, Rat, Aminoguanidine

PC045

Effect of NAN-190 and Vilazodone Interaction on Penicillin-Induced Epileptiform Activity

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AIM: Penicillin causes a structural GABAA receptor antagonist and when administered to the brain cortex, eliminates GABA inhibition resulting in acute focal epilepsy-like epileptic activity in human. Vilazodone is a new antidepressant having selective serotonin (5-HT) reuptake inhibitor and 5-HT1A receptor partial agonist. NAN-190 is a selective 5-HT1A receptor antagonist. The aim of this study was to investigate the effect of NAN-190 and vilazodone interaction on penicillin-induced epileptiform activity.

METHODS: 24 male Wistar rats were used in our study (n: 6). Epileptiform activity was induced by administering 500 IU Penicillin-G to the cortex (intracortical) in a volume of 2.5 microliters with a Hamilton microinjector. Electrocorticogram (ECoG) recordings were recorded online for three hours after 500 IU penicillin injection. The frequency and amplitude of epileptiform activity were analyzed offline. 30 minutes after penicillin injection, vilazodone (10 mg/kg); NAN-190 (5 mg/kg) and vilazodone + NAN-190 were administered intraperitoneally. This study was approved by the Animal Experiments Local Ethics Committee (OMU HADYEK) and supported by OMU Project Office (PYO.TIP.1904.17.018). One-way analysis of variance and Post Hoc Tukey tests were used for statistical analysis.

RESULTS: Compared with the control group, vilazodone (10 mg/kg) significantly reduced the spike frequency throughout the experiment ($p<0.05$). NAN-190 (5 mg/kg) significantly increased spike frequency after 70 minutes ($p<0.05$). When NAN-190 + vilazodone were applied, the spike frequency decreased significantly between 30-40 minutes ($p<0.05$). No statistically significant difference was found between the groups in terms of amplitude values ($p>0.05$).

CONCLUSION: Vilazodone showed anticonvulsant effect on penicillin-induced epileptiform activity and blocked the proconvulsive effect of NAN-190. Further studies are needed to explain the interaction mechanism between NAN-190 and vilazodone by molecular and biochemical studies.

Keywords: Vilazodone, Epilepsy, Penicillin, Rat, NAN-190

PC046

Investigation of Effects of Trans-Cinnamaldehyde in PTZ-Induced Kindling in Rats

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AIM: Trans-cinnamaldehyde (TCA) shows neuroprotective effects in neurological disorders such as Alzheimer and Parkinson's disease with potent anti-inflammatory and anti-oxidant actions. The aim of the current study is to investigate the effects and mechanism of TCA in pentylenetetrazole (PTZ) induced kindling model of epilepsy.

METHODS: Adult male Sprague-Dawley rats weighing 220-240 g (n=28) were randomly divided four groups (Control, PTZ, TCA 10 mg/kg, TCA 30 mg/kg). Kindling was induced with PTZ injections (35 mg/kg, i.p.) every other day (mean 13 times) and seizure stage was observed during 30 minutes after PTZ injections. Rats were accepted as kindled when showed stage 4 or 5 after three consecutive injections of PTZ according to the Racine's scale. To obtain electrocorticographic (ECoG) recordings, superficial bipolar electrodes were implanted to the skull in contact with the dura through the frontooccipital direction. After 7day healing period, TCA (10 and 30 mg/kg) was injected i.p. for 14 days. Twenty-four hours after the last drug administration, PTZ injection was repeated and ECoG recordings were obtained. All rats were decapitated after twenty-four hours of last PTZ injection and total brain tissues were homogenized. Brain-derived neutrophic factor (BDNF), cAMP response element binding protein (cREB), N-methyl-D-aspartate receptor 2B subtype (NMDA-2B) expression levels were calculated with western blotting.

RESULTS: TCA, at a dose of 30 mg/kg (but not 10 mg/kg), decreased the first myoclonic jerk latency, and increased seizure severity and total spike number compared to PTZ group ($p<0.05$). PTZ administration increased the expression levels of NMDA-2B, cREB and BDNF compared to control group ($p<0.05$). PTZ-induced these increases were found to be enhanced with the administration of both doses of TCA ($p<0.05$).

CONCLUSION: Subchronic TCA administration increased PTZ-induced epileptic seizures. We suggested that this increase might be mediated by increased expressions of BDNF and cREB proteins and NMDA-2B receptors.

Keywords: Cinnamaldeyhde, Pentylenetetrazol, Epilepsy, Rat

PC047

The Effect of Hemopressin on Epileptiform Activity in the Pentylenetetrazole Kindling Rat Model

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AIM: Hemopressin, α9 amino acid nanopeptide derived from α chain of hemoglobin. However, it is not clear whether hemopressin is agonist or antagonist of cannabinoid receptors (CB1) receptors. The aim of this study was examined its effect on pentylenetetrazole (PTZ) kindling model.

METHOD: 28 Male Wistar albino rats weighing (230-260 g) were used. To establish kindling model; the animals were injected a sub-convulsive (35mg/kg/ intraperitoneally (i.p)) dose of pentylenetetrazole for three days per week for maximum 29 injections. Subsequently, various doses of hemopressin (0.015 µg, 0.030 µg and 0.6 µg, intracerebroventricularly) were administered 30 minutes before PTZ (35 mg/kg /i.p) injection. An ECoG recording was started when the PTZ injected and last for 30 minutes. The epileptiform activity frequency and amplitude were analyzed.

RESULTS: The 0.015µg dose of hemopressin statistically has no significant effect on the parameters of ECoG recordings in comparing to the control group on the total spike wave discharge (SWD) numbers, spike wave count in each SWD, total SWD time, spike amplitude average values and behavioral seizure score and myoclonic jerk latency during the 30-minute recording period ($p>0.05$). The dose of 0.030 was reduced only the number of spikes in each cluster ($p<0.05$) without altering other parameters. The 0.6 µg dose of hemopressin significantly reduced the SWD number, the number of spikes in each cluster, and the total SWD time ($p<0.05$), while significant increment was observed in myoclonic jerk latency compared with the control group ($p<0.05$). However, there was no statistically significant difference in behavioral seizure score and spike amplitude mean values ($p>0.05$).

CONCLUSION: Our results revealed that the most effective dose of hemopressin is 0.6 µg; suggesting acting as a CB1 receptor agonist.

Keywords: Electrocorticography, Epilepsy, Epileptiform, Hemopressin, Pentylenetetrazole, Rat

PC048

Effect of Ginkgo biloba Extract EGb 761 on Intracellular Calcium Level and Excitability in WAG/Rij Rat Cortical Neuron Culture

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AIM: The standardized extract of Ginkgo biloba (EGb 761) is widely used in the treatment of different health problems, including dementia, both as a phytotherapeutic preparation in traditional and complementary medicine and as a drug in modern medicine. However, there are clinical and experimental studies suggesting that Ginkgo biloba extract and its other products may cause epileptic seizures. The aim of the present study is to investigate the effect of EGb 761 doses on neuronal excitability in WAG/Rij rat cortical neuron culture by using calcium-imaging technique.
METHOD: Experiments were conducted with the permission of Istanbul Medipol University Animal Experiments Local Ethics Committee dated 12/07/2017 and numbered 35. Cortical neuron culture obtained from WAG/Rij rats (P1-P4) was used in the experiments. Measurement of intracellular calcium levels was performed under the confocal microscope using Fluo-4 calcium indicator dye. Neuronal excitability was induced by 30 mM KCl. Cultured cells were exposed to concentrations of 50, 100, 200 and 400 µg/ml of EGb 761. Intracellular calcium luminescence values were expressed as relative fluorescence change (ΔF/F0) after normalizing in percent. Experimental groups were compared using Kruskal-Wallis and Mann-Whitney U tests. $p<0.05$ was considered statistically significant.
RESULTS: 100 and 200 EGb 761 caused an increase in intracellular calcium levels. Increase in doses of 100 and 200 µg/ml of EGb 761 was found to be statistically significant ($p<0,001$).
CONCLUSION: EGb 761, a standardized extract of Ginkgo biloba, was found to increase intracellular calcium levels in WAG/Rij rat cortical neuron cultures, leading to increased excitability. This increase in neuronal excitability should be considered for epileptic patients or healthy individuals who use Ginkgo biloba extract EGb 761.This study was supported by TUBITAK (Project No: 115S348)
Keywords: Ginkgo biloba, EGb 761, Absence epilepsy, WAG/Rij, neuronal excitability, Calcium imaging

PC049

The Effect of CB1 Receptor Agonist and Antagonist on the Epileptiform Activity in a Pentylenetetrazole Kindling Rat Model

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AIM: CB1 receptor play an important role in epilepsy. We examined the effect of CB1 receptor agonist (ACEA) and CB1 antagonist (AM-251) on the epileptiform activity in a pentylenetetrazole kindling rat model.

METHOD: Animals were injected sub-convulsive dose of PTZ (35mg/kg/i.p) for three days per week. The kindled rats received various doses of ACEA (1.25, 2.5, and 7.5 µg/ICV) 70 minutes before PTZ (35 mg/kg/i.p) injection, and various doses of AM-251 (0.125, 0.25, 0.50, and 1 µg/ICV) 30 minutes before PTZ (35 mg/kg/i.p) injection. An ECoG recording was started after PTZ injection. This study was approved by the Local Ethical Committee of Exprimental Animal (OMU HADYEK).

RESULTS: 7.5 µg dose of ACEA reduced the total SWCs number, spikes of each SWC, total SWCs time and behavioral seizure score, while increased myoclonic jerk latency ($p<0.05$) without altering in spike amplitude. Dose of 1.25 µg was non-effective. While 2.5 µg dose only reduced the total SWCs, spikes number and the total SWCs time ($p<0.05$) compared with the control group. The 0.5 µg dose of AM-251, decreased the total SWCs number and myoclonic jerk latency ($p<0.05$), while increased the spikes number in each SWC and total SWCs time ($p<0.05$). The 0.125 µg dose of AM-251, decreased the total SWCs number ($p<0.05$) only. The 0.25 µg dose of AM-251, decreased the total SWCs number and spikes for each SWC ($p<0.05$) only. The 1 µg dose of AM-251 was non-effective compared with the control group.

CONCLUSION: The most effective dose of ACEA is 7.5 µg acting as CB1 receptor agonist. While the 0.5 µg dose of AM-251 which revealed to act as a CB1 receptor antagonist induced no changes on the investigated parameters. However, low dose of AM-251 showed agonist effects on total SWC and spikes for each SWC parameters.

This study was supported by TUBITAK (project number 215S808).

Keywords: Electrocorticography, Epilepsy, ACEA, AM-251, pentylenetetrazole, Rat

PC050

The Effect of Isoflurane and Ketamine/Xylazine on Epileptiform Activity in Genetic Absence Epilepsy (Wag\Rij) Rats Model

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AIM: The aim of this study was to establish a simple and safe method of anesthesia in animals that used in experimental studies. So, we examined the effect of Isofluorane and ketaminee/xylazin on epileptiform activity in genetic abscence epilepsy (Wag\Rij) rats.

METHODS: In this study, 14 male of Albino Wag/Rij rats weighing 170-190 g are used. ECoG activities were recorded as control during the first two hours for isofluorane group (n=7) and ketaminee /xylazin group, then isofluorane (3-4% induction, 1-2% maintenance) and ketamine (60mg/0.13ml/kg/i.p) /xylazin (80mg/0.10ml/kg/i.p) were administered and ECoG recorded for another 2 hours. The frequency and amplitude of epileptiform activity were analyzed off-line and statistically analyzed by Graphpad Instat 3 (paired t test, one-tail p value). This study was approved by the local Ethical Committee (OMU HADYEK, 2018/51).

RESULTS: Isofluorane significantly decreased the total SWDs and total spikes ($p<0,001$), while the mean duration of the spikes and the time scale for first 20 minutes not affected ($p>0.05$). Isofluorane also abolished the total SWDs activity after 20 minutes till the end of the experiment. The combination injection of Ketamine and Xylazin significantly decreased the total SWD, total spikes, mean duration of the spikes and the time scale for first 20 minutes ($p<0.05$).

CONCLUSION: Our data revealed that both isoflurane and ketamine/xylazin significantly decreased the SWDs, so it should be used cautiously especially while using these anesthetics in studying experimental epilepsy investigations.

Keywords: Epilepsy, Wag\Rij, isoflurane, Ketamine, Xylazine, Rat

PC051

The Effect of Chloral Hydrate and Urethane on Epileptiform Activity in Wag\Rij Rats

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AIM: Despite the common use of chloral hydrate and urethane in expermintal studys so far there is no study showing the effect of Chloral Hydrate and Urethane on epileptiform activity of genetic absence epilepsy Wag\Rij rats model. In this study we examined the effect of these two anesthetics on epileptiform activity.

METHODS: In this study, 14 male of Albino Wag/Rij rats weighing (170-190 g) are used. ECoG activities were recorded as control during the first two hours for chloral hydrate group (n=7), and urethane group. Then chloral hydrate (175mg/Kg/intraperitoneally (i.p) for the first group) and urethane (1.25g/1ml/i.p for the second group) administered and ECoG recorded for another 2 hours. The frequency and amplitude of epileptiform activity were analyzed off-line and statistically analyzed by Graphpad Instat 3 (paired t test, one-tail p value). This study was approved by the local Ethical Committee (OMU HADYEK, 2018/51).

RESULTS: After administration of the chloral hydrate, total spike wave discharge (SWD), total spikes and mean duration of the spikes significantly decreased ($p<0.05$), chloral hydrate abolished the SWD within 10 minutes of administration. Urethane administration caused inhibition of all SWDs, so we were not able to calculate SWDs parameters.

CONCLUSION: Our results revealed that after the injection of chloral hydrate; the epileptiform activity reduced dramatically, while urethane totally inhibited SWDs activity. Therefore, chloral hydrate is a better anesthetic for the experimental epilepsy models compared to urethane.

Keywords: Epilepsy, Wag\Rij, chloral hydrate, urethane, electrocorticography, Rat

PC052

Protective Effect of Cup Therapy Model in Rats on Epileptic Seizures by Determination of Different Anatomic Region

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AIM: Epilepsy is caused by multifactorial factors and is a progressive disease characterized by recurrent seizures. Cupping is known to have a therapeutic effect on aretaeus uterus, cholera, ileus prolapsus and epilepsy in the 2nd century AD. Although there have been human studies of cupping, scientific evidence-based research on animal models of epilepsy has not been developed. We aimed to investigate the protective effect of cupping on seizures in modeling of rats by different anatomical regions. The study received ethical approval with number of 2019/27 by BAIBU HAYEK.

METHODS: A total of 42 Wistar Albino rats were used. Groups; Group 1 (G1): Servical 7(C7) + paralumbal + vacuum Group 2 (G2): C7+ paralumbal + incision, Group 3 (G3): Epilepsy, Group 4 (G4): Diazepam, Group 5 (G5): paralumbal + vacuum, Group 6 (G6): paralumbal + incision. Ketamine / xylazine and 90/10 mg / kg were administered as anesthetics. In specially designed 1 cm cups, rats were vacuumed with scalpel at different anotomic regions for 5 minutes. After 24 hours, rats were administered subcutaneous pentylenetetrazole at a dose of 35 mg / kg and epilepsy behavior scoring was performed for 20-30 minutes. The parameters; the third stage is the first moment (min), the first generalized seizure (min) and the modified stage. Statistical analysis of the groups was evaluated by SPSS. Statistical analysis of the results was performed by One-Way ANOVA ($p<0.05$).

RESULTS: In the modified stage, G6 was found to be statistically significant compared to G3. No significant difference was observed other analyzes ($p<0.05$).

CONCLUSION: In the modified stage, G6 group suppressed seizure compared to G3. However, G2 group showed no protective effect. Consequently, the need for investigating the reasons for the protective effect of cupping on seizures by experimental rat modeling is thought to be an important step for future studies.

Keywords: Cupping, epilepsy, pentylenetetrazole (PTZ)

PC053

The Effect of Canabinoids on Epileptic Activity in WAG/Rij Rats and the Role of Purinergic P2X7 Receptors in This Effect

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AIM: Absence epilepsy is a generalized, non-convulsive epilepsy. WAG/Rij rats are genetic model of absence epilepsy. P2X7 receptors (P2X7R) are ATP sensitive cation channels. CB1 is cannabinoid receptor and has been shown to be effective in many epilepsy models, alike P2X7R. There is limited information about P2X7R and CB1 interactions. Therefore, we aimed to investigate the effect of CB1 agonist ACEA and antagonist AM-251 and their interaction with P2X7R agonist BzATP and antagonist A-438079 on epileptic activity in WAG/Rij rats.

METHODS: In this study, 6-8 months aged, 49 male WAG/Rij rats (n=7) were used. The electrodes were placed on the skulls of the animals. Baseline electrocorticography (ECoG) recordings were taken. ACEA 7.5 µg intracerebroventicular (i.c.v.) AM-251 0.5 µg i.c.v, BzATP 100 µg i.c.v.; A-438079 20 µg i.c.v. and BzATP-AM-251; A438079-AM-251; BzATP-ACEA; A-4380799-ACEA groups created. Then ECoG recordings continued. Data were evaluated using Paired-Samples T Test and One-Way ANOVA then Tukey test in SPSS 15.0. This study was carried out with permission of OMU Animal Experiments Local Ethics Committee.

RESULTS: ACEA, BzATP-ACEA, A-438079-ACEA groups were anticonvulsant ($p<0.001$) and there wasn't significant difference between each other in seizure activity ($p>0.05$). AM-251 was proconvulsant ($p<0.05$). BzATP-AM-251 group significantly reduced seizures compared to control group and AM-251 group ($p<0.01$). A-438079-AM-251 group wasn't effective compared to control group ($p>0.05$), but it significantly reduced the proconvulsant effect of AM-251 ($p<0.05$).

CONCLUSION: ACEA, was anticonvulsant on WAG/Rij rats, and P2X7R activation didn't alter this effect. AM-251 was proconvulsant. However, A-438079 altered this effect to the control level, and BzATP turned it into anticonvulsant direction. Studies have shown that A-438079 stops cell death due to CB1 activation. This suggests that cannabinoid activation depends on P2X7R activity. BzATP may have produced this effect by affecting cannabinoid release. This study was supported by OMU BAP (PYO.TIP.1905.15.002).

Keywords: Absence, epilepsy, canabinoid, P2X7, WAG/Rij

PC054

Electrophysiological and Biochemical Effects and Interaction of P2X7 Receptors and Memantine on Epileptic Activity in WAG / Rij Rats

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AIM: Absence epilepsy is a generalized, non-convulsive epilepsy. WAG/Rij rats are genetic model of absence epilepsy. P2X7 receptors (P2X7R) are ATP sensitive cation channels and have been shown to be effective in various epilepsy models. There are no studies on the effect and interaction of P2X7R and glutamate receptor NMDA on absence epilepsy. Therefore, the effect and interaction of P2X7R agonist BzATP and antagonist A-438079 and NMDA antagonist memantine were investigated in WAG/Rij rats by using the electrophysiological and biochemical analysing methods.

METHODS: In this study, 42 male, 6-8 months aged WAG/Rij rats (n=7) were used. Electrodes were placed on the skulls of the animals. Baseline electrocorticography (ECoG) recordings were taken. BzATP 100 µg i.c.v; A-438079 20 µg i.c.v.; memantine 5 mg/kg i.p. and BzATP-memantine; A-438079-memantine groups were injected. Rats were decapitated for biochemical analysis and blood samples were taken; advanced protein oxidation products, malondialdehyde, superoxide dismutase, catalase, glutathione, glutathione peroxidase and glutathione reductase were measured. Data were evaluated using Paired-Samples T Test and One-Way ANOVA then Tukey test in SPSS 15.0. This study was carried out with permission of OMU Animal Experiments Local Ethics Committee (2015/56).

RESULTS: In the present study, BzATP and A-438079 were ineffective on seizure activity in WAG/Rij rats ($p>0.05$); the effect of memantine was anticonvulsant and antioxidant ($p<0.05$). BzATP did not change the effect of memantine on spike and wave discharges (SWD) ($p>0.05$), but decreased its antioxidant effect ($p>0.05$), and A-438079 decreased the effect of memantine on SWDs ($p<0.05$).

CONCLUSION: Findings show that, P2X7R doesn't directly affect SWDs and doesn't change oxidant parameters in WAG/Rij rats, but changes memantine's anticonvulsant and antioxidant effects. This suggests that P2X7R and NMDA intersect in multiple mechanisms and locations. Further molecular and cellular studies are needed to clarify this relationship.

This study was supported by OMU BAP (PYO. TIP. 1905. 15.002).

Keywords: absence, epilepsy, NMDA, memantine, P2X7, WAG/Rij

PC055

Electrophysiological Evaluation of the Effect of Minoxidil on Penicillin-G-Induced Epilepsy in Rats

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AIM: Epilepsy is a disease that affects 1% of the world population. Epilepsy occurs when the balance between GABA and glutamate is compromised in the brain. Potassium channel openers expose the depolarized cell to a hyperpolarized state, allowing the cell to return to the resting membrane potential. Minoxidil, a vasodilating agent, is also an adenosine-3-phosphate (ATP) -dependent potassium channel opener. This study was aimed to evaluate the effect of minoxidil on epileptiform activity in an experimental epilepsy model induced by penicillin-G in rats
.
METHODS: 35 male Wistar Albino rats were used. The animals were divided into 5 groups, each containing 7 rats. The animals were anesthetized with 1.25 mg / kg urethane. Epileptic activity was induced by penicillin-G (1000 IU) injection by drilling 1.5-2 mm lateral, 1 mm in front of bregma origin and into depth of 1.5-2 mm. After 5 minutes of basal activity recordings, penicillin injection was performed. After seizures occurred, drugs were administered and 120 min ECoG recordings were taken. Data were analyzed by using ANOVA or Kruskall-Wallis analysis methods in SPSS.20 program. The study was conducted by BAIBU Animal Local Ethics Committee (HAYEK) with permission from 2018/44.

RESULTS: As a result of statistical analysis, it was found that there was a significant difference in frequency and amplitude of control, minoxidil and DMSO groups with the other groups ($p <0.05$). The difference between the Penicillin-G Epilepsy group and the Penicillin-G Epilepsy + Minoxidil groups was not statistically significant ($p> 0.05$). However, on average, minoxidil decreased frequency and amplitude in penicillin-G induced epilepsy model animals.

CONCLUSION: As a result of the 120 minute recording, it provides a decrease in the number of thorn waves and the amplitudes of the waves and therefore it is thought that minoxidil used as vasodilator may be effective on epilepsy.

Keywords: Epilepsy, Potassium Channels Openers, Minoxidil

PC056

Effects of Centrally-Injected Neuropeptide S on Epileptic Seizures, Anxiety and Learning and Memory; Role of Gender

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AIM: Neuropeptide S (NPS) is a peptide which has been shown to exert important effects on sleep-wake cycle and anxiety. It also contributes to learning, memory and epileptic seizures. In this study, we aimed to investigate the effects of intracerebroventricularly (i.c.v.)-injected NPS on epileptic seizures, anxiety, learning and memory and to find out whether these changes are gender-dependent.

METHODS: First group of rats (n=28 for each gender) were pretreated with NPS (0.1, 1, 10 nmol/5 µl; i.c.v.) or saline (5µl; i.c.v.) 30 minutes before Elevated Plus Maze (EPM), which was used to assess anxiety. Then, epileptic seizures were induced by pilocarpine (400mg/kg; i.p.) and latency to status epilepticus (SE) was recorded. Second group of rats (n=28 for each gender) were subjected to 4-day acquisition trials with the hidden platform in the Morris Water Maze (MWM) and time to find the hidden platform (escape latency) was recorded. On the 5th day probe trial was applied to assess the memory. Rats were pretreated with NPS (0.1, 1, 10 nmol/5µl; i.c.v.) or saline (5µl; i.c.v.) 30 minutes before each acquisition and the probe trial. One-way ANOVA test was used for statistical analysis.

RESULTS: NPS did not significantly affect the latency to SE. In the EPM, NPS (1nmol/5µl) significantly decreased the time spent in the closed arms and increased the time spent in the open arms, with respect to the saline group ($p<0.01$). In the MWM, escape latency in all groups decreased significantly on the 4th day compared to the 1s day ($p<0,001$ for all groups). None of the applied doses of NPS produced statistically significant differences in the MWM parameters compared with saline-treated rats. There was no gender-dependent effect of NPS in any of the tests applied
.
CONCLUSION: Centrally-injected NPS did not have any significant effects on epileptic seizures, learning and memory, but exerted a significant dose-dependent anxiolytic effect, independent from gender difference.

Keywords: Neuropeptide S, Status epilepticus, Learning, Memory, Anxiety

PC057

Effects of Nicotine Withdrawal on Sucrose Preference in Nicotine Preferring Rat Lines

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AIM: Stress response and negative affect induced by withdrawal plays important roles in development of drug addiction. Nicotine-preferring (NP) rat line is generated using selective breeding method. We aimed to reveal the regulatory effect of inherited genetic background on nicotine withdrawal-induced negative affect. We studied differences in basal and withdrawal induced-anhedonia between NP rat lines and their controls.

METHODS: This study involved 4 groups (n=12): Control Males (CM), Females (CF), NP Males (NPM), Females (NPF). Sucrose preference test was performed for seven days, followed by forced oral nicotine (50 µg/ml) administration for eight weeks. Sucrose preference was repeated during withdrawal which lasted 9 days. Data were analyzed using repeated measures ANOVA, multivariate ANOVA and post-hoc Duncan tests.

RESULTS: There was a main effect of line ($p\leq0,05$) and sex ($p\leq0,05$) on hourly sucrose consumption data at 1st, 2nd, 4th, 6th and 24th hours on the first day of withdrawal. There was a line X sex interaction. When basal and withdrawal data were compared, there was a main effect of treatment ($p=0.042$), days ($p\leq0.001$), line ($p\leq0.001$) and sex ($p\leq0.001$). There was line X sex ($p\leq0.001$) and line X treatment ($p=0.039$) interactions. CF, compared with other groups, consumed more sucrose during basal and withdrawal conditions. Declined withdrawal sucrose consumption in all groups indicated anhedonia. There was a dramatic sex difference in basal and withdrawal sucrose consumption between control groups. In NP groups, there was no sex difference in basal sucrose consumption while a sex difference has emerged during withdrawal.

CONCLUSION: The group with the least anhedonia was CF. NPF experienced more anhedonia than CF. Anhedonia was prominent especially in male groups. Sex difference decreased in NP rats with females performing similar to males. Supported by Ege University, Scientific Research Projects Commission (Research Fund Grant TYL-2018-20412), approved by Institutional Animal Ethics Committee of Ege University, Izmir, Turkey (EÜHADYEK approval number: 2019-001).

Keywords: Anhedonia, nicotine, sucrose preference

PC058

Effect of Prenatal Exposure to Radiofrequency Electromagnetic Fields on the Rat Hippocampus: A Generation Study

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AIM: The aim of our study was to investigate effects MAPK proteins on hippocampal levels in two-generation male rat brain the prenatally exposure to 2450 MHz radiofrequency-electromagnetic field (RF-EMF).

METHODS: Wistar Albino genus 12 female and 4 male rats were used this study. They were divided into a control and three exposure groups including a male and three female rats. The exposure groups were exposed by 2450 MHz RF-EMF 12h/day through experiment. Control group was not exposed. 1st groups were exposed male but not exposed female rats. 2nd group were exposed both male and female rats. 3rd group were not exposed male rat and were exposed female rats. Before 30 days from fertilization was exposed RF. At the end of 30 days all groups were fertilized. When male rats were two months old, six male rats from each group were sacrificed under general anesthesia and hippocampus was taken. Hippocampal levels of MAPKs of all male rats were measured using Western Blotting technique. Other male and female rats were used in the second generation studies using the same experimental protocols.

RESULTS: In first generation male rats; there were statistically significant difference between control and exposure groups in pERK level ($p<0.05$) but there was no statistically significant difference between control and exposure groups in ERK, p38 and p-P38 levels. In second generation male rats; p-ERK and p-P38 MAPK levels were statistically significant decreased in the second group compared to control ($p<0.05$). There were not statistically significant difference between control and exposure groups in total protein level.

CONCLUSION: Study findings confirmed that phosphorylation levels of pERK and p-P38 were significantly increased after EMF exposed in exposure groups. These findings indicated that EMF exposed rats may lead to changes in the function of MAPK pathway affecting cognitive processes such as learning and memory. ERU-SRP: Project number: TCD-2017-7275.

Keywords: RF-EMF, generation, brain, ERK/MAPK, p38/38.

PC060

A Novel Method for Measuring the Flicker Fusion Frequency: Determination of the Flicker Fusion Frequency by Arduino

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AIM: Flicker Fusion Frequency (FFF) is the lowest frequency in which flickering light appears to be permanently on and it is a tool to use for diagnosis and evaluation of some diseases such as Alzheimer's disease, hepatic encephalopathy and optic neuritis. Our objective is to develop a real-time, low-cost, and easy-to-use device and to determine FFF of young adults under different colors and light parameters.

METHODS: Forty volunteers, 20 of them were women, were included in the study. The average age was 21.4±1.8 (19-24) years. We developed an Arduino (microcontroller) controlled device. FFF values were determined for each color as cone-sensitive and rod-sensitive. The cone-sensitive procedure was conducted in room brightness (5 lux), centrally whereas the rod-sensitive procedure was conducted in dark room. Paired sample test is used to compare cone-sensitive and rod-sensitive FFF. Student's t test is used to compare genders, and finally color differences were tested by Levene's test.

RESULTS: Average FFF values were determined for each color as cone-sensitive and rod-sensitive. Values were given as period. "On" value is 11.87±0.97 milliseconds for cones, 14.13±2.39 for cones in white; 13.12±0.97 for cones, 14.33±2.65 for rods in red; 12.53±1.2 for cones, 15.30±2.52 for rods in blue; 12.17±1.17 for cones, 13.88±2.19 for rods in green. There was statistically significant difference in four color for cone-sensitive and rod-sensitive measurements ($p<0.001$). There was statistically significant difference in each color ($p<0.005$). There was a difference between white-red, white-blue, red-blue and red-green in the center and white-blue, red-blue and red-green in the periphery ($p<0.005$). There was not significant difference between genders in four colors for cone-sensitive or rod-sensitive angle.

CONCLUSION: We developed sensitive, low-cost and easy-to-use FFF device and obtained normal data of FFF for young adults. We plan to use this device in the diagnosis and follow-up of various diseases in the future.

Keywords: Flicker fusion frequency, visual system physiology, robophysiology

PC061

Assessing Empathy Like Social Behavior in Valproic Acid Induced Autism Model of Rats

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AIM: Autism Spectrum Disorders (ASD) are neurodevelopmental disorders with repetitive behaviors, social interaction and communication deficits which have genetic and environmental roots. Prenatal valproic acid (VPA) exposure increases autism risk in humans and used in experimental models. Empathy is a common problem in autism patients, and yet it is not investigated in ASD model by in utero VPA exposure. Aim of the study is to assess whether empathy can be modeled by this experimental design.

METHODS: Wistar Albino pregnant females received either 400mg/kg/ml VPA (n=3) or same volume of saline (n=2) i.p. on embryonic day 12.5. On postnatal day 20 (P20) rats were separated from mother and testing began on P22 (nVPA=26, ncontrol=23). Rats were tested for empathy on P30 and P60 in a 25x60x30cm Plexiglas box and restrainer. Restrained sibling rat was placed at the center of the box and subject rat's behavior was recorded for 10 minutes. Subject rats were not trained before test and were not given any reinforcements. Besides testing for empathy, rats were assessed for malformations and tested for olfactory discrimination, social performance, pre- pulse inhibition and locomotor activity. Statistical analysis was made on Sigma Plot version 12.5, and Student T test was used.

RESULTS: To assess empathy, attentive time of subject rat with sibling and subject's frequency of attempt to open restrainer's door were measured. VPA group spent less attentive time with sibling on P30 and P60 compared to controls ($p<0.05$; $p<0.001$). Although there were no differences between groups on P30 for frequency of attempt to open restrainer's door, VPA group scored less on P60 ($p<0.001$).

CONCLUSION: For the first time in literature assessment of empathy in autism models has been showed. Other tests' results confirm autism like symptomatic effects of prenatal VPA exposure. Our study shows VPA's effects on neurologic and social development.

Keywords: Autism, Empathy, Rat, VPA

PC062

Investigation of the Effect of Repeated Acetaminophen Usage on Hippocampus, Prefrontal Cortex and Liver IGF-1 And MMP-2 Levels in Rats

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AIM: Acetaminophen is one of the most widely used over-the-counter drug in the world for the treatment of pain and fever. It's known that acetaminophen usage impaired hippocampus related learning and memory. Insulin-like growth factor-1 (IGF-1) and matrix metalloproteinase2 (MMP2) are important for cellular survival, maintenance and tissue integrity. Aim of this study was to investigate dose dependent effects of acetaminophen on hippocampus, prefrontal cortex and liver tissues.
METHODS: Twenty-eight outbred male Sprague Dawley rats were divided into four groups: (1) Control (n=7), (2) 100-mg/kg acetaminophen group (n=7), (3) 200-mg/kg acetaminophen group (n=7), (4) 400-mg/kg acetaminophen group (n=7). Acetaminophen was administrated once-a-day, for 11 days; by oral gavage. Twenty-four hours after the last acetaminophen administration, all animals were sacrificed and liver, hippocampus and prefrontal cortex removed for analyses. Tissue IGF-1 and MMP2 levels were measured by ELISA and serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured by colorimetric method. Hippocampus and prefrontal cortex morphologies were evaluated histologically. All statistical analyzes were performed with SPSS, version 11 (SPSS, Chicago, IL). Significant differences between groups were analyzed by one-way ANOVA and post-hoc Bonferroni test.
RESULTS: Hippocampal IGF-1 and MMP2 levels were shown to decrease only after high dose -400mg/kg-acetaminophen administration accompanied by pathological changes in histology (IGF-1 levels: compared with control and 100-mg/kg group, $p<0.05$; compared with 200-mg/kg group, $p<0.006$. MMP-2 levels: compared with control and 100 mg/kg acetaminophen group, both $p<0.05$). The prefrontal cortex was not affected. Liver IGF-1 and MMP2 levels were observed to decrease in all experimental groups. Serum ALT and AST levels were found to be increased in the 200-mg/kg and 400-mg/kg acetaminophen groups ($p<0.0001$).
CONCLUSION: This study not only demonstrates the dose-dependent hepatotoxic effect of acetaminophen, but also hippocampal toxic effect of acetaminophen in high doses, accompanied by a decrease in IGF-1 and MMP-2 levels.

Keywords: acetaminophen, hippocampus, IGF-1, liver, MMP2, paracetamol

PC063

Effects of GDNF on Neurovascular Structures During Recovery Process After Cerebral Ischemia

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AIM: Stroke is the second leading cause of death and the most common cause of permanent disabilities worldwide. Glial cell-line derived neurotrophic factor (GDNF) is one of the powerful candidate therapeutics for stroke treatment. In this study, efficiency of prolonged GDNF expression achieved by lenti-viral vectors was investigated as a potential treatment strategy for stroke.

METHODS: In the study, 8-12 weeks C57BL6 mice were treated with lenti-viral-GDNF (Lv-GDNF) or lenti-viral-GFP (Lv-GFP) vectors intra-striatally. Ten days after injections, middle cerebral artery occlusion (MCAO) was performed throughout 90 minutes followed by 24 hours of reperfusion and 30 minutes followed by 72 hours or 52 days reperfusion. For analyzing acute structural and molecular effects infarct size, swelling, blood-brain-barrier (BBB) permeability, apoptosis and neuronal survival were performed. In long term, by applying grip-strength, open-field and rota-rod tests functional recovery was assessed. Also, neurogenesis and angiogenesis were examined via BrdU/NeuN and BrdU/PECAM immuno-stainings. Independent sample t test was used for between group statistics.

RESULTS: Infarct size, edema and BBB permeability were found to be apparently lower in Lv-GDNF treated animals ($p=0.003$; $p=0.001$; $p=0.045$). Number of surviving neurons were greater while number of apoptotic neurons were fewer in the ischemic hemisphere upon Lv-GDNF administration ($p=0.044$; $p=0.044$). Furthermore, newborn cell populations were demonstrated to be higher depending on GDNF ($p=0.040$). Gripping ability, motor activity and mobility of animals were significantly better in Lv-GDNF group ($p=0.026$; $p=0.047$; $p=0.045$). Also, axonal projections from contra to ipsi-lesional hemisphere at the levels of red and facial nucleus were found to be increased after GDNF treatment ($p=0.023$; $p=0.045$).

CONCLUSION: Lenti-viral mediated GDNF expression was demonstrated to decrease infarct size, edema, BBB permeability and apoptosis whereas increase cell survival, functional recovery and plasticity after MCAO. To this end, genetically modulated lenti-viral GDNF expression can be a reliable and effective way for stroke treatment.

Keywords: GDNF, Cerebral Ischemia, Lenti-virus

PC064

Protective Effects of Polyphenols on Neuronal Rotenone Toxicity and Apoptosis

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AIM: Rotenone, a widely used pesticide, is known to cause oxidative stress by affecting mitochondria and is associated with neurodegenerative diseases. Curcumin and resveratrol are natural polyphenols. The aim of this study was to determine the neuroprotective efficacy of curcumin and resveratrol in human neuroblastoma cell line (SH-SY5Y) induced by rotenone toxicity.

METHOD: Firstly, rotenone toxicity was determined in SH-SY5Y cells by using 1,5, 50, 100, 150, 200, 250, 500,1000 nM doses, and the effective dose (LD50) was found to be 200 nM. The cells were treated with Curcumin (10, 50, 100, 500, 1000 nM) and Resveratrol (1, 5, 10, 50, 100 µM) for 24 hours prior to toxicity, then Rotenone was applied for 24 hours (200nM). Cell survival was evaluated with MTS (Cell proliferation test by Methyl-tetrazolium-salt), their reproductive/colony forming ability was measured by clonogenic test. The role of caspase-mediated apoptosis and the effects of antioxidants were evaluated by elisa method (Caspase-3 Cell Death Detection). One-way ANOVA was used for statistical analysis.

RESULTS: Resveratrol was shown to increase cell viability with a dose of 1, 5, 10, 50µM and Curcumin with 10, 50, 100, 500, 1000 nM ($p<0.05$). As the dose of resveratrol used increased, the protective effect was replaced by toxicity and toxic effects were observed at 100µM dose. Resveratrol was found to be effective in increasing colony formation ability at doses of 1, 5, 10, 50, 100 µM and curcumin at 10, 50, 100, 500, 1000 nM doses ($p<0.05$). It was observed that both polyphenols were not significantly effective on caspase-3 dependent apoptosis at all doses but they caused a low decrease in active caspase-3 levels ($p>0.05$).

CONCLUSION: The results of the study showed that rotenone increased cell death in the SH-SY5Y cells, whereas low doses of curcumin and resveratrol polyphenols (1.5, 10 µM Resveratrol; 10, 50, 100, 500 nM Curcumin) maintained viability and increased colony forming ability compared with rotenone. The lack of a significant effect on caspase-3-dependent apoptosis revealed the need to evaluate other possible mechanisms underlying their protective effects. Supported by Ege University BAP Project no: TYL-2018-20049.

Keywords: Apoptosis, curcumin, neuronal toxicity, resveratrol, rotenone

PC065

The Effects of the Methyl-Beta-Cyclodextrin and Myriocin on Blood-Brain Barrier Integrity in Septic Rats

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AIM: A pathophysiological mechanistic factor in septic encephalopathy is impairment of blood-brain barrier (BBB). Methyl-beta-cyclodextrin (MβCD) disrupts caveolae, and myriocin inhibits sphingolipid synthesis in plasmalemma. We evaluated the effects of MβCD and myriocin on BBB permeability in septic rats induced by cecal ligation and puncture (CLP).

METHODS: Evans blue (EB) and horseradish peroxidase (HRP) were used to assess BBB permeability. Brain sections were immunostained for claudin-5, glucose transporter (GLUT)-1 and caveolin-1.

RESULTS: Claudin-5 fluorescence intensity in cerebral cortex increased in MβCD, myriocin, and CLP+myriocin, and decreased in CLP and CLP+MBCD, however the intensity in hippocampus decreased in all groups compared to sham ($P<0.01$). Caveolin-1 fluorescence intensity in cortex increased in CLP+myriocin, and decreased in the other groups, while in hippocampus, the intensity increased in all groups compared to sham ($p<0.01$). GLUT-1 fluorescence intensity in cortex increased in CLP, CLP+MβCD, and CLP+myriocin, and decreased in MβCD and myriocin, while the intensity in hippocampus decreased in all groups compared to sham ($p<0.01$). Both MβCD and myriocin significantly decreased EB-dye content in brains of septic animals ($P<0.01$). Ultrastructurally, HRP-positive vesicles increased in cortical and hippocampal endothelial cells in CLP, MβCD and myriocin, but were decreased in septic animals by MβCD and myriocin ($p<0.01$). Increased HRP-positive vesicles were also noted in parenchyma of both regions in CLP and myriocin, whereas in septic animals, they were decreased by MβCD and myriocin ($p<0.01$).

CONCLUSION: Our results revealed that although MBCD and myriocin led to BBB disruption in sham-operated animals, both drugs provided protective effects on BBB integrity in septic conditions.
Keywords: Blood-Brain Barrier, Sepsis, Tight Junction proteins, Inflammation

PC066

Investigation of the Effects of Lithium After Long-Term Spinal Cord Injury

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AIM: Spinal cord injuries (SCI) cause neuronal damage and functional loss in the sensory and motor pathways. After SCI cellular therapies, neuroprotective agents and physical therapy methods are being developed as treatment methods. However, there is no effective treatment that can be used in clinical practice. Lithium is known to have positive effects in neurodegenerative diseases. We aimed to investigate the effect of lithium on the functional recovery, neuronal survival and axonal plasticity after SCI on mice.

METHODS: BalB/c male mice (8-12 week old) were used and spinal cord injury was induced by semi-incision on T10 level. After SCI, daily lithium injection was performed intraperitoneally at 0.2 mmol/kg and 2 mmol/kg doses (n: 12) for 56 days. Behavioral tests were performed to evaluate the functional recovery. Neuronal survival and atrophy were measured by cresyl violet staining. Axonal plasticity was investigated after injection of BDA. Statistical analysis was performed by one-way ANOVA method.

RESULTS: The 0.2 mmol/kg injected group showed faster functional recovery compared with the control group. According to baseline, the total distance traveled by the control group on day 28 was 33%, whereas it was 59% ($p <0,05$) in the 0.2 mmol/kg group. The correct stepping rate increased on the 42th day in the 0.2 mmol/kg group, compared to control group. Cresyl violet staining results showed that the white matter of rostral segments atrophy areas were significantly less and neuronal survival was significantly increased in 0.2 mmol/kg group. The dorsal and lateral funiculus of the rostral segment were evaluated with biotinylated dextran amine (BDA) tracer application, which showed that axonal plasticity was increased in the 2 mmol/kg group.

CONCLUSION: It has been found that lithium treatment contributes to functional recovery, neuronal survival and axonal plasticity after injury. These results suggest that lithium may have long-term treatment potential after SCI.

Keywords: Spinal cord injury, lithium, neuronal recovery

PC067

The Role of Opioid Receptors in the Antinociceptive Effect of Oxytocin in Visceral Pain Induced By Colorectal Distension

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AIM: Oxytocin is a peptide hormone secreted from hypothalamic paraventricular and supraoptic nuclei. Studies have shown that oxytocin may have antinociceptive/analgesic effects in addition to the functions of providing uterine contraction and control of milk ejection reflex. The aim of this study is to investigate the antinociceptive effect of oxytocin in visceral pain induced by colorectal distension and the role of opioid receptors in this effect.
METHODS: In our study, male Sprague Dawley rats were used. Rats were anesthetized with ketamine + chlorpromazine (100 mg/kg ip + 0.75 mg/kg ip) combination and two Ni/Cr wire electrodes were placed in the external oblique muscle. The catheter was inserted into the jugular vein for drug administration. Following the surgery, rats were placed in Bollman cages for 7 days and acclimated to the experimental conditions. Colorectal distension (CRD) was created by inflating a 6-7 cm long balloon, which was placed at the descending colon and rectum, to 80 mmHg. Electromyographic activity (visceromotor response) caused by colorectal distension was recorded every 10 minutes for 90 minutes before and after administration of the drugs. After determining the suitability of the data for normal distribution, one-way analysis of variance (ANOVA) test was performed and Tukey-Kramer post-hoc test was used for multiple comparisons between groups. $p < 0.05$ was considered statistically significant. Ethical permission was approved by OMÜ HADYEK, 2019/04.
RESULTS: Exogenously administered oxytocin (5-80 µg/kg, iv) reduced visceromotor response starting from 10th minute in different ratios (%20-%70) in a dose-dependent manner ($p < 0.05$-0.001). The antinociceptive effect of oxytocin (40 µg/kg, iv) was completely inhibited by nonspecific opioid receptor antagonist naloxone (0.5 mg/kg) administered intravenously 10 minutes before oxytocin ($p < 0.01$).
CONCLUSION: Our results show that intravenous oxytocin has antinociceptive effect on visceral pain induced by CRD and opioid receptors play a role in this effect.

Keywords: oxytocin, visceral pain, antinociception, colorectal distension, naloxone, opioid receptor

PC068

Investigation of the Role of Opioidergic and Nicotinergic System in Antinociceptive Effect of Nicotine in Visceral Pain Model Induced by Colorectal Distension in Rats

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AIM: Nicotine is exogenous ligand with different effects on peripheral and central nervous system by binding to nicotinic acetylcholine receptors. Nicotine has been found to be antinociceptive in many somatic experimental pain models but its effect on visceral pain models has not been investigated. In our study, we investigated antinociceptive effect of nicotine and the role of opiodergic and nicotinergic receptors in this effect.
METHOD: In this study 6 Sprague-Dawley (250-300 g) rats was divided into groups as follows: Control, nicotine (1,5-10 mg/kg) dose groups, mecamylamine alone (0.25 mg/kg), mecamylamine (0.25 mg/kg) + nicotine (5 mg/kg), naloxone alone (0.05 mg/kg) and naloxone (0.05 mg/kg) + nicotine group. In order to obtain electromyographic recordings, the rats were placed with two Ni/Cr wire electrodes and a jugular cannula for drug administration under ketamine (100 mg/kg, ip) anesthesia. Colorectal distention was induced by an inflatable colorectal apparatus placed in the colons of rats. In all groups, the noxious stimulus is produced by colorectal distension (CRD) following this noxious stimulus, visceromotor response (VMR) was obtained and measured by recording EMG activity gained from electrodes implanted into the external oblique muscle. The overall effect of treatments was also represented as area under the curve (AUC) of time-response function with Excel computer program. The AUC was calculated from time plot of postdrug. After checking the data for normal distribution, one-way analysis of variance (ANOVA) test was performed and Tukey-Kramer post-hoc test was used for multiple comparisons between groups. $P < 0.05$ was considered statistically significant. Ethical permission was approved by OMÜ HADYEK, 2015/197.
RESULTS: Nicotine (1.25-10 mg/kg) administered intravenously showed dose-dependent antinociceptive effect (EAA values for the control group: 6+111; for nicotine doses (1.25, 2.5, 5 and 10 mg/kg -341+638,440+286, 2538+220;1827+405 respectively; $p < 0.05$-0.001). The antinociceptive effect of nicotine (5 mg/kg) was completely inhibited by the non-selective nicotinic receptor antagonist mecamylamine ($p < 0.001$) and was partially reduced with the nonselective opioid antagonist naloxone ($p < 0.05$).
CONCLUSION: These results suggest that nicotine has antinociceptive effect in visceral pain model induced by colorectal distension via nicotinergic and partly opioidergic receptors.

Keywords: Antinociception, Colorectal Distension, Nicotine, Rat, Visceral Pain

PC069

The Effects of SNr-DBS on Cerebellum in 6-OHDA Rat Model of Parkinson's Disease

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AIM: Parkinson's disease (PD) is a chronic neurodegenerative disease caused by loss of neuromelanin-containing dopaminergic neurons in the nigrostriatal pathway. Deep brain stimulation (DBS) is a method of treatment for PD. This study was planned to investigate the effect of DBS on cerebellum which was applied to the substantia nigra pars reticulata (SNr) and to determine the role of brain derived neurotrophic factor (BDNF) in this effect in rats with the experimental model of PD.

METHODS: In this study, adult male Wistar rats were randomly divided into 4 groups as: 1) Control (n=12), 2) Parkinson (n=12) (Bilateral striatal PD model, AP:0,7,L:3,4,V:5.0, relative to the bregma), 3) Sham (Parkinson+electrode) (n=20) (SNr bilateral electrodes, AP:-4,8,L:2.5,V:-7, relative to the bregma) and 4) DBS (Parkinson+DBS) (n=20). The DBS group was subjected to electrical stimulation for three hours in a day for two weeks. Gait analysis were evaluated and then the immunohistochemical staining were performed. Data were assessed using one-way ANOVA followed by Tukey Post Hoc or Student-Newman Keuls tests.

RESULTS: The front and back foot step lenghts of the animals decreased in Parkinson group compared to control group ($p<0.001$) which were improved by DBS treatment ($p<0.001$). Front and rear foot sole widths increased in Parkinson group compared to control group ($p<0.01$) which were decreased by electrical stimulation ($p<0.001$, $p<0.05$). BDNF containing cells in cerebellum were found to be increased with DBS treatment ($p<0.05$). c-Fos containing cells in cerebellum Purkinje cells and TH+ cell numbers in substantia nigra (SN) were counted and the numbers were shown to be increased after DBS in Parkinson group ($p<0.05$).

CONCLUSION: Our results suggest that the DBS treatment of SNr increases BDNF levels in cerebellum which improves the motor deficits in PD.

This study was supported by Akdeniz University Scientific Research Projects Coordination Unit (Project Number: TTU-2016-1883) and the procedures were reviewed and approved by Akdeniz University Local Committee on Animal Research Ethics (Protocol no:2016.03.08).

Keywords: Deep brain stimulation, BDNF, Parkinson's disease, Cerebellum, c-Fos

PC070

Possible Mechanism of Agmatine in Rotenone-Induced Parkinson's Disease Model in Rats

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AIM: Agmatine is a decarboxylation product, which is synthesized from arginine. Neuroprotective, antioxidant effects of exogenously administered agmatine has been already known. Main aim of this study was to investigate the effects and mechanism of agmatine in rotenone-induced Parkinson's disease model.

METHODS: In this study 18 male Sprague-Dawley rats (220-240 g) were used (OMUHADYEK_2018-04). Experimental Parkinson's disease model was created with intranigral and intrastriatal injection of rotenone (0.5µg/1 µl) under stereotaxic surgery. After ten day of surgery, apomorphine test was performed in order to validate Parkinson's disease model. Apomorphine test was repeated after 14 day agmatine (100 mg/kg, i.p.) administration. Rats were decapitated after evaluation of motor coordination with open-field and pole tests. After decapitation brain tissues were isolated for biochemical, molecular and histopathological analysis. All data obtained from experiments was analyzed with one-way analysis of variance (ANOVA) test using SPSS (v21) software.

RESULTS: Agmatine administration decreased apomorphine induced rotation number. Additionally, agmatine decreased motor coordination impairment and intensity of bradykinesia which was the results of rotenone toxication. Furthermore, agmatine prevented rotenone induced lipid and protein oxidation and increased SOD, CAT levels which play role in oxidative stress. Besides, agmatine increased expression levels of cREB, BDNF and ERK1/2 in the striatal tissue. Histopathological analysis showed that neuronal loss, which is a result of rotenone injection, decreased in agmatine administered group significantly ($p<0.05$).

CONCLUSION: In this study, relation of agmatine with antioxidant system and cREB, BDNF, ERK1/2 was firstly demonstrated in rotenone-induced Parkinson's disease. This work was supported by TUBITAK (218S237).

Keywords: Agmatine, Rotenone, Parkinson's disease, Rat

PC071

The Neuroprotective Effects of Neuropeptide W in Newborn Rats with Cerebral Palsy

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AIM: Cerebral palsy (CP), which develops during perinatal period by oxidative events in brain, and makes life difficult with permanent motor disorders, has no preventive/ therapeutic medical treatments. Neuropeptide W (NPW), isolated from hypothalamus, has analgesic and antiepileptic effects. The aim was to investigate possible neuroprotective effects of NPW on oxidative brain injury in newborn rats induced with cerebral palsy.
METHODS: To induce CP, under isoflurane anesthesia right common carotid arteries of seven-day-old Sprague-Dawley rats were ligated. Following surgery, pups were allowed to recover with their mothers for 120 minutes, then exposed to 92% nitrogen + 8% oxygen for 150 minutes within an incubator (37°C). Immediately after ischemia-hypoxia, CP- rats were treated intraperitoneally with saline (n=6) or NPW (0.1, 1 or 10 μg/kg/day; n=21) and treatments were continued for 3 days. The pups in sham-control group were kept with their mothers after skin incisions were closed (n=6). On postnatal 10th day, rats were decapitated to determine cerebral malondialdehyde and glutathione levels, myeloperoxidase activity and luminol/lucigenin chemiluminescence (CL) levels and histopathological damage. Data were analyzed by ANOVA and Student's t-test.
RESULTS: While antioxidant glutathione levels in saline-treated CP group were not different from control group, they were elevated in 0.1 and 1 μg/kg NPW-treated groups ($p<0.05$). Compared with control, malondialdehyde levels in saline-treated CP group were increased ($p<0.001$), indicating enhanced lipid peroxidation; but a tendency to decrease was observed with all NPW doses ($p>0.05$). CL levels, showing oxygen radicals, were increased with CP ($p<0.001$), but decreased with 0.1 and 10 μg/kg NPW doses ($p<0.01$-0.001). Increased myeloperoxidase activity in damaged brain tissue ($p<0.05$) was reduced only in 0.1 μg/kg NPW ($p<0.05$). Neuronal damage observed in cortices and hippocampi of saline-treated CP group was reduced by NPW, mostly at 0.1 μg/kg dose.
CONCLUSION: NPW exerts dose-dependent neuroprotective and antioxidant effects in hypoxic-ischemia-induced brain injury.

Keywords: Neuropeptide W, oxidative damage, brain, hypoxia-ischemia.

PC072

The Effect of Central Neuropeptide-S on MPTP-induced Behavioral Changes in Mice

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AIM: This study was designed to investigate the effects of central neuropeptide-S (NPS) treatment on methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced impaired behavioral functions.
METHODS: In this study, male C57Bl/6 mice were randomly divided into three groups (n=15): Groups consist of Control, MPTP (20 mg/kg; i.p) and NPS-treated (0.1 nmol; icv) group (treatment was administered MPTP injection). Nigral microdialysis for dopamine, glutamine and glutamic acid were measured seven days after MPTP injection. Elevated plus maze and sucrose preference tests were used to assess anxiety and depression-like behaviours, respectively. Data were analyzed with ANOVA followed by Tukey post hoc test. Protocols were approved by the Animal Ethical Committee of Akdeniz University (B.30.2.AKD.0.05.07.00/103).
RESULTS: Administration of NPS did not significantly change the time spent in the closed arm, as well as the number of open arm and closed arm entries compared to MPTP groups. However, MPTP injection caused to a significant decrease in the time spent in the open arm ($p<0.05$). In vivo brain microdialysis was performed to quantify the amount of extracellular dopamine, glutamine and glutamic acid levels in substantia nigra (SN), compared with the control animals, MPTP decreased these levels in microdialysates significantly ($p<0.05$). The MPTP-induced decreases in dopamine, glutamine, glutamic acid levels were prevented by NPS treatment ($p<0.05$). In the sucrose preference test, MPTP group showed a decreased preference for sucrose when compared to control animals ($p<0.0001$). This effect was significantly reversed by NPS treatment ($p<0.0001$).
CONCLUSION: NPS appears to be a novel therapeutic approach for treatment of behavioral changes on experimental model of Parkinson's disease.

Keywords: Parkinson's Disease, Neuropeptide-S, Sucrose Preference, Anxiety, Depression-like Behaviors

PC073

Neuroprotective Effect of Neuropeptide-S on Cognitive Functions in the Experimental Model of Parkinson's Disease

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AIM: This study aims to determine the effects of neuropeptide-S (NPS) treatment on cognitive parameters in the experimental model of Parkinson's disease

METHODS: Mice (three months old, C57Bl/6, male) were randomly divided into three groups, namely the control group, the MPTP group and MPTP-injected + NPS treated (received intraperitoneal injection of MPTP and intracerebroventricular (icv) injection of NPS, 0.1 nmol for 7 days). They were injected (i.p) with 20 mg/kg MPTP to create the Parkinson's Disease (PD) mouse model and the control group received saline with an inter injection interval of 12 h. Radial arm maze test was used to determine working memory and tyrosine hydroxylase (TH) immunoreactivity was assessed by immunofluoresans method in nigral sections. The levels of dopamine, glutamic acid and glutamine were detected in hippocampal tissue samples. Data were analyzed with ANOVA followed by Tukey post hoc test. Protocols were approved by the Animal Ethical Committee of Akdeniz University (B.30.2.AKD.0.05.07.00/103).

RESULTS: In the RAM test, the number of reference memory errors (RME) decreased in the MPTP+NPS-treated group compared to MPTP-induced Parkinsonian model. In addition, the number of working memory errors (WME) was attenuated by NPS treatment. The levels of dopamine, glutamine and glutamic acid in the hippocampal tissues were diminished with MPTP injection ($p<0.05$). These levels increased with NPS treatment but did not reach a significant level. Whereas the hippocampal glutamine level enhanced in the NPS-treated group. In control mice, extensive immunoreactivity for TH was detected which was abolished by the injection of MPTP. However, NPS treatment reversed the loss of nigral TH-positive cells in SN ($p<0.05$).

CONCLUSION: The analysis of RAM behavior data shows that NPS treatment does have positive effects on the MPTP-induced PD model in cognitive functions.

Keywords: Working memory, Neuropeptide-S, Parkinson's Disease, Cognitive functions

PC074

Effects of Taurine on Learning, Memory and Anxiety in Very Elderly Rats with Experimental Alzheimer's Disease Model

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AIM: The aim of this study was to investigate the effect of taurine (2-aminoethanesulfonic acid), a broad-spectrum cytoprotective agent in neurodegenerative process induced by amyloid beta 1-42 (Aβ 1-42) injection, on spatial learning, memory performance and anxiety in old rats.

METHODS: In this study, 30 old (28±4 months) male Wistar albino rats were used. Rats were divided into 5 groups as control, sham, Aβ 1-42, taurine, Aβ 1-42+taurine. Taurine was added to the drinking water of the animals at a dose of 1000 mg/kg/day and given for 6 weeks. After taurine administration, the animals were injected intracerebroventricular (icv) Aβ 1-42 (into the lateral ventricles, 5 µl) by stereotaxic surgery. All animals received Morris water tank and elevated plus maze test. Spatial learning and memory performance and anxiety like behavior of the animals were evaluated. For statistical analysis; Kruskal Wallis and Mann Whitney U test, Friedman and Wilcoxon test were used and Bonferroni correction was applied. $p<0.01$ was considered significant. Ethics committee approval was received for our study (G.Ü. ET-17.058).

RESULTS: In our study; Aβ 1-42 injection increased platform discovery time and impaired spatial learning and memory performance in rats ($p<0.01$), and taurine supplementation did not make a significant difference on learning and memory performance ($p>0.01$). In elevated plus maze test, Aβ 1-42 injection increased the number of entries into open and closed arm and motor activity in rats ($p<0.01$). Chronic taurine supplementation increased the time spent in closed arms ($p<0.01$).

CONCLUSION: Our study showed that, the chronic administration of taurine did not make a significant difference on cognitive functions in old rats during the course neurodegenerative process due to icv Aβ 1-42 injection, and it may also cause anxiety.

This work was supported by the project G.Ü.-BAP 01/2017-30.

Keywords: Alzheimer's Disease, Anxiety, Memory, Learning, Taurine

PC075

Effect of Taurine Supplementation on Oxidative Stress in Liver Tissue in Very Old Rats with Experimental Alzheimer's Disease Model

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AIM: Amyloid beta(Aβ) aggregates in the brain are known to play a central role in the pathogenesis of Alzheimer's disease. Rodent studies have shown that the liver plays an important role in the elimination of Aβ. The aim of this study was to investigate the effect of administration of taurine, which has antioxidant properties and synthesized mainly in the brain and the liver, on oxidative stress parameters in liver tissue in very old rats with experimental Alzheimer model.

METHODS: In our study, 30 Wistar albino male rats, approximately 30 months old, were divided into 5 groups (Control, Sham, Aβ 1-42, Taurine+Aβ 1-42 and Taurine). Intracerebroventricular(icv) injection of Aβ 1-42 (into lateral ventricles,5 µl) was applied by stereotaxic surgery to rats in Taurine+Aβ 1-42 and Aβ 1-42 groups after 6 weeks of oral 1000 mg/kg/day taurine pre-supplementation. Rats in the other groups were injected with the same amount of vehicle. Two weeks later, rats were sacrificed and MDA and GSH levels in liver tissues were measured by spectrophotometric method. Kruskal Wallis test was used for data analysis, $p<0.05$ was considered significant.

RESULTS: Although MDA levels were increased in the Aβ 1-42 group, this increase was not statistically significant ($p>0.05$). There was no significant difference between the groups in terms of GSH levels.

CONCLUSION: In our study, the fact that icv Aβ 1-42 administration did not lead to a significant change in liver MDA and GSH levels in very old rats may be due to the fact that intra-brain administration did not show sufficient effect on peripheral tissues. In addition, there was no difference between the groups in terms of oxidative stress since all rats experienced stereotaxic surgical stress. The fact that taurine pre-supplementation did not yield a significant difference can be explained by the lack of oxidant damage to induce the antioxidant effect of taurine.

Keywords: Alzheimer's model, GSH, liver, MDA, oksidative stress, taurine

PC076

Effect of *Ginkgo biloba* Components on Locomotor Activity in WAG/Rij Rats

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AIM: *Ginkgo biloba* extract EGb 761, which is prescribed in some types of dementia and is also used without a prescription to improve cognitive performance, is a widely used herbal product. In an experimental study, however, it has been suggested that chronic EGb 761 reduces motor activity. The aim of the present study was to investigate the effects of ginkgolide A, B, C and bilobalide on the locomotor behavior of WAG/Rij rats with genetically absence epilepsy using open field and rotarod behavior tests.

METHODS: Ginkgolide A, B, C and bilobalide were administered intraperitoneally at a dose of 6 mg/kg for 7 days. The animals were subjected to the open field and the rotarod behavior tests before drug administration, after the 1st dose and 7th dose. Locomotor performance of WAG/Rij rats was evaluated by the number of crossed squares and rearings in the open field test and the latency to fall from the platform in the rotarod test. In addition, the anxiety level of the rats was determined by the number of fecal boli in the open field test. Behavior data were analyzed using Mann-Whitney U test after Kruskal-Wallis variance analysis. The study was conducted with the permission of SBÜ Animal Experiments Local Ethics Committee 2017-1054.

RESULTS: Ginkgolide C and bilobalide significantly reduced the number of crossed squares after the first dose ($p <0.05$). In addition, bilobalide significantly reduced the number of rearings after 1st and 7th doses ($p <0.05$). Rotarod test showed that all the active components of EGb 761 were not effective on the latency to fall from the platform.

CONCLUSION: It was concluded that EGb 761, *Ginkgo biloba* extract, may reduce locomotor activity through some active components such as ginkgolide C and bilobalide. This study was supported by TÜBİTAK (Project no: 115S348).

Keywords: {Ginkgo biloba}, open-field test, rotarod test, WAG/Rij rat

PC077

mRNA Expression Levels of TRPV1, TRPV2, TRPV3 TRPV4, TRPM2, TRPM4, TRPM7, TRPA1 and TRPC6 Channels in Multiple Sclerosis Patients

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AIM: Transient receptor potential (TRP) channels have been expressed in many cells, including immune cells. It was understood that TRP channels play a role in the formation of various pathological conditions due to effect of immune response. Microglial activation in Multiple Sclerosis (MS) is accompanied by blood – brain barrier disturbance, lymphocytes and macrophages infiltration. Relapsing-Remitting Multiple Sclerosis (RRMS), which is the first stage and the most common type of MS, is important for early planning of treatment. In this study, we investigated the level of transient receptor potential melastatin 2 (TRPM2), TRPM4, TRPM7, transient receptor potential ankyrin 1 (TRPA1), Transient Receptor Potential Vanilloid 1 (TRPV1), TRPV2, TRPV3, TRPV4 and transient receptor potential canonical 6 (TRPC6) mRNA expression associated with inflammatory process in peripheral blood mononuclear cell (PBMC) of RRMS patients.

METHODS: Thirty five controls and thirty patients with RRMS were included in the study. PMBC was isolated from the blood of the participants. TRPV1, TRPV2, TRPV3, TRPV4, TRPM2, TRPM4, TRPM7, TRPA1 and TRPC6 PBMC mRNA expression levels were measured by qRT-PCR.

RESULTS: In our study, we found that the expression of TRPV1, TRPV3, TRPV4, TRPM7 and TRPC6 mRNA in PBMC in RRMS patients was significantly lower than in the control group ($p<0.05$).

CONCLUSION: In this study, it was shown that, for the first time, the expression of TRPV1, TRPV3, TRPV4, TRPM7 and TRPC6 mRNA in PBMC were decreased in RRMS patients. Further research is needed to fully understand the relationship between these TRP channels and MS.

Keywords: TRP channels, mRNA, expression, Multiple Sclerosis

PC078

The Effect of Thymoquinone on the Calcitonin Gene-Related Peptide Release and Dural Mast Cell Degranulation Induced by Compound-48/80

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AIM: Overactivation of dural mast cells induces neurogenic inflammation underlying migraine pathophysiology. Main migraine mediator calcitonin gene-related peptide (CGRP) reinforces neurogenic inflammation by activating dural mast cells. Although anti-inflammatory effects of a phytochemical agent thymoquinone were demonstrated, its effects on the dural mast cell-mediated neurogenic inflammation and CGRP release are not known. We aimed to investigate effects of thymoquinone on the mast cell degranulating agent compound-48/80-induced dural mast cell degranulation and CGRP release from neuronal structures associated with migraine pain in rats.

METHODS: Adult male Wistar rats in groups (n=7) received single-dose intraperitoneal injection of 0.2 ml saline, 2 mg/kg compound-48/80, 10 mg/kg thymoquinone+compound-48/80, 50 mg/kg cromolyn+compound-48/80, 0.2 ml vehicle (0.1% ethanol)+compound-48/80 and thymoquinone alone, respectively. CGRP levels as neurogenic inflammation marker in plasma, trigeminal ganglia, brainstem and cerebrum and diencephalon samples of brain were measured using ELISA. Dura mater was stained with toluidine blue. Dural mast cells were evaluated for their number and degranulation. Data were compared by Kruskal-Wallis test. Ethics committee approval no: 2016/14.

RESULTS: Compound-48/80 increased CGRP levels in plasma and structures associated with neurogenic inflammation including trigeminal ganglia, brainstem and brain (cerebrum and diencephalon) ($p<0.01$). Thymoquinone alleviated these increments ($p<0.05$) and mast cell stabilizer cromolyn completely blocked ($p<0.01$). Compound-48/80 evoked dural mast cell degranulation ($p<0.001$) without affecting their numbers. Thymoquinone and cromolyn prevented dural mast cell degranulation induced by compound-48/80, respectively ($p<0.001$). Thymoquinone alone did not affect these parameters in control rats ($p>0.05$).

CONCLUSION: Thymoquinone prevented compound-48/80-induced neurogenic inflammation by stabilizing dural mast cells. Thus, thymoquinone may be a promising candidate for mast cell stabilizer of natural origin in preventing neurogenic inflammation and consequently migraine pain.
Grant-number: 2016.08.02.1082(BAIBU-BAP)

Keywords: CGRP, mast cell stabilization, migraine, neurogenic inflammation, thymoquinone.

PC079

Oxidative Stress and Sirtuin2 Changes in Different Parts of the Brain in Aging: Protective Effect of Melatonin

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AIM: Sirtuin2 (SIRT2) is a member of the sirtuin family called the long life protein. SIRT2 has been shown to increase in brain tissue with aging and SIRT2 inhibition is protective in age-related neurodegenerative diseases. In this study, the effects of SIRT2, malondialdehyde (MDA) and glutathione (GSH) levels on brain regions of young and old rat total cerebral cortex, hippocampus, and cerebellum and the effect of melatonin administration were investigated.

METHODS: In this study, 24 Wistar albino rats (3 months young, n = 12; 22 months old n = 12) were divided into four groups: Young-Control (1% ethanol + PBS sc) Young-MLT (10 mg/kg+ 1% ethanol + PBS sc), Elderly-Control, Elderly-MLT. Tissues were isolated after 30 days of injection. SIRT2 protein expressions were determined by Western blotting and tissue level was determined by ELISA. MDA as an indicator of oxidative stress and GSH levels as antioxidant were measured by spectrophotometer. ANOVA, LSD and Pearson correlation tests were used for statistical analysis ($p < 0.05$).

RESULTS: It was found that aging increased MDA and SIRT2, decreased GSH, in cerebral cortex and hippocampus. There was no change in age-related SIRT2 and MDA in the cerebellum. MLT application decreased MDA levels and SIRT2 expression and increased GSH levels in cerebral cortex and hippocampus in elderly rats $p < 0,05$). MLT administered to young rats reduced MDA in the hippocampus but did not affect GSH. SIRT2 values determined by Western blotting and ELISA kit were correlated. MDA levels were positively correlated with tissue SIRT2 levels and negative relationship with GSH.in cerebral cortex and hippocampus regions.

CONCLUSION: Our results support that SIRT2 inhibition may be a therapeutic target in the prevention of neurodegeneration in aging.

This work was supported by the Scientific and Technological Research Council of Turkey (Project No. 216S258).

Keywords: Aging, melatonin, oxidative stress, sirtuin2,

PC080

Ameliorative Effect of Pre-Exercising on Seizure-Induced Oxidative Injury of Skeletal Muscle and Brain in Rats

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AIM: Tonic-clonic contractions during status epilepticus result in skeletal muscle destruction. Although aerobic exercise was shown to be beneficial, by reducing susceptibility to seizures and improving memory, patients who have experienced prolonged seizures during exercise avoid participating in sports activities. It was aimed to evaluate the possible protective effects of exercising prior to seizure on seizure-induced oxidative injury in the skeletal muscle and brain.

METHODS: Sprague-Dawley male rats were randomly assigned as sedentary (n=16) and exercising groups (n=16) on a treadmill (30 min/day) for 10 days. On 11th day, passive avoidance test was performed in all rats to obtain basal values for memory performances. Then, half of sedentary and exercise groups were injected intraperitoneally with pentylenetetrazol (PTZ; 45 mg/kg), seizures were video-taped and scored with Racine scale. Rest of sedentary and exercise groups without PTZ injection constituted control groups. In skeletal muscle and brain samples, myeloperoxidase activity, malondialdehyde and glutathione levels, luminol and lucigenin-enhanced chemiluminescence levels were measured, and histopathological analyses were made. ANOVA and Student's t-test were used for statistical analyses.

RESULTS: The frequency of tonic-clonic contractions, average seizure scores and memory performances were similar in sedentary and exercise groups. Exercise had no effect on brain tissue in control groups, while elevated oxidative parameters in sedentary-PTZ group ($p<0.001$) were reduced in exercise-PTZ group ($p<0.01$). Skeletal muscle glutathione, luminol and lucigenin levels were elevated in exercise-control group ($p<0.05$). Increased lucigenin levels and myeloperoxidase activity in sedentary-PTZ group ($p<0.05$-0.001) were suppressed with exercise prior to seizure ($p<0.05$-0.01). Histopathological evaluation of muscle tissue in sedentary-PTZ group revealed abnormal organization of myofibers and neuronal loss in some brain areas, while regular myofibrillar and neuronal morphology were observed in exercise-PTZ group.

CONCLUSION: Although seizure susceptibility/severity or memory performance were not affected, ten-day exercise alleviated seizure-induced oxidative injury in brain and skeletal muscle

Keywords: Epileptic seizure, Exercise, oxidative damage, memory dysfunction

PC081

Neuroprotective Effects of Suberosin on Glutmate Excitotoxicty in Primary Cortical Neurons

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AIM: Glutamate is one of the major excitatory neurotransmitter of central nervous system. Excessive increase in glutamate release is known to cause excitotoxicity and neuronal deaths in many neurodegenerative diseases because of prolonged activation of glutamate receptors. The antiproliferative effects of suberosin found in coumarin-derived plants have been shown on many cancer cell-lines. The effects of some coumarin species on nervous system have also been reported. In this study; it was aimed to investigate neuroprotection of suberosin isolated from Ferulago cassia roots with CH_2Cl_2 extract in primary cortical neuron cell (PCNC) culture.

METHODS: This study was approved by Ataturk University Local Animal Experiments Ethics Committee. Suberosin was isolated from the roots of dichloromethane extract of Ferulago cassia and compound structure was elucidated by Nuclear Magnetic Resonance and Mass Spectroscopy methods. PCNC's were obtained from newborn Sprague Dawley rats. In order to stimulate glutamate excitotoxicity, glutamate at a concentration of $6x10^{-5}$ M was applied to the culture medium. Suberosin (10µM-1mM) was then added to the medium at different concentrations and allowed to incubate for 24 and 72 hours. MTT test was used to determine proliferative effect. Total Oxidant Status (TOS) and Total Antioxidant Status (TAS) analyzes were performed to evaluate reactive oxygen species.

RESULTS: Suberosin: Colourless crystal, C15H16O3 and ESIMS m/z 245.31 [M+H]+. According to MTT analysis, cell viability decreased after $6x10^{-5}$ M exposing of glutamate. It was determined that cell viability was increased following suberosin administration. The most significant increase was observed at concentrations of 100-500 µM suberosin administration. Consistent with MTT method, TAS-TOS analysis results showed that suberosin decreased oxidant level and increased antioxidant level.

CONCLUSION: It has been shown that suberosin has a protective effect on glutamate excitotoxicity in PCNC and it was concluded that suberosin can be used as a therapeutic agent against glutamate excitotoxicity

Keywords: Glutamate, Primary Neuron Culture, Suberosin

PC082

Capparis Spinosa L. in an Animal Model of Sciatic Crush Injury

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AIM: Capparis spinosa L. (capparis) is a perennial plant rich in flavonoids which may potentially exert anti-inflammatory and neuroprotective actions. This study was aimed to investigate the effectiveness of Capparis on serum markers.

METHODS: The left sciatic nerve of adult Wistar albino rats were crush-injured (n=7) or sham-operated (n=7) or the crush-injured animals received Capparis extract (500 mg/kg, p.o.) (n=8) for 6 weeks following the injury. The controls (n=6) weren't undergone any intervention. Subsequently, blood serum was obtained and tumor necrosis factor-alpha (TNF-α), nerve growth factor (NGF), prostaglandin E2 (PGE2), and interleukin-10(IL-10) were measured. Either one-way ANOVA or Kruskal-Wallis test was used in the statistical analyses. Ethical consent was acquired (2017/1-4).

RESULTS: In the non-treated crush-injured animals, TNF-α and NGF were decreased ($p<0.05$) while only TNF-α was decreased in the Capparis-treated crush-injured animals ($p<0.05$). No significance was found in PGE2 and IL-10 levels ($p>0.05$).

CONCLUSION: The inverse relation between TNF-α and fibrosis is known and hence, we hypothesize that lower TNF-α in the nerve-injured animals may correspond to established fibrosis while noting that Capparis was unable to alter TNF-α levels. Although NGF is expected to be locally increased in injured neurons, its circulating levels are independent of neurons due to being released by numerous extra-neuronal tissues such as adipocytes and mast cells and hence it was increased by exercise. We presume that lower NGF levels in the non-treated nerve-injured animals may reflect decreased physical activity which was recovered by Capparis. PGE2 is a dual-action prostaglandin which have both pro-inflammatory and anti-inflammatory effects and IL-10 is an anti-inflammatory cytokine which fluctuates following the injury; however, their levels don't sustain increased for weeks. We believe that our statistically non-significant results for TNF-α and PGE2 may be originated in the time of sampling which was 6 weeks after the injury. Nevertheless, Capparis was found to influence neither TNF-a nor PGE2.

Keywords: Capparis, sciatic crush injury, nevre

PC083

Effect of Acute Gabapentin on Open Field Test Behavior in Balb/c mice Administered with MK-801

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AIM: In our study, the effect of acute gabapentin on locomotor activity and anxiety-like behavior in Balb/c mice administered with MK-801 was evaluated in the open-field test.

METHODS: In present study, 8-10 weeks old 19 male adult Balb/c mice were used. Mice were administered uncompetetive N-methyl-D-aspartate (NMDA) receptor blocker MK-801 (0.5mg/kg dose, 0.1mL/kg body weight). The same volume of saline (0.9%NaCl) was injected intraperitoneally to the mice in the control group. Gabapentin was administered at a dose of 100 mg/kg 30 min. after MK-801 administration. Mice were tested with open-field test 30 min. after injection. The locomotor activity and anxiety-like behavior of the mice were recorded with a video-camera for 5 min and scored with the ETHOVISION XT program. Data were analyzed using Mann-Whitney-u test was used following Kruskal-Wallis. Ethics committee approval C.U. animal experiments were taken from the local ethics committee with the decision number 3/8, dated 09.05.2019.

RESULTS: The time spent in the center of the MK-801 group compared with the control group increased, latency to the center and the frequency of rearing decreased ($p<0.05$). Gabapentin administration after MK-801 injection decreased the frequency of rearing in mice compared to the group of administered gabapentin ($p<0.05$) and did not significantly change the latency to the center and the time spent in the center.

CONCLUSION: MK-801-induced NMDA blockade reduced anxiety-like behavior in the open-field test. Gabapentin did not change this effect of MK-801.In conclusion, it can be argued that the effects of NMDA receptor blockade in the open-field test cannot be altered by the increase in acute GABA level.

Keywords: Balb/c mouse, gabapentin, MK-801, open field test, schizophrenia.

PC084

Bisphenol A (BPA) Led to Anxiety-Like Behaviors in Eisenia Fetida Invertebrate Model

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AIM: Anxiety is a behavioral mechanism in animals to tackle with difficult situations. Fear and anxiety share the same physical and mental symptoms, like avoidance, hypervigilance and an increased alert level to avoid damage. Some stereotype behaviours in invertebrate animals are used to create anxiety model. Bisphenol A is an important endocrine disruptor and it is used in industry for production of resins and polycarbonate plastic. Detrimental effects Bisphenol A such as disruption of reproductive hormones, growth retardation, renal and genetic toxicity have been reported. The aim of this study is to evaluate the effect of Bisphenol A on the anxiety-like behaviour and locomotor activity in Eisenia fetida.

METHODS: 24 Eisenia fetida (1 years old, 9cm. and n= 8) were used in the present study. Subjects adapted for 4 weeks. For experiment, 150 and 300 mg/kg/day of BPA were used. Each worm was removed from its shelter and placed into an exposure chamber containing test compound or saline for 30 minutes. After 30 min, each worm was placed in to experiment chamber (modified light dark box test) and recorded via camera 10 min. Light zone time, light/dark zone entrance number, locomotor activity, dark zone entrance latency and velocity were analyzed. All the results were presented as mean ± standard error of the mean (SEM). The data were evaluated by analysis of variance (ANOVA) followed by Student's t-test and Neuman–Keuls post hoc test.

RESULTS: Light zone time, light/dark zone entrance number and dark zone entrance latency were decreased between 150 and 300 mg/kg/day of BPA groups with dose-dependent ($p <0.05$, in 150 mg/kg group; $p<0.01$, in 300 mg/kg group). Locomotor activity and velocity were also decreased significantly in 150 and 300 mg/kg/day of BPA groups compere to control ($p< 0.01$).

CONCLUSION: BPA increased anxiety-like behaviour of Eisenia fetida with dose dependent manner. Locomotor activity and speed were similarly impaired in both dose groups.

Keywords: Anxiety model, Bisphenol A (BPA), Eisenia fetida, Light/Dark Box Test

PC085

Di (2-Ethylhexyl) Phthalate (DEHP) Triggered off Anxiety Like Behaviors in Eisenia Fetida

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AIM: Di(2-ethylhexyl) phthalate (DEHP) is well known endocrine disruptor. DEHP can cause adverse effects on organism, or its progeny. DEHP is known to have toxic effects on organs and hormones of the reproductive system. It has been shown that DEHP is hepatocarcinogenic to the liver and cause skeletal and cardiovascular system anomalies in rodents. It can be found in food and beverage processing, and in many other commercial products such as epoxy resin cans, dental sealants, personal care products, baby bottles, building materials, flame retardant materials, optical lenses, materials for the protection of window glazing, DVDs, and household electronics. The aim of this study is to evaluate the effect of DEHP on the anxiety-like behaviour and locomotor activity in Eisenia fetida.

METHODS: 24 Eisenia fetida (1 years old, 9cm. and n= 8) were used in the present study. Worms were left for adaptation for 4 weeks. Saline was applied for control group. For experiment, 100 and 200 mg/kg/day of DEHP were used. Each worm was removed from its shelter cage and placed into an exposure chamber containing test compound or saline for 30 minutes. After 30 min, each worm was placed in to experiment chamber (modified light dark box test) and recorded via camera 10 min. Light zone time, dark time zone, light/dark zone entrance number, locomotor activity, dark zone entrance latency and velocity were analyzed. All data were analyzed by one-way analysis of variance (ANOVA) followed by a Tukey's post hoc test for multiple comparison.

RESULTS: Light zone time was decreased and dark zone time was increased ($p < 0.01$). Also, light/dark zone entrance number and dark zone entrance latency was decreased between the groups ($p < 0.01$). Locomotor activity and velocity were also decreased significantly in 100 and 200 mg/kg/day of DEHP groups compere to control ($p < 0.01$).

CONCLUSION: DEHP increased in Eisenia fetida without dose-dependent.

Keywords: Anxiety-like behaviours, Eisenia fetida, Di(2-ethylhexyl) phthalate (DEHP), light dark box test

PC086

Depression and Anxiety Levels of Renal Transplantation Patients

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AIM: Anxiety and depression are the most common mental health problems. In chronic renal failure, long-term hospital treatment such as dialysis, anxiety and depression can be seen due to the inability of the kidney to function and other stressors. The aim of this study was to investigate the state of anxiety and depression in hemodialysis patients undergoing transplantation.

METHODS: Presented study was performed in 110 kidney transplant patients who came to Ankara İbni Sina Hospital. It was performed in 110 patients who underwent renal transplantation to determine their status and categorize their emotional status. The control group was not used. Beck Depression and Anxiety Scales were applied to patients who had kidney transplantation at İbni Sina Hospital of Ankara University. Statistical analysis was performed by One Way Anova and Tukey Test to determine the difference between groups. Significance $p < 0.05$ was admitted significantly.

RESULTS: Patients with intermediate and severe levels of anxiety and depression were found to be higher than mild or nonsymptomatic patient ($P < 0.05$). Our presented findings, the prevalence of anxiety in 110 renal transplant patients in hospital was 25.45%; the prevalence of depression was 14.54%.

CONCLUSION: According to the prevalence of anxiety and depression in the world population, the prevalence of both depression and anxiety was found to be high in organ transplant patients According to past studies, compared to dialysis patients anxiety and depression prevalence was found lower in transplant patients. Patients' health gains rather than loss of health led to a positive increase in their emotions. Patients should be followed up by liaison psychiatry because of the negative thoughts that may occur in the future such as recurrent kidney loss, repetition of dialysis treatment and organ transplant failure.

Keywords: Anxiety Prevelance, Depression Prevelance, Kidney Transplantation

PC087

Effect of Fasudil Inhibition of Rho / Rho-kinase on Hippocampal UDG Responses

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AIM: Rho-kinase (ROCK) has an important role in formation of long-term potentiation (LTP) in presynaptic and postsynaptic hippocampal neurons. Studies reported increased ROCK levels in Alzheimer's or cognitive impairment. Increased ROCK expression may result with dendritic spike losses. In our study, we investigated synaptic plasticity changes by infusing ROCK inhibitor Fasudil to rat hippocampi without pathological disorders.

METHODS: Control (n = 8) and Fasudil (n = 8) groups were composed of Wistar-Albino male rats. The anesthetized animal skull was fixed to the stereotaxic system and stimulated with electrode entering the perforating path. After basal recording (15 min), Serum physiological and Fasudil infusion (10µm infusion dose dissolved in saline) were given to the dentate gyrus with high frequency stimulation (HFS) and recorded simultaneously; followed by recording of maintenance phase (60 min). Population Spike (PS) amplitude and Excitatory Post Synaptic Potential (EPSP) slopes were evaluated and statistical analyzes (I/O; ANOVA, LTP; student-t test) were performed. Our study was approved by the ethics committee of Erciyes University, numbered 18/090.

RESULTS: In I/O evaluation, PS amplitude was statistically significantly increased. There was no statistically significant difference between groups. When posttetanic and maintenance PS amplitudes were evaluated following HFS protocol for LTP, both posttetanic ($t14 = 3.25$ $p = 0.006$) and maintenance PS amplitudes ($t14 = 4.82$, $p < 0.001$) showed significant decrease in Fasudil group. EPSP slope of Fasudil infusion in both posttetanic ($t14 = 4.82$, $p < 0.001$) and maintenance periods ($t14 = 3.68$, $p = 0.002$) showed significant decrease.

CONCLUSION: Our study revealed that ROCK-signaling pathway is important for dentate gyrus synaptic plasticity. In the literature, we found no study that searches in vivo effect of ROCK on hippocampal plasticity function. Thus, our study is unique. Increase of ROCK protein expression's effect on forms of hippocampal plasticity are planned to be researched in the future.

Keywords: Fasudil, hippocampus, long term potentiation, Rho-kinase

PC088

The Effects of Visual Multi Go and NoGo Tasks on Event Related Potential Components

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AIM: In everyday life, the successful maintenance of cognitive and motor functions often requires the simultaneous or sequential execution of multiple inhibition or activation tasks. In cognitive electrophysiology, the go-nogo paradigm is an experimental design used to measure both response activation and response inhibition processes in the brain. In this study, we aimed to investigate the effects of visual multi go and nogo tasks on event related potential (ERP) components.

METHODS: Thirty-six healthy volunteers aged 22.08±1.20 years participated in the study. ERPs were recorded from 30 Ag-AgCl electrodes (international 10/20 system) using three different equiprobable visual go-nogo paradigm. The first go-nogo paradigm contained one go and one nogo stimulus, while the second paradigm contained three different go stimuli and the third paradigm contained three different nogo stimuli. The amplitude and latency values of ERP components in the averaged responses to go and nogo stimuli were measured and then analyzed by repeated measures analyses of variance (ANOVA).

RESULTS: Statistical analyses indicate that the amplitudes of P3 potential were significantly lower in response to multi go and multi nogo stimuli compared with go and nogo stimuli conditions ($p=0.001$ and $p=0.001$, respectively). Also, interaction of the nogo stimuli conditions and antero-posterior distribution of nogo P3 amplitudes was significant. Decrease of the amplitude of multi nogo-P3 potential at the fronto-central areas was bigger than that at the parietal areas ($p=0.006$). However, latencies of P3 potentials were not significantly different among go and nogo stimuli conditions ($p>0.05$).

CONCLUSION: Our results suggest that the processing time of the visual multi go and multi nogo stimuli by the brain are similar to that of the visual go and nogo stimuli, whereas increase in the difficulty of the task in multi go and multi nogo responses increases the uncertainty in processing of the visual stimuli in the brain.

Keywords: Go-nogo paradigm, event related potential, P3 potential

PC089

The Effect of GLP-1 Receptor Agonist on Hippocampal-Mediated Learning and Memory in REM Sleep Deprived Rats

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AIM: Substantial evidence has shown that REM sleep deprivation may affect learning and memory. Glucagon-like peptide 1 (GLP-1) receptors have been defined in numerous brain region such as hippocampus that plays an important role in memory. The aim of this study was to investigate the effects of GLP-1 analogue (exenatide) on memory and oxidative stress markers in sleep deprived (SD) rats.

METHODS: 32 male Wistar albino rats (200-250g) were randomly divided into 4 groups. 1) Control, 2) Exenatide treated control, 3) SD, 4) Exenatide treated SD. Multiple platform method was used to induce REM sleep deprivation for 72 hours. Treatment of exenatide (0,5µg/kg) was applied by daily subcutaneous injection for duration of experiment. The Morris water maze (MWM) test was used to detect the effects of exenatide on learning and memory. At the end of study hippocampus tissues were collected. Tissue levels of malondialdehyde (MDA) and reduced glutathione (GSH) were assessed spectrophotometrically. Kruskal-Wallis test was applied for statistical comparison of groups, followed by analysis with the Dunn test to determine differences between the groups.

RESULTS: The results showed that there was no significant difference in MDA and GSH levels between groups ($p>0.05$). In the hidden platform test, exenatide treatment was not effective on memory of rats. Probe test (on 1. day) results have indicated that rats in SD group significantly spent less time in the target quadrant compared with the control and exenatide treated groups ($p<0.05$). Exenatide administration alleviated the impaired memory of SD rats significantly after 24 and 48 h of SD ($p<0.05$).

CONCLUSION: REM sleep deprivation caused learning and memory disruption without changing the oxidative balance in the hippocampus. The results showed that exenatide treatment may be useful in reducing SD-induced memory impairment.

Keywords: Exenatide, GLP-1, learning and memory, REM sleep deprivation

PC090

Determining the Ideal Object Size in the Novel Object Recognition Test

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AIM: The novel object recognition test is among the tests that are used to evaluate hippocampus-dependent recognition memory performance. This study was designed with the aim of determining the ideal size of objects in the novel object recognition test.

METHODS: Adult male Wistar rats were engaged in the novel object recognition test with the objects of a size of 2, 4,6, 8 and 10 cm. In the familiarization session, the animals encountered identical objects (f1-f2) for 5 minutes while they came upon the n1 object which was substituted for the f2 object in the short-term memory session (1.5 h). The f1 object was changed with the n2 object and the animals were observed for 5 minutes in the long-term memory session (24 h). One-way ANOVA and paired sample t-tests were used for the statistical analyses.

RESULTS: The count and duration of interest to the objects were the highest toward the 6-cm objects (respectively 7.4 [arbitrary] and 17.6 s; 3.5 [arbitrary] and 5.4 s; $p<0.05$) and the lowest toward the 2-cm objects (respectively 2.2 [arbitrary] and 6.5 s; 1.5 [arbitrary] and 2.7 s; $p<0.05$) in the familiarization and long-term memory sessions. In the short-term memory session, the interest count and duration were found to be the highest toward the 8-cm objects (respectively 3.7 [arbitrary] and 7.4 s; $p<0.05$) and the lowest toward the 4-cm objects (respectively 1.2 [arbitrary] and 2.2 s; $p<0.05$).

CONCLUSION: We believe that the ideal object size is 6-8 cm in the novel object recognition test in which the interest to the object is associated with memory.

Keywords: Novel object recognition test, long term memory, short term memory

PC091

Cognitive Deterioration Following Strength Training in Adolescents

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AIM: Studies have demonstrated that aerobic exercise improves several aspects of cognition such as attention, executive functions, memory and processing speed. However, it is not clear how elite-level strength training affects cognitive function during adolescence. The aim of this study was to determine how a single session of strength training affects cognition in highly trained adolescents.

METHODS: Motor functions, ability of sustaining attention and executive functions of 25 elite female weightlifters were evaluated through finger tapping performance, simple visual reaction time (S- VRT), complex visual reaction time (C-VRT), simple recognition visual reaction time (SR-VRT) and complex recognition visual reaction time (CR-VRT) tests. Weightlifters were tested before and after a training session. In addition to descriptive statistics, t test and Wilcoxon test was used for inferential analysis.

RESULTS: There was a significant increase in mean CR-VRT of weightlifters after training (before: 491.9 ± 80.55 ms, after: 568.3 ± 104.23 ms) ($p<.01$). In SR-VRT and CR-VRT tests, rate of true answers decreased significantly after training (SR-VRT, before: %99.1 after: %96.9; CR-VRT, before %94.3 after: %91.4; $p<.05$). Total number of taps and mean inter-tap intervals did not show any difference among weightlifters before and after training ($p>.05$).

CONCLUSION: Adolescent weightlifters' executive functions are deteriorated following a training session. In future studies, the duration of this deteriorating effect of strength training can be investigated.

Keywords: adolescence, cognition, executive skill, reaction time, weightlifting

PC092

The Effect of Music on Subjective Time Perception

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AIM: The nature of time and how it is perceived is one of the important topics of psychology. It is controversial whether time perception of an individual is an innate characteristic or a cognitive process gained through experience and environment. In this study, it has been investigated whether music is effective on subjective time perception.

METHODS: This study included 11 healthy young adult volunteers (M/F, 0/11; Mean age±SD, 28.1±1.0 year) who gave consent. Subjective time perception was measured by prospective time-production and retrospective verbal time estimation tests. Volunteers were engaged in various activities (reading and isometric hand-grip) in the presence and absence of music and were asked to estimate passed time during the activity. In prospective measurements, the volunteers were asked to produce a pre-determined time interval by using reaction time device in the presence or absence of music. The estimated time rate (ETR) was calculated by dividing estimated time by actual time. An ETR<1 was accepted slower whereas an ETR>1 was accepted faster time perception. The results obtained in the presence and absence of music were compared with paired t-test.

RESULTS: Retrospective estimation was comparable in the presence versus absence of music (mean±SD 64.0±32.8 vs 67.0±32.4 sec, $p>0.05$). Prospective time production was similar in the presence or absence of music (72.6±18.6 vs 70.6±22.9 sec, $p>0.05$). All participants reported that they liked the music played. Prospective and retrospective ETRs similar with or without music (0.94±0.25 vs 0.90±0.27 and 0.81±0.36 vs 0.84±0.46 sec, respectively; $p>0.05$ for both).

CONCLUSION: It was concluded that the presence of music during various activities such as reading and physical exercise failed to affect retrospective time perception in healthy young adult women. The presence of music led no change in the results of prospective time production test.

Keywords: Cognitive psychology, estimated time ratio, music, subjective time perception,

PC093

Evaluation of Biceps Brachii Muscle Oxygenation and Differences in Oxygenation During Exercise and Resting States with Multichannel fNIRS

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AIM: Near infrared spectroscopy (NIRS) has recently become an important and rapidly developing noninvasive and inexpensive method for functional evaluation of skeletal muscle oxidative metabolism. The aim of this study is to develop a paradigm that demonstrates changes in muscle oxygenation in exercise and resting states and then to use this paradigm in pathological conditions such as muscle diseases. In this study, oxygenation of biceps brachii muscle during elbow flexion exercise and resting state of healthy participants were recorded with multichannel fNIRS system.

METHODS: This study included 14 healthy participants aged between 23-34 years, body mass index between 18.6 and 27.7, without chronic diseases and no implants to prevent elbow movement. The rhythmic elbow flexion exercise with the paradigm created in Nirstim program was performed by the participants. Contraction-induced oxygenation changes were recorded by fNIRS optodes placed on the dominant arm biceps brachii muscles. In this study, 7 channels were created with 3 sources and 3 detector optodes for recording. The use of a 7-channel system to evaluate oxygen delivery in contraction and resting states is an untested method in current studies. Paired t-test was used for statistical analysis of oxyhemoglobin / myoglobin levels recorded from each channel.

RESULTS: In fNIRS analysis, it was seen that oxyhemoglobin/myoglobin levels in biceps brachi were decreased with exercise and increased in resting state. In the statistical analysis, it was seen that the change levels of oxyhemoglobin/myoglobin concentration in exercise and resting states were significantly different in all channels (Channel1 $p=0.004$; Channel2 $p<0.01$; Channel3 $p<0.01$; Channel4 $p<0.01$; Channel5 $p<0.01$; Channel6 $p<0.01$; Channel7 $p=0.005$).

CONCLUSION: Spatial differences and changes in oxygen metabolism during exercise and resting states are demonstrated by the paradigm we have created. This paradigm can be used as a predictor for the onset or progression of muscle diseases especially myasthenia gravis disease.

Keywords: Biceps Brachii, fNIRS, Muscle Oxygenation

PC094

Neuro-Cortical Activity Variations Depends on Psycho-Physiological States

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AIM: The universal emotions defined independently of cultures, are induced by stimuli depending on subjective experiences, and cause neuro-physiological changes. Therefore, analysis of emotional EEG has been used for emotion recognition in order to detect cortical dysfunctions originated from psychiatric disorders. The aim of this study is to propose a new emotional EEG marker.

METHODS: 14-channel EEG series, downloaded from a dataset called DREAMER, were measured from 9 females and 14 males aged between 22-33 years old with 128 Hz sampling frequency with respect to international 10-20 placement system in response to watching 18 different video films. The largest principal components of full-band EEG phase space trajectories were used as emotional EEG markers. Firstly, statistical differences between males and females in emotional states were calculated through one-way ANOVA test, then these differences were transformed into cortical maps.

RESULTS: No significant differences ($p>0.5$) were observed in basic emotions, while meaningful differences ($p<<0.5$) were obtained in a mixed type emotion (amusement) between them. Regarding cortical maps, ignorable group differences ($p>=0.8$) were mostly observed at right temporal lobes. Regarding deep learning applications, emotional states, fear and excitement, calm and anger, surprise and amusement, sadness and amusement, happiness and surprise, happiness and sadness, were classified with the accuracies of %97.28, %94.47, %95.75, %94.15, %92.38, %91.83 respectively. Regarding histograms (Figure-2), the lowest EEG complexity levels were generated in calm and disgust, while the largest levels were observed in happiness and anger. In females and males, identical neuro-cortical functions were generated in basic emotions, whereas their responses were affected by subjective experiences in mixed type emotions.

CONCLUSION: The lower EEG complexity levels are correlated with the lower affective scores (valence and arousal). For recognition of emotional state, the largest principal component of full-band EEG phase space trajectories is proposed as new affective marker.

Keywords: EEG, emotion recognition, neuronal complexity, brain

PC095

The Effect of Nutrition with High Fructose Corn Syrup on Two Forms of Hippocampal Synaptic Plasticity

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AIM: In this study, long-term potentiation (LTP) and long-term depression (LTD) were recorded in corn syrup-fed rats in order to understand the effect of high-fructose nutrition on learning and memory processes.

METHODS: The study was conducted with 60 (100 ± 15 gr; 20 / group) 21 days old male Wistar Albino rats from Erciyes University Experimental Animal Research Center. Young male rats separated from their mother on the 21st day (1) unrestricted standard rat feed and tap water, (2) unrestricted feed and High Fructose Syrup solution (8%; 0.24 Kcal / mL) and (3) unrestricted feed and sucrose solution (10%, 0.4 Kcal / mL) for at least 60 days. Field potentials were recorded from the right dentate gyrus by stimulation of the right medial perforating pathway. LTP, high frequency stimulation; LTD was induced by low frequency stimulation. Th study was approved by Erciyes University Animal Experiments Local Ethics Committee.

RESULTS: As a result of the input / output curves analysis of the study groups before induction, the interaction between stimulation intensity and group was significant ($p < 0.01$). There was no significant difference in EPSP slope between high fructose corn syrup and sucrose groups (117 ± 5% and 123 ± 3%; $p > 0.05$), but significant increase was found in high fructose corn syrup group (262 ± 23%; = 0,03). In contrast, low frequency stimuli produced low amplitude LTD in sucrose and control rats, while it produced LTP in rats fed with high fructose corn syrup.

CONCLUSION: These findings indicate that feeding with foods containing high levels of fructose disrupts the balance between two forms of synaptic plasticity and thus may adversely affect learning processes. It was concluded that feeding with foods containing high fructose reduces synaptic deletion and makes it difficult to store new information.

Keywords: High fructose corn syrup, sucrose; Long-term empowerment; Long-term suppression; learning, memory.

PC096

Effect of Infusion of Methylene Blue into the Dentate Gyrus in Metaplasticity

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AIM: Methylene blue (MB) is an inhibitor of guanylate cyclase whose antiseptic properties are well known. Recent studies have shown that MB has positive effects on learning. Synaptic plasticity is the basis of learning and memory. Long term potentiation (LTP) and depression (LTD) forms of synaptic plasticity, can be considered as a change in synaptic strength due to the frequency of stimulation. Priming impulses (metaplasticity) affects learning by causing changes in LTP and LTD responses. The aim of the present study was to investigate the effect of MB infused into the dentate gyrus on metaplasticity.

METHOD: Sixteen Wistar type young adult rats were used. Anesthetized rat heads were fixed to the stereotaxic system and electrical stimuli were given through perforating way. Dentate gyrus was also infused with MB or serum physiologic (SF) and responses to stimuli were recorded. Metaplasticity was evaluated as population spike (PS) amplitude, and Excitatory Post Synaptic Potential (EPSP) slope were evaluated. Statistical analysis was performed with selected tests according to suitability. This study was approved by Erciyes University Ethics Committee and supported (18/139, Project TYL-2018-8661).

RESULTS: We found that priming of synapses with LFS differentially affected subsequent LTP induction in spite of similar magnitude of LTD of fEPSP slope. HFS could induce an LTP of fEPSP in the MB group whereas rats in the saline infusion group do not express a significant LTP. Nevertheless, a persistent LTP of population spike could be elicited in spite of priming in both groups. The PS at 5-min post-HFS period was significantly higher than baseline (saline:197,5 ± 12,9% and MB:233,5±12,8% and MB:209,3 ±19,4%;$t14=2,00$, $p=0,065$).

CONCLUSION: These results suggest that MB is a potential neuroprotector in learning deformations. MB seems to be able to benefit cognitive function by modulating metaplastic LTP response in neurodegenerative diseases such as Alzheimer's disease

Keywords: Metaplasticity, Methylene Blue, Hippocampus

PC097

A Novel Approach that Makes Diagnosing Sleep Breathing Disorders Easier by Analyzing in a Computer Environment the Physiological Features of Sound Tapes Recorded from Snorers. A New Product Diagnosing Sleep Breathing Disorder at Home

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AIM: Diagnosing prevalent sleep breathing disorders, such as primary snoring and obstructive sleep apnea syndrome (OSAS), has become viable by polysomnography (PSG) reputed globe wide as the golden standard method of diagnosis. PSG lasting overnight (at least 6 hours) with multiple electrodes and cables affixed to the patients' body; it allows analysis of only one patient per night in a room created in a hospital setting. Appointment period is very long (6 months-2 years) and is a system that bother the patient during the night. The aim of this study is to develop a novel method and innovative product that can make diagnosis of sleep breathing disorder easier by analyzing in a computer environment the physiological features of sound tapes recorded from snoring individuals.

METHODS: Numbers of apnea numbers recorded from 4 female and 1 male volunteers (Age; 49.2 ± 6.76 and BMI; 42.6 ± 8.16) having been diagnosed with sleep breathing disorder and snoring have been compared between classical PSG and our novel method. The new method analyzes the snoring sounds recorded during sleep and reaches the estimated number of apneas. Applied algorithms: Zero Crossing Rate, Energy, Spectral Flux, Spectral Centroid, etc.

RESULTS: In the end there was not a statistically significant difference measured between both methods (Paired Sample Test: p=0,708; Pearson Correlation Coefficient: 0,999***). The results showed 95.7% sensitivity, 97% specificity and 96.9% accuracy.

CONCLUSION: The novel method is a simple, convenient, effective and innovative product developed to assist diagnosing widely prevalent primary snoring and OSAS among patients intimidated or unwilling to enter operational sleep labs, who are unable to set an appointment or can only arrange appointment to a distant future; instead they can receive the same procedure in their homes and their own beds, inside their familiar environment with no disturbance and interference of electrodes and cables.

Keywords: Sleep, Electrophysiology, PSG, Snoring Signal Analysis

PC098

Possible Role of Nitric Oxide Synthase in Low-Frequency Stimulation-Induced Long-Term Potentiation in Aged Hyperthyroid Rats

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AIM: There is evidence that aging is associated with neurodegenerative diseases caused by thyroid dysfunction. Long-term depression (LTD) is the form of synaptic plasticity has a critical role in neurodegenerative memory disorders. In this study, we investigated the involvement of thyroid hormones in oxidative intracellular redox status and relationship between aging changes in hyperthyroidism and LTD induction.

METHODS: The study was performed on young and old Wistar albino male rats (n=26). In each group, 7 rats were used for electrophysiological recordings and 6 rats were used for antioxidant enzyme studies. Hyperthyroidism was induced by intraperitoneal injection of L-thyroxine 0.2 mg/kg/day for 21 days, starting on the 40th postnatal day. LTD responses were recorded from dentate gyrus by inducing perforating pathway with low-frequency stimulation. Nitric oxide synthase (NOS) and catalase (CAT) activity were measured using a commercial ELISA kit. Malondialdehyde (MDA) levels were measured according to method developed by Ohkawa et al.

RESULTS: LFS failed to induce a reliable LTD of synaptic efficacy and of neuronal output in euthyroid young and aged rats ($p>0.05$). However, same stimulus elicited a significant LTD in young hyperthyroid rats, but a significant LTP in aged hyperthyroid rats ($p<0,001$). Hyperthyroidism didn't alter age-dependent decrease in catalase activity and age-dependent increase in MDA levels, but higher levels of NOS levels were found in aged hyperthyroid rats compared to young hyperthyroid rats ($p<0.001$).

CONCLUSION: The study findings suggest that L-Thyroxine-induced changes in synaptic plasticity may show interaction with age. Because the increase in NOS levels may be indicator of glutamate toxicity. Therefore, increasing activity of NOS may be an indicator of this L-thyroxine-induced changes and may explain atypical changes in synaptic connectivity observed in hyperthyroidism leading to cognitive impairment in this disease.
This research was financially supported by the Erciyes University Research Found grant numbers: TYL-2016-6549 and TDK-2017-7696.

Keywords: Synaptic plasticity, Long-term depression, Nitric oxide synthase, Malondialdehyde

PC099

Effect of Nesfatin-1 on Oxidative Stress Parameters in Experimental Epilepsy Model

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AIM: Epilepsy is defined as a sudden and excessive activity of neurons involving some part or whole nervous system. In the present study, the effect of Nesfatin-1 on oxidative stress parameters was investigated in penicillin-induced epilepsy models.

METHODS: A total of 35 adult male Wistar rats were used and rats were divided into 7 groups (n=5) as control and Nesfatin-1 groups (at 12.5, 25, 50, 100, 200, 400 pmol doses). All rats were anesthetized with the urethane (1.25 g/kg, i.p.). Epileptiform activity was induced by penicillin (400IU, i.c.) and after the 30th minutes of penicillin application, Nesfatin-1 doses was injected (i.c.v.). The experiment was terminated 180 minutes after the onset of epileptic activity. Then, the rats were decapitated and the brain tissues were stored at -80°C for biochemical analysis. Superoxide dismutase (SOD), malondialdehyde (MDA), glutathione (GSH), glutathione reductase (GR) and glutathione peroxide (GPx) levels in brain tissue were measured by ELISA method. Statistical analysis of the data was performed by the One-Way ANOVA and Tukey tests.

RESULTS: Nesfatin-1 showed no effect on SOD and MDA ($p>0.05$). There was significant decreased in the levels of GSH in Nesfatin-1 (12.5 pmol) compared to control, 100, 200 and 400 pmol groups ($p<0.05$). GR levels were found to be significantly increased Nesfatin-1 25, 50, 100, 200 and 400 pmol groups compared to control group ($p<0.05$). GPx levels was significantly higher in Nesfatin-1 400 pmol group compared to control and all other Nesfatin-1 groups ($p<0.05$).

CONCLUSION: The effect of Nesfatin-1 on epilepsy is thought to be mediated by the glutathione enzymes. GR activity may be elevated as a protective against oxidative stress products occurring during epileptic activity. Further studies are needed to elucidate the dose-dependent effects of Nesfatin-1 on glutathione enzymes in epilepsy.

This study was supported by Amasya University (Project number: FMB-BAP 17-0288).

Keywords: Oxidative stres, Experimental epilepsy, Nesfatin-1, Neuropeptide

PC100

The Effects of *Ginkgo Biloba* on Picrotoxin-induced Epileptiform Activity in Rats

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AIM: *Ginkgo biloba* standardized leaf extract (EGb 761) has been extensively used in some modern medical applications, particularly in cognitive performance problems. However, several clinical and experimental studies have suggested that EGb 761 and other ginkgo products may be associated with epilepsy. The aim of the present study was to investigate the effects of EGb 761 on the epileptiform activity induced by picrotoxin (PTX) in male Wistar rats.

METHOD: In the experiments, 8 weeks old male Wistar rats divided into 6 groups were used. The animals were intraperitoneally injected with saline, 50, 100, 200 mg/kg EGb 761, 300 mg/kg sodium valproate or 100 mg/kg topiramate for 14 days. Epileptiform activity induced by PTX (10 µg, i.c.v.) was observed and recorded by electrophysiological method. EEG data related to epileptiform activity were analyzed by Mann-Whitney U test after Kruskal-Wallis. This study was approved by the Karadeniz Technical University Animal Experiments Local Ethics Committee (Protocol No: 2014/46).

RESULTS: Administration of 200 mg/kg EGb 761 significantly increased the spike frequency of PTX-induced epileptiform activity ($p<0.05$). In addition, it was found that EGb 761 increased dose-dependent spike amplitude and decreased latency of epileptiform activity, but these effects were not statistically significant. Although sodium valproate (300 mg/kg) injection decreased spike frequency, this effect was not statistically significant. In addition, no changes were observed in the topiramate group (100 mg/kg).

CONCLUSION: According to the findings, *Ginkgo biloba* extract EGb 761 increases PTX-induced epileptiform activity. It should be noted that high-dose EGb 761 may lead to an increase in neuronal excitability in patients receiving *Ginkgo biloba* extract EGb 761.

Keywords: Epileptiform activity, Ginkgo biloba, Picrotoxin, Rat

PC101

Effect of Infusion of Lithium Carbonate into the Dentate Gyrus in Long-Term Depression

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AIM: Lithium (Li) has been shown to inhibit various enzymes directly in vitro such as inositol monophosphatases, bisphosphate 3′-nucleotidase, cyclooxygenase and isoforms of glycogen synthase kinase 3 (GSK-3). GSK3β is constitutively active in cells under resting / unstimulated conditions and is primarily regulated through inhibition of its activity by phosphorylation. Although, accumulating evidence is delineating a neuroprotective and neurotrophic role for Li, the short-term effects Li on the long-term depression (LTD) are still unknown.

METHODS: Sixteen Wistar type young adult rats were enrolled to this study. Field potentials were recorded from the Dentate Gyrus, stimulating perforant pathways, in rats acutely treated with LiCO3 and their corresponding control rats. LTD was induced by prolonged 1-Hz low-frequency stimulation. Lithium Carbonate at the dose of 10 mM was infused by a Hamilton pump starting from LTD induction.

RESULTS: Considering saline infusion experiments, we found that prolonged 1-Hz stimulation induced a durable LTD of synaptic strength (87.9±3.2% of pre-LFS baseline). This type of LTD was completely inhibited by GSK3β (102.5±3.9; n = 8 /group; t14= 2.86; p = 0.012). Interestingly, population spike amplitude was not depressed, but rather potentiated to 153.8%±8.1% of baseline in saline infusion experiments, a value which was not significantly, but slightly higher than that in Li infusion experiments (128.9%±8.9% of baseline; t14= 2.08; p = 0.056).

CONCLUSION: Despite most data suggest that lithium always yields neuroprotective effects against neuropathological conditions; we concluded that short-term treatment of lithium disrupts hippocampal synaptic plasticity underlying forgetting mechanism.

Keywords: Lithium, Long-term plasticity, Hippocampus, Glycogen Synthase Kinase 3

PC102

Investigation of Task-Neglect in Stroop Test by Event Related Potentials

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AIM: In Stroop test, task is to indicate print color of single color name words while ignoring word meaning. Prolongation in reaction times and increase in number of errors are observed in stimuli with color-word incongruency condition. Increased frequency of congruent stimuli increase effort for sustaining attention and induce task neglect which is reported lead to impairment in task performance. Although Stroop test involves several cognitive processes, event-related potential (ERP) components related with Stroop test is quite limited. We aimed to find ERP component(s) that are indicative of sustained attention during Stroop test by inducing task neglect.

METHODS: 11 healthy volunteers (5 women, 6 men) participated in the study. EEG was recorded while two versions of the computer-based Stroop test were applied. In one block congruent and incongruent stimuli were equal (standard version), while in the other block 80% of the stimuli were congruent and 20% of them were incongruent (task-neglect version). In the grand average ERPs N450 wave was apparent in the incongruent stimuli waveforms. This wave was evaluated in the post-stimulus 400-550ms. Repeated-measures ANOVA designs were used for the statistical analyses.

RESULTS: Stroop effect occurred independent from the task neglect (reaction times for incongruent stimuli were longer, p=0.025). In task neglect version of Stroop test, more errors were committed (p=0.002). Regardless from the version of Strop test, N450 peak was more negative in response to the incongruent stimuli (p=0.001). Follow-up analyses on both version of the test revealed significantly more negative N450 peaks in the incongruent condition (standard Stroop, p=0.003; Stroop with task-neglect, p=0.026). N450 amplitude did not differ based on the task version.

CONCLUSION: In line with literature, we observed more errors when task neglect is induced. N450 wave occurred apparently in the incongruent condition. However, N450 or any other ERP component was not an indicator for goal neglect.

Keywords: Event related potentials, neurophysiology, Stroop test

PC103

The Short-Term Effects Lithium Carbonate on Metaplasticity of Long-Term Potentiation in vivo

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AIM: Among several targets, lithium has been shown to directly inhibit glycogen synthase kinase 3 alpha and beta (GSK3α and GSK3β). GSK3β is constitutively active in neurons under unstimulated conditions and is primarily regulated through inhibition of its activity by phosphorylation. Although, accumulating evidence is delineating a neuroprotective and neurotrophic role for Li, the short-term effects Li on metaplasticity of long-term potentiation (LTP) are still unknown.

METHODS: Sixteen Wistar type young adult rats were enrolled to this study. Field potentials were recorded form the Dentate Gyrus, stimulating perforant pathways, in rats acutely treated with LiCO3 and their corresponding control rats. The long-term potentiation was induced by a tetanic stimulation protocol 5-min after prolonged 1-Hz low-frequency stimulation. Lithium Carbonate at the dose of 10 mM was infused by a Hamilton pump starting from LTP induction.

RESULTS: Considering saline infusion experiments, we found that prolonged 1-Hz stimulation inhibited metaplastic LTP of synaptic strength (81.1±6.7% of pre-LFS baseline). Metaplastic LTP inhibition was not observed in Li infusion experiments (115.5±5.8; n = 8 /group; t14= 3.85; p = 0.002). Nevertheless, PS amplitude was not depressed, but rather potentiated to 162.9%±12.8% of baseline in saline infusion experiments, a value which was not significantly, but slightly lower than that in Li infusion experiments (214.9%±25.1% of baseline; t14= 1.84; p = 0.086).

CONCLUSION: Despite most data suggest that lithium always yields neuroprotective effects against neuropathological conditions; we concluded that short-term treatment of lithium disrupts the ability of synaptic plasticity to be modified by prior experience.

Keywords: Lithium, Hippocampus, Learning and Memory, Long-term Potentiation, Metaplasticity

PC104

Effect of Tadalafil in Penicillin-Induced Epileptiform Activity

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AIM: Epileptiform activity induced by the administration of penicillin into the brain cortex is one of the commonly used experimental models and mimics partial seizures in humans. Tadalafil, a phosphodiesterase type-5 enzyme inhibitor commonly used in erectile dysfunction and pulmonary hypertension, produces its effects on the nitric oxide pathway by inhibiting cGMP degradation. Nitric oxide pathway plays an important role in the pathogenesis of epilepsy. The aim of this study was to investigate the effect of tadalafil in penicillin-induced epileptiform activity.

METHODS: Wistar male rats (n=36) were randomly divided into 6 groups. Epileptiform activity was induced by the injection of 500 IU Penicillin-G to the brain cortex by a Hamilton microinjector in a volume of 2.5 microliters. The solvent of tadalafil, sterile physiological saline, was given to the control group. Tadalafil, at the doses of 2.5, 5, 10, 25 and 50 mg/kg, was administered intraperitoneally 30 minutes after penicillin injection. Spike activities were recorded for 180 minutes after drug injection and compared with the control group. After verifying that the data were normally distributed, one-way analysis of variance (ANOVA) and Tukey-Kramer post-hoc tests were performed for multiple comparisons. The study was approved by local ethics committee (OMU HADYEK).

RESULTS: Tadalafil did not statistically change the spike frequency and amplitude at any given doses compared to the control group (p>0,05).

CONCLUSION: Studies have shown that at the doses of 10 and 20 mg/kg, tadalafil administration increases the generalized seizures induced by pentylenetetrazole. In our study, tadalafil did not show a significant change in spike frequency and amplitude. We suggested that the difference of the experimental model could cause this effect. In the next stage of this study, the effect of chronically administered tadalafil will be investigated in penicillin-induced epileptiform activity.

Keywords: Tadalafil, Epilepsy, Penicillin, Rat

PC105

The Role of 5-HT1A Serotonin Receptor on the Effect of 5-Hydroxytryptophan in Penicillin-Induced Epileptiform Activity

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AIM: 5-Hydroxy tryptophan (5-HTP) is a serotonin precursor. Vilazodone is an antidepressant which is a 5-HT1A receptor agonist. NAN-190 is a selective 5-HT1A receptor antagonist. The aim of this study was to investigate the role of 5-HT1A serotonin receptor on the effect of 5-HTP on penicillin induced epileptiform activity.

METHODS: In our study, thirty male albino Wistar rats were used. All rats were divided into five groups (n:6): I- Penicillin group (Control); II-5-HTP (50 mg/kg, intraperitoneally (i.p)) group; III- 5-HTP (50 mg/kg, i.p) + vilazodone (10 mg/kg, i.p) group; IV- 5-HTP (50 mg/kg, i.p) + NAN-190 (5 mg/kg, i.p) group; V- 5-HTP (50 mg/kg, i.p) + NAN-190 (5 mg/kg, i.p) + vilazodone (10 mg/kg, i.p) group. Epileptiform activity was induced by using a Hamilton microinjector to administer 500 IU of Penicillin-G to the cortex (intracortical) in a volume of 2,5 microliters. 30 min after the injection of penicillin, drugs were applied. This study was approved by the Animal Experiments Local Ethics Committee (OMU HADYEK) and supported by OMU Project Office (PYO.TIP.1904.17.018). One-Way Anova and Post Hoc Tukey tests were used for statistical analysis.

RESULTS: Compared with the control group, 5-HTP (50 mg/kg) significantly reduced spike frequency throughout the experiment ($p<0.05$). When 5-HTP and NAN-190 were applied together, spike frequency decreased significantly between 30-70 and 90-180 minutes ($p<0.05$). When 5-HTP and vilazodone were administered together, the spike frequency decreased significantly during the experiment ($p<0.05$). When 5-HTP, vilazodone and NAN-190 were applied together, all the subjects lost their lives. No statistically significant difference was found between the groups in terms of amplitude values ($p>0.05$).

CONCLUSION: 5-HTP showed an anticonvulsant effect on penicillin-induced epileptiform activity. Vilazodone increased the anticonvulsant effect of 5-HTP; NAN-190 reduced. Further studies are needed to explain the interaction mechanism of 5-HTP, vilazodone and NAN-190 on epilepsy.

Keywords: Vilazodone, Epilepsy, Penicillin, Rat, NAN-190

PC106

The Effects of Melatonin Administration on Vasomotor Activity of Thoracic Aorta in Rats with Experimental Hyperthyroidism

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AIM: Hyperthyroidism is a common endocrine disorder with multiple aetiologies, manifestations and potential therapies. Effects of the principal hormone of the pineal gland melatonin (MEL) on vascular tissues are still vague. The aim of this study was to investigate the effects of MEL on isolated aortic rings of rats with hyperthyroidism and its role in the vascular reactivity to contractile agents such as, potassium chloride (KCl) and phenylephrine (PHE).

METHODS: Thirty-four male rats were divided into four groups: Control, hyperthyroid, melatonin, hyperthyroid+ melatonin. Hyperthyroidism was induced by ip 0.3 mg/kg/day L-Thyroxin for 2 weeks. MEL administration was used as 3 mg/kg/day via i.p and in vitro MEL administrion was used as a 10-4/10-10 M doses in the bath. PHE and KCI were implemented to the bath with a protocol and dose-response curves were obtained. Data were analyzed statistically by ANOVA using Tukey test ($p<0.05$). The study was approved by the Ethical Committee of Ataturk University.

RESULTS: The aortic rings from the hyperthyroid group had significantly lowered contractile responses compared with the rats in the control group ($p<0.05$) and the in vivo MEL administration attenuated the decreases in contraction responses compared with the hyperthyroid group. KCl-induced contraction responses showed that contractile responses from the MEL group increased compared with all other groups, whereas hyperthyroid and hyperthyroid+melatonin groups showed a decrease in contraction responses compared with the control group. The decrease in the contraction response in the hyperthyroid group was significantly higher than the melatonin+hyperthyroid group ($p<0.05$).

CONCLUSION: PHE and KCl-induced contractions were significantly suppressed in the thoracic aortic rings isolated from rats with L-thyroxine-induced hyperthyroidism. The responses of contraction of aortic rings that decreased due to hyperthyroidism, partially attenuated by in vivo and in vitro melatonin administration. In summary, MEL prevents the decrease of vascular resistance induced by hyperthyroidism. The study was supported by Ataturk University (BAP, 2017/6152).

Keywords: Hyperthyroidism, melatonin, vascular reactivity.

PC107

Optimization of Cortisol Measurement in Human Hair

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AIM: Cortisol is secreted as an end product of the hypothalamo-pituitary-adrenal axis in response to stress reactivity. Its measurement in hair represents retrospective cortisol secretion because it accumulates in the hair as it grows. Aim of the current study was to optimize the method of cortisol measurement in the hair.

METHODS: For that purpose, bulk hair samples belonging to 20 male individuals were either pre-washed with isopropanol or not. Afterwards, they were either cut into small pieces by a scissors or smashed by the help of liquid nitrogen. The samples prepared were extracted into methanol by the help of temperature (16 h at 52 C), ultrasound (2 h) or ultrasound (2 h) + temperature (16 h at 52 C). Samples were prepared in duplicate and were analyzed ELISA for cortisol measurement (n=480). Kruskal-Wallis was used to analyze the data as the data did not have a normal distribution. Data were presented as median (min-max) and an alpha level less than 0.05 were denoted as significant.

RESULTS: The analyses show that there was no significant difference between washing and not washing procedures (19.5 vs. 20.6, respectively; P=0.247). Cutting the hair into small pieces yielded slightly lower but significant cortisol levels (17.4 vs.22.0 pg/mg, P=0.002). There was no difference between temperature, ultrasound or temperature+ultrasound (20.2, 19.7, 19.6 pg/mg, respectively, P=0.971).

CONCLUSION: Hair cortisol measurement was successfully validated and it seems that any of the methods described can be used. Although, smashing the hair with the help of liquid nitrogen and a pestle yielded higher cortisol levels, this was accepted as a minimal increase when compared to wider distribution of hair cortisol levels. The method provides a tool to measure chronic stress levels retrospectively. Supported by the Scientific Research Unit (BAP, TDK-2017-812), İnönü University, Malatya.

Keywords: Human Hair cortisol, Method Optimization, Hypothalamo-pituitary-adrenal axis

PC108

The Relationship Between Basal Metabolic Rate, Body Composition and Lipid Profile with Vitamin D in Obese Male Subjects

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AIM: According to body mass index (BMI) used in World Health Organization's classification of obesity is defined as 30.0-34.99 kg/m2 class I obese, 35.0-39.99 kg/m2 class II obese and ≥40 kg/m2 class III obese. The aim of this study was to determine the relationship between vitamin D, basal metabolic rate, body composition and lipid profile in obese male subjects.

METHODS: 234 obese male subjects who applied to Obesity Policlinic of Goztepe Training and Research Hospital, Istanbul Medeniyet University were included in our retrospective study (Ethics Committee Number: 2019/0211). Body composition analyzes of the obese males were measured with bioelectrical impedance analyzer (TANITA-48M) and blood parameters were determined by biochemical tests. Shapiro-Wilk, Spearman's rho and Pearson correlation tests were used for data analysis and $p<0.05$ was considered as statistically significant.

RESULTS: According to the obesity classification, 97 males (41.45%) were class I obese, 79 males (33.76%) were class II obese and 58 males (24.79%) were class III obese. The mean age of obese males was 46.24±12.2. The mean vitamin D values were found 18.46±15.18; while the number of obese men with normal vitamin D values was 19 (8.1%), the number of obese men with deficient or insufficient vitamin D levels was 214 (91.45%). Only 1 (0.42%) obese male had vitamin D intoxication. Negative correlation was found between total cholesterol and vitamin D levels in obese males with normal vitamin D values. High-density lipoprotein and vitamin D levels positively correlated in class II obese males. It was determined that vitamin D decreased as body mass index and fat percentage increased in class III morbidly obese males ($p<0.05$).

CONCLUSION: Vitamin D supplementation may be important due to the high prevalence of vitamin D deficiency in obese males.

Keywords: Obese males, Vitamin D, lipid profile, body composition

PC109

Intracerebroventricular MOTS-C Infusion Increases Peripheral Uncoupling Proteins in Rats Generated From Experimental Obesity Model

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AIM: Obesity is a chronic disease that is based on genetic and environmental interaction due to the increase in body fat mass as a result of the energy being more than the energy consumed. Mitochondrial derived peptide (MOTS-c) is a peptide discovered in 2015. Studies have shown that MOTS-c plays an active role in cell metabolism while reducing obesity. Uncoupling protein (UCP) synthesized from the inner membrane of mitochondria plays a role in the function of mitochondrial membrane and regulation of cellular energy. This study was conducted to investigate the effects of icv MOTS-c infusion on peripheral UCPs in rats with experimental obesity model.

METHODS: Forty male Wistar-Albino rats were used in the study. The rats were divided into 4 groups (n=10). 21-days-old rats were fed with high fat diet (Research Diet) for 12 weeks. Obesity model was confirmed by Lee index scoring. Then, rats other than the control group were anesthetized and osmotic mini-pumps were connected to brain infusion kits placed in the lateral ventricles. The sham group received 5 µl/h of yBOS and the study groups received 5µl/h of 10 and 100 µM MOTS-c infusion for 14 days. In the 15th day, the rats were decapitated and muscle, white and brown fat tissue samples were collected. UCP3 mRNA levels from muscle, UCP1 from white and brown fat tissues were determined by RT-PCR method.

RESULT: MOTS-c infusion was found to increase UCP1 mRNA levels in white and brown fat tissues and UCP3 mRNA levels in muscle tissue ($p<0.05$).

CONCLUSION: The results of the study show that MOTS-c can play important physiological roles in energy metabolism through UCPs. The mechanisms by which MOTS-c performs the roles it plays in increasing UCP activity should be explored through more comprehensive studies.

This study was supported by TUBITAK with Project number 116S744.

Keywords: MOTS-c, UCP1, UCP3, obesity, infusion

PC110

Effect of Systemic Adropin Administration on Oxidative Stress in Diabetic Rat Liver Tissue

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AIM: Adropine is a peptide molecule. In 2008 Kumar et al. described it as an agent that produces strong metabolic effects on various tissue types. This hormone-acting peptide is encoded by Energy Homeostasis Associated Gene (ENHO), which is expressed in the brain and liver. In our study; we aimed to investigate the effects of Adropin, which is known to have positive effects on glucose intolerance and insulin resistance; on oxidant antioxidant levels in liver tissue of diabetic rats.

METHODS: Adult male Wistar albino rats (n=28) were divided into 4 groups. Diabetes was induced by intraperinoneally administrated single dose of Streptozocin (STZ-65 mg/kg in 0.1M citrate buffer). A single dose of citrate buffer was administered to the control groups.72 hours after STZ administration a basal blood glucose level above 250 mg/dL were considered diabetic.10 weeks after STZ administration, adropine was administered intraperinoneally twice daily at a dose of 450 nmol/kg/day was applied for 10 days. At the end of the period, rats were sacrificed by taking blood from their hearts under 45 mg/kg ketamine 5 mg/kg xylazine anesthesia. Liver tissue oxidant (Malondialdehyde, MDA) and TAS-TOS levels were evaluated. Results were compared with Kruskal Wallis and Tukey tests, $p<0.05$ values were considered significant. Ethical Comittee for the Use and Care of Laboratory Animals of Gazi University approved the procedures used in this study.

RESULTS: TOS increased in the diabetes group ($p<0.05$) however, Adropine administration caused some decrease but these changes were not significant. While TAS decreased significantly ($p<0.05$) in the diabetes group, TAS significantly increased in Adropine-treated diabetic rats. While MDA, which is an indicator of lipid peroxidation, increased significantly ($p<0.05$) in the diabetes group compared with control, Adropin did not cause a significant change in elevated MDA levels.

CONCLUSION: Our results indicate that systemic adropine increases the level of antioxidant in diabetic liver tissue but does not significantly change the increased oxidant stress with diabetes. We suggest that evaluation of different parameters with different administration time and dose studies will provide support to the literature.

Keywords: Adropin, Liver, Diabetes, Oxidative stress

PC111

Metabolic Effect of Moderate Swimming Exercise on Elderly Rats

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AIM: The aim of the study is to investigate the effects of regular, moderate exercise on metabolic changes occur in liver, muscle and adipose tissues with aging.

METHOD: In the study 32 male Sprague-Dawley rats (300-500 g) aged between 11-12 months and 15-16 months old were used. The study was randomly separated into four groups and 8 rats in each group. Groups; Control (C1/11-12 months), Exercise (E1/11-12 months), Control (C2/15-16 months), Exercise (E2/15-16 months). 30 minutes /per day, 5 days / week training period 8 weeks, moderate swimming exercise was applied.

RESULTS: Histopathologically, no significant difference was observed between the groups ($p>0.05$). On immuno-histochemical evaluation; Expressions of Hif-1, TNF-alpha, iNOS and Caspase-3 were found statistically meaningful to increase in expression on liver, muscle and adipose tissue in K1 and K2 groups and decrease of expression in E1 and E2 groups ($p=0.001$).

CONCLUSION: It has been demonstrated that aerobic activity of swimming exercise protects against hypoxic state, closes apoptotic pathway in metabolic organs and may have protective effect against oxidative stress and inflammation caused by aging

Keywords: Fat, Liver, Muscle Metabolism, Swimming Exercise

PC112

Evaluation of the Relationship Between HbA1c Level and 25 Hydroxyvitamin D and Vitamin B12 in Type 2 Diabetes Mellitus Patients

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AIM: Beginning with insulin resistance in the early stages, pancreatic β-cell dysfunction also plays an important role in type 2 diabetes mellitus (DM) pathogenesis. The disease is observed in all age groups, with rapidly increasing global prevalence and significant chronic complications. Cobalamin (B12) support lowers homocysteine in the body. In type 2 DM, homocysteine levels are higher than in normal individuals. Hyperhomocysteinemia is a risk factor for cardiovascular diseases. The aim of this study is to determine whether there is a correlation between HbA1c levels with 25-hydroxyvitamin D, fasting glucose levels and B12 vitamin.

METHODS: This retrospective study used data from measurements of HbA1c, fasting blood glucose, 25-hydroxyvitamin D and B12 vitamin in 155 patients (116 female, 39 male) with type 2 DM diagnosis attending Uşak University Faculty of Medicine Education and Research Hospital Endocrinology Clinic. Statistical analysis was performed with Spearman correlation analysis.

RESULTS: Of patients, 74.8% were female and 25.16% were male. The mean age of patients was 56±10.19 years, with body mass index (BMI) of 32.12±4.86 kg/m2. When compared with normal value intervals, HbA1c value was 7.02±6.65%, fasting blood glucose was 155.29±133 mg/dL, 25-hydroxyvitamin D was 16.09±13.39 ng/mL and B12 vitamin had mean value of 413.24±356 ng/L. The results of correlation analysis identified a weak but significant positive correlation between 25-hydroxyvitamin D and B12 vitamin ($p<0.05$) ($r=0.242$). Additionally, there was a weak but significant positive correlation identified between fasting blood glucose and BMI values ($p<0.05$) ($r=0.162$).

CONCLUSION: In our study, the correlation between HbA1c levels with fasting blood glucose values, 25-hydroxyvitamin D and B12 vitamin in type 2 DM patients was found to be statistically significant. We consider this result will form significant clinical data in terms of monitoring type 2 DM patients and taking precautions against diseases with risk in advanced periods like hyperhomocysteinemia.

Keywords: Type 2 DM, 25- Hydroxyvitamin D, Vitamin B12.

PC113

Perinatal and Adolescent High Fat Diet Induced Changes in Autonomic Outflow and Phenotype

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AIM: Exposure to high fat diet (HFD) during perinatal age and adolescence has been shown to induce neuroplastic changes in autonomic circuitry. Using rats exposed to maternal and adolescent HFD, this study was designed to investigate the changes in autonomic outputs.

METHODS: 10-week age Wistar male rats were divided into two groups as; rats born from the pregnant rats fed with HFD from prenatal day-14 to postnatal day-21 (perinatal HFD) and rats fed with HFD from 4-week age (adolescent HFD). In anesthetized (ketamine 60 mg/kg; xylazine 6 mg/kg, ip) 10-week age male rats, electrocardiography (ECG) was recorded and heart rate variability (HRV) was analyzed. Rats then were sacrificed and epididymal fat tissues were removed and weighed. Data were analyzed with Kruskal Wallis followed by Mann Whitney-U test. Experimental protocols were approved by the Animal Ethical Committee of Akdeniz University (2017.09.005).

RESULTS: Compared with control rats, high frequency component (HF) was found to be lower; low frequency component (LF) and LF:HF an indicator of sympatho-vagal balance was found to be higher in both HFD-fed groups, especially in male rats exposed to maternal HFD. As compared with control rats, the weights of epididymal fat tissues per gram of each animal were higher in both HFD-fed groups, especially in male rats exposed to HFD in adolescence.

CONCLUSION: The present data indicate that perinatal HFD resulted in long-lasting alterations in autonomic signaling rather than phenotypic features, while exposing HFD in adolescence caused phenotypic changes rather than affecting autonomic signaling.

Keywords: Heart rate variability, high fat diet, sympathetic tone, visceral fat.

PC114

Effects of Ghrelin on Energy Balance on Brain Tissue of Sepsis-Induced Rats

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AIM: Sepsis, which is described as the increased and irregular response of host to inflammation and multiple organ failure were reported as one causes of mortality and morbidity. Sepsis mediated encephalopathy has a high incidence in intensive care hospitalization. Lipopolysaccharide (LPS) is a molecule in a glycolipid structure which is obtained from the cell wall of the Gram-negative bacteria. Sepsis was reported to damage the brain blood flow, and decreased its activity consequently resulting with mitochondrial dysfunction and energy imbalances in the studies with lipopolysaccharide. We aimed to investigate the effects of an antioxidant peptide-ghrelin, which is known as the growth hormone endogenous ligand, on energy balance in the brain tissue of sepsis-induced rats.

METHODS: Adult Wistar albino male rats were divided into 4 groups as the control (n:8), LPS (5 mg/kg i.v., and 5 mg/ kg i.p after 12 hours) (n:10), Ghrelin (10 nmol/kg i.v.) (n:10), and LPS+Ghrelin (n:10) (Ethics number: 2013/123) in the study. The brain tissues of the rats were taken out under anesthesia 24 hours after the first injection. The tissues were homogenized in acid medium. The AMP, ADP, ATP, Creatine, Creatine phosphate levels were measured with high performance liquid chromography (HPLC) method from homogenates. Statistical analysis was performed by one-way variant analysis, and Tukey test.

RESULTS: In the LPS group, AMP, ATP, Creatine and Creatine phosphate levels were found significantly lower ($P<0.01$; $P<0.01$; $P<0.05$; and $P<0.01$, respectively) compared with the levels in other groups, and ADP levels were significantly higher ($P<0.01$). No significant difference was detected between the other experimental groups ($P>0.05$).

CONCLUSION: In conclusion, exogenously administered Ghrelin appears to be an effective agent in regulating the disturbed energy balance in LPS induced sepsis. We suggest that Ghrelin performs this effect by regulating lipid and glucose metabolisms in the central nervous system.

Keywords: Ghrelin, LPS, sepsis, brain, energy

PC115

Determination of the Effects of In Vivo Melatonin Application on Thyroid Hormone Levels in Kidney Tissue of Experimental Hyperthyroid Rats

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AIM: The aim of this study was to determine the effect of melatonin, an inhibitory neuroendocrine hormone, on T3, T4 and TSH levels in renal tissue of experimental hyperthyroid rats.

METHODS: In this study, 23 male Wistar Albino rats were used. The groups were divided into four groups as control (n=5), hyperthyroidism (n=6), melatonin (n=6) and hyperthyroidism+melatonin (n=6). L-thyroxine was administered at a dose of 0.3 mg/kg/day for 14 days to produce experimental hyperthyroidism. Melatonin was injected intraperitoneally 3 mg/kg/day at 21:00 in the evening for 14 days. Abdominal regions of rats were opened after the injection applications were completed. Rat (T3, T4, TSH) ELISA kit was used to determine the hormone levels in kidney tissues. Statistical analysis was performed by using ANOVA test with SPSS program and values of $p < 0.05$ were considered significant. Ethical consent was obtained by the Scientific Ethics Committee of Experimental Animals of Atatürk University with the letter 42190979-E.1700019841 dated 17/01/2017.

RESULTS: In our study, the lowest T3 level was found to be in the melatonin-treated group. However, this decrease was not statistically significant. There was a significant increase in T3 level in hyperthyroid group compared with melatonin group ($p<0.05$). T4 levels increased in all groups. However, there was a statistically significant increase in hyperthyroidism group compared with the control group ($p<0.05$). TSH levels were higher in hyperthyroid groups and it was statistically significant ($p<0.001$).

CONCLUSION: In our study, the effects of melatonin on thyroid hormone levels in rat kidney tissue were determined in hyperthyroidism. In our study, when compared with the control group, it was found that the levels of hormones in the kidney tissues of rats with hyperthyroidism increased and Melatonin administration decreased the levels of these hormones.

This study was supported by Atatürk University BAP Unit with project number TDK-2017-6152.

Keywords: Hyperthyroidism, Kidney, Melatonin, Thyroid hormones

PC116

Effect of Fructose-Induced Metabolic Syndrome on Spatial Learning and Memory Tests

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AIM: Metabolic Syndrome (MetS) is a fatal endocrinopathy in which systemic disorders such as abdominal obesity, glucose intolerance, dyslipidemia, and hypertension begin with insulin resistance. MetS has been suggested to be a risk factor for cognitive decline and memory impairment. In this study, the possible effects of MetS on spatial learning and memory in rats were investigated using Morris Water Maze (MWM).

METHODS: 10 Wistar male rats were used in the study, 5 control and 5 MetS groups. MetS were formed by adding 20% fructose to the drinking water for 13 weeks. The control group received only tap water during this period. Fasting plasma insulin levels for MetS confirmation were measured. Learning and memory tests were performed with MWM. The latency time of the rats was measured for their learning performance, a memory test was performed on the 1st and 5th days. Swimming speeds were measured to confirm the motor functions. The results were given as ± standard error and the difference between the groups was evaluated using Mann-Whitney U test and SPSS package program. The study protocol was approved by Pamukkale University Animal Experiments Ethics Committee

RESULTS: Plasma insulin levels of MetS group were higher than control group. There was no difference between the learning performances of the rats in each experimental group. No significant difference was found between swimming rates. This shows that the motor functions of rats are intact. There was no significant difference between the two groups in the recall tests obtained on days 1 and 5.

CONCLUSION: In the MetS model, it was seen that learning and memory test results in MWM did not deteriorate significantly compared with control. The small number of rats in groups is a limitation of the study. The results obtained in this study are consistent with similar studies.

Keywords: Memory, metabolic syndrome, spatial learning

PC117

Determination of Acetylcholinesterase Enzyme Activity in Liver Tissues of Rats with Hyperthyroidism

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AIM: Acetylcholinesterase (AChE) is an important enzyme that plays an important role in various morphometric processes, cell adhesion and migration, apoptotic pathways and tumor suppression. AChE levels are also used as a possible marker of liver function tests in pesticide intoxications. Liver has an important role in the transport, storage and metabolism of thyroid hormones. Hypermetabolic state caused by increased oxygen consumption in hyperthyroidism has indirect effects on liver. The aim of this study was to investigate how AChE enzyme activity is affected in liver tissues of rats by hyperthyroidism.

METHODS: 14 adult male Wistar albino rats weighing 250-300 g were used in this study. Rats were divided into two groups as control (C, n:7) and hyperthyroidism (H, n:7). 0.5 cc %0.9 NaCl was given for C group, 0, 3 mg/kg/gün L-thyroxine intraperitoneally for 14 days. Rats were sacrificed on the 15th day and blood and liver samples were taken. Blood samples were measured for T3, T4 and TSH levels and hyperthyroidism was evaluated. AChE enzyme activity in rat liver tissue were analyzed using Ellman spectrophotometric method. Statistical analysis was performed using t-test in Graphpad program.

RESULTS: AChE enzyme activity was determined in two different experimental groups (C and H). It was found that AChE activity in C group was 5,644 ± 0,412 EU / mg protein and H group was 4,362 ± 0,387 EU / mg protein. As a result of study, liver AChE enzyme activity in group H decreased by 22.71% compared to group C and it was found to be significant as $p < 0.001$.

CONCLUSION: According to the results of this study, hyperthyroidism decreased liver AChE enzyme activity, which plays an important role in physiological processes. This suggests that rat liver in hyperthyroidism increase the likelihood of injury due to decreased AChE activity.

Keywords: Acetylcholinesterase, Hyperthyroidism, Liver

PC118

Oxidative and Histological Changes in Pancreatic Tissue in the Aging Process

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AIM: Aging is a very important risk factor for metabolic diseases. Pancreatic aging increases atrophy, decreased secretions, insulin resistance and oxidant stress. In our previous study, Salermide (SLM) administered to elderly rats decreased oxidant stress in various brain regions. On this basis, our aim is to investigate the effects of SLM application on pancreatic tissue oxidative stress levels and morphological structure in aging.

METHODS: Four groups were formed using aged (22 months, n=12) and young (3 months, n=12) Wistar albino rats and experimental applications were started. Rats; 1-Young Control (YC), 2-Young Salermide (Y-SLM: 1mM SLM, 25 µl/100 g, ip), 3-Aged Control (AC: Dimethyl sulfoxide (DMSO: 100 µl/bw, ip)), 4-Aged Salermide (A-SLM: 1mM SLM, 25 µl/100 g, ip) Malondialdehyde (MDA) in pancreatic tissue with TBARS formation, Glutathione (GSH) modified Ellman, total oxidant level (TOS) and total antioxidant level (TAS) with commercial kits oxidative stress index (OSI) was calculated. Langerhans island area and island size were measured for histological evaluations. ANOVA, LSD and Pearson r were used for statistical analysis ($p < 0.05$).

RESULTS: TAS levels were significantly higher in young rats than in aged controls (p=0,013). Aging significantly increased MDA and OSI values compared with younger controls (p=0,031; p=0,000). With aging, a significant increase was observed in the Lanhergans islet area (p=0,009). Langerhans found the island size indistinguishable between groups. Aged SLM significantly decreased MDA compared to aged control group (p=0,039); there was no significant change in GSH value. Pancreatic TAS level with GSH (p=0,041); TOS levels were positively correlated with OSI and MDA (p=0,000; p=0,004). Pancreatic OSI was positively correlated with Langerhans island area (p=0,038). Aging led to localized micro and macro vesicular fat, perivascular infiltration and congestion between islet cells and atrophy. Aged rats showed decreased acinar atrophy and lymphocytic infiltration with SLM.

CONCLUSION: SLM application may be effective in reducing oxidant stress, atrophy in pancreatic injury with aging.

Keywords: Aging, Pancreas, Oxidative Stress, Histological Changes

PC119

The Effects of Intracerebroventricularly Administered Salusin-β on levels of GnRH in Rats

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AIM: Salusin-β (Sal-β) is a bioactive peptite-structured and multifunctional hormone which originates from preprosalusin. This hormone, known to be present in the hypothalamus, is also known to affect the pituitary gland through hypothalamic responses of hypothalamus secretions. The aim of this study is to explain the endocrinological effects of Sal-β on male reproductive system.

METHODD: On the research, 40 Wistar Albino rats were used. Those animals were divided into 4 groups in a way that their body weights are closed to each other (n=10). No application was made to the control group. To experiment group, for seven days long, artificial cerebrospinal fluid (CSF), 2 and 20 nmol/kg/240µl/days infusion of salusin β was applied in intracerebroventricular (icv) way. After seven days, animals were decapitated and brain (hypothalamus) tissue samples were collected. Using the collected hypothalamus samples, GnRH mRNA levels of the groups were determined by RT-PCR method.

RESULTS: It was found that applied Sal-β increased GnRH mRNA level in both concentrations. (P <0.05).: The data obtained at the end of the study show that Sal-β causes an increase in GnRH mRNA level in rats.

CONCLUSION: These results suggest that Sal-β can play important roles on the hypothalamic- pituitary-testicular axis. This study was supported by Scientific Research Fund of the Inonu University (Project no: TSG-2017-952).

Keywords: Salusin-β, Hypothalamus, GnRH

PC120

Investigation of the Effect of Melatonin and Luzindole on Inflammatory Cytokines in Kidney and Liver Tissues in Type 2 Diabetes

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AIM: Type 2 diabetes mellitus is a chronic metabolic disorder. Its prevalence is increasing steadily all over the world. Inflammation is one of the main causes of complications observed in Type 2 diabetes mellitus. Melatonin is a hormone released from pineal gland with circadian rhythm which has anticancerogenic, antiapoptotic and antioxidant effects. Melatonin is also associated with inflammation. In this study, we investigated the effect of melatonin and a selective melatonin receptor (MT2) antagonist luzindole, on inflammation in type 2 diabetes mellitus.

METHODS: 2.5 months old Sprague Dawley male rats were divided into 4 experimental groups consisted of 10 rats each. Control group, type 2 diabetes mellitus group, type 2 diabetes mellitus group treated with Melatonin (500 µg/day); type 2 diabetes mellitus group treated with Luzindole (0.25 g/kg) and Melatonin. Type 2 diabetes was induced with nicotinamide (100mg/kg) and streptozotocin (50 mg/kg). All chemicals were administered intraperitoneally. 6 weeks later rats were sacrificed, kidney and liver tissues were collected. Inflammatory cytokines, IL-1beta, TNF-alpha, IL-6 and NFkB protein levels were measured by Western Blot and immunohistochemistry.

RESULTS: All inflammatory cytokine levels were increased significantly in type 2 diabetes group comparison with the control group ($p<0.05$). Our data indicated that inflammation markers of melatonin treated group decreased significantly when compared with type 2 diabetes group ($p<0.05$) both in kidney and in liver tissues. However, luzindole was found to reduce the anti-inflammatory effect of melatonin in terms of cytokines in both kidney and liver tissues ($p<0.05$). One way ANOVA test was used for statistical analysis.

CONCLUSION: We observed that melatonin decreased inflammatory cytokine levels in kidney and liver tissue of diabetic rats. However, luzindole, MT2 receptor selective antagonist, reduced the antiinflammatory effects of melatonin. Melatonin might reveal its antiinflammatory effect through its MT2 receptors.

Keywords: Melatonin, Type 2 Diabetes Mellitus, Inflammation, MT2 Receptor

PC121

Investigation of Apelin Hormone Levels According to Body Mass Index and Waist Height Ratio Classification in Type 2 Diabetes Mellitus

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AIM: Apelin, an adipokine, has a close relationship between body composition and insulin sensitivity. This study was conducted to determine whether there is any relationship between apelin hormone, Body Mass Index (BMI) and Waist Height Ratio (WHtR) classification in patients with type-2 diabetes mellitus (T2DM) and in healthy individuals.

METHODS: The study included 47 individuals with T2DM and 48 healthy subjects. After acquiring the voluntary consent, anamneses were recorded, anthropometric and hormonal examinations were performed. Apelin level was measured by ELISA method. SPSS 21 package program (Kruskal-Wallis and Mann-Whitney U tests) was used in the statistical analyses.

RESULTS: In our study, apelin levels were compared between the groups according to WHtR classification in control and patient individuals; among the control subjects, in the group with high WHtR (12.54 ng/L), apelin hormone level was found to be lower than normal (36.65 ng/L) and slightly higher group (36.81 ng/L) ($p<0.05$). According to WHtR classification, apelin levels were similar and no statistically significant difference was found between the groups ($p>0.05$). Apelin levels of individuals with high WHtR classification in the control and patient groups were compared; apelin hormone levels were significantly increased in the patient group (39.02 ng/L) compared to the control group (12.54 ng/L) ($p<0.05$). In our study, when we compared apelin hormone levels between the groups according to BMI classification in control and patient individuals; apelin level was similar between the groups ($p>0.05$). When the apelin levels of the obese individuals in the control and patient groups were compared; apelin levels were significantly higher in the patient group (39.20 ng/L) than in the control group (12.60 ng/L) ($p<0.05$).

CONCLUSION: According to the data obtained from the study, apelin hormone is an important predictor of DM susceptibility when taking account of T2DM risk determinant BMI and WHtR classification. (M.K.U. BAP #2017/16550)

Keywords: Type 2 diabetes mellitus, apelin, waist height ratio, body mass index

PC122

Visceral Adipose Index and SIRT1 Gene Expression Relationship with Type 2 Diabetes Mellitus

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AIM: Apelin and sirtuin-1 are effective in lipid and glucose metabolism in adipose tissue, liver, pancreas and many tissues and have an important role in the regulation of metabolic homeostasis. In this study, we aimed to determine the relationship between visceral adipose index (VAI), sirtuin-1 gene and apelin hormone type-2 diabetes mellitus (T2DM).

METHODS: 95 individuals (47 healthy controls, 48 patients with T2DM) were included in the cross-sectional study. Anthropometric measurements such as weight, height and waist circumference were taken to determine the VAI and lipid accumulation products (LAP) index scores. Blood samples were also taken from the participants to determine HDL-C, triglyceride, apelin hormone level and sirtuin-1 gene expression. Apelin hormone levels were measured by ELISA method and sirtuin-1 gene expression levels were measured by RT-PCR method. The analysis of the data was performed with SPSS v.21 package program (Student's t-test, Mann-Whitney U test).

RESULTS: VAI was higher in the patient group (3.5±3.48) than in the control group (2.13±1.27) ($p <0.05$). Sirtuin-1 gene expression was 1.05±0.45 in the control group and 1.1±0.69 in the patient group. When the patient group was compared with the control group, there was no statistically significant difference in sirtuin-1 gene expression ($p>0.05$). In addition, average apelin hormone levels of the participants, there was a statistically significant difference between the patient and control groups (44.07± 4.51 ng/L and 37.12±32.67 ng/L) ($p<0.05$). LAP index was 54.18±1.96 in the controls and 97.73±76.9 in the patients. A significance was found between the two groups ($p<0.05$). There was no correlation between VAI and sirtuin-1 gene and apelin. However, there was a strong positive correlation between VAI and LAP index (control; $r=0.904$, $p<0.001$ and patient; $r=0.912$, $p<0.001$).

CONCLUSION: In conclusion, larger cohort studies are needed to evaluate the association of VAI and sirtuin-1 gene expression levels with T2DM. (M.K.U. BAP #2017/16550)

Keywords: Type 2 diabetes mellitus, visceral adipose index, SIRT1, apelin hormone

PC123

Histopathological Evaluation of Boronphenyl alanine and Zinc Containing Nanoemulsion Formulations on Wound Healing in Streptozocin Induced Diabetic Rats

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AIM: Diabetes Mellitus (DM) is a chronic metabolic disease that is caused by lack or absence of insulin hormone secretion. Boron and zinc (Zn) are involved in biological processes, especially on wound healing in humans. We have investigated wound healing effects of nanoemulsion (NE) formulations containing boronphenylalanine (BPA) and/or Zn histopathologically on streptozocin-induced diabetic rats.
METHOD: The nanoemulsion formulations containing BPA (BPA-NE), Zn(Zn-NE), BPA+Zn(BPA+Zn-NE) and blank nanoemulsion (BlankNE) were prepared. Diabetes model was formed by intraperitoneal streptozocin injection and the dorsal regions were shaved to create an excisional wound model. Rats were randomly divided into 8 groups. (Group1: Control; Group2: DM control; Group3: DM+NE; Group4: DM+BPA-NE-1 (equivalent to 10µM BPA); Group5: DM+BPA-NE-2 (equivalent to 25µM BPA); Group6: DM+Zn-NE (equivalent to 50µM BPA); Group7: DM+Zn+BPA-NE-1, Group8: DM+BPA+Zn-NE-2). Wound region of rats was treated with 100µL/cm² NE once a day for 14 days. Lastly, the rats were sacrificed and tissue samples of wounds were taken for histopathological examination. The tissue sections were stained by the hematoxylin-eosin and Gomorrah modified aldehyde fuchsin and examined under a light microscope. The study was approved by Ataturk University Local Ethics Committee for Experimental Animals.
RESULTS: In group 1, granulation of wound dermis, collagen production and reepithelization near wound lips were observed, in group 2, large cavities and intensive granulation on the wound edges were seen and in group 3, repitelization formation and production of partial collagen fibers were found. In the granulation tissues of remained groups [groups4-8], abundant collagen fibers, less elastane and full wound healing were observed during the initial period of healing. Particularly in Group 4, complete reepithelization was seen and wound area was completely closed.
CONCLUSION: In this study, it was concluded that BPA alone and / or in combination with Zn may be an alternative compound in the treatment of diabetic wound.

Keywords: Boronphenyl alanine, Zinc, Diabetes Mellitus, Wound healing

PC124

Determination of Glutathione Reductase Enzyme Activity in Melatonin Administered Rats's Heart Tissue

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AIM: Glutathione reductase (GR) is a flavoenzyme that converts oxidase glutathione into reduced glutathione using nicotinamide adenine dinucleotide phosphate. Melatonin, an inhibitory neuroendocrine hormone, is involved in the regeneration of cells, strengthening the immune system, regulating sleep rhythm and body temperature. It is also one of the most effective antioxidants with lipophilic properties. The aim of this study was to determine the level of GR enzyme activity in heart tissues of rats treated with melatonin.
METHODS: 14 adult male Wistar albino rats (weighing250-300g) were divided into two different groups as control and melatonin. The rats in the melatonin group (n:7) received 3mg/kg/day melatonin and the rats in the control group (n:7) were administered 0.9% NaCl intraperitoneally for 14 days at 21:00 o'clock. The rats in the melatonin group received 3mg/kg/day melatonin and the rats in the control group were administered 0.9%NaCl intraperitoneally for 14 days. The rats were euthanized by cervical dislocation under anesthesia as a result of injection applications and thoracic regions were opened and heart tissue was taken. Enzyme activity was measured spectrophotometrically by using Beutler method. Enzyme activity levels of control group and melatonin treated rats were compared. The data obtained were evaluated by Student's t test. Significance level was accepted as $p<0.05$. This study was approved by the local ethics committee of Ataturk University for animal experiments
RESULTS: GR enzyme activity levels were found to be 4,842 ± 0,314 EU/mg protein in the control group and 5,467± 0,372 EU/mg protein in the melatonin treated group. When melatonin group and control group were compared, it was found that enzyme activity level increased by 12.9% and this increase was statistically significant ($p<0.001$).
CONCLUSION: Melatonin, a powerful antioxidant hormone, increased rat cardiac GR activity significantly compared to control group in this study. This result suggests that melatonin strengthens the antioxidant defense mechanism in heart tissue.

Keywords: Heart, Glutathione reductase, Melatonin.

PC125

Coriandrum Sativum Effect on Intestinal Tissue Damage Result from Liver Ischemia Reperfusion Injury

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AIM: Hepatic ischemia reperfusion injury (IRI) is not only pathophysiological process involving the liver, but also complex systemic process affecting multiple organs including small intestine. Due to IRI, absorption of nutrients from the intestines will be disrupted and the blockage of portal vein will occur. Coriandrum sativum has anti-inflammatory and antioxidant effects on brain and kidney ischemia reperfusion injury. It is widely consumed in Northern Cyprus. The aim was to investigate the effects of liver IRI on small intestine and possible protective effect of Coriandrum sativum on light microscopic level.

METHODS: The experimental procedure was approved by the Near East University Animal Experiments Local Ethics Committee (2019/01-57). 32 female Wistar Albino rats, 450-500g, aged 6-7 months were used. Four groups; sham, ischemia / reperfusion, ischemia / reperfusion + Coriandrum sativum and Coriandrum sativum. During the experiment, 60 minutes ischemia and 60 minutes reperfusion were performed. In the treatment group, Coriandrum sativum was given daily by gavage dose of 300 mg / kg, starting 3 days before ischemia and 1 hour. At the end of the reperfusion period, the duodenum of the small intestine was removed and fixed with 4% paraformaldehyde. Villus lengths and mucosal layer thickness were measured. Using SPSS 17.0 package program Kruskal Wallis and Man Whitney U statistical tests were used to compare each group.

RESULTS: Histologically, there was significant epithelial loss, congestion in lamina propria, hemorrhage and shortening of the villi in the IR group when compared with control and CS groups. In the treatment group, tissue damage was found to be less than in the IR group. Compared with IR group, villus lengths and mucosal layer thickness were found to be closer in the treatment group than the control group ($p < 0.05$).

CONCLUSION: Coriandrum sativum has a protective effect against small intestine injury.

Keywords: Hepatic ischemia reperfusion injury, small intestine, Coriandrum sativum

PC126

Investigation the Role of Docosahexaenoic Acid (DHA) in Inflammatory Response in TNBS-Induced Colitis Model

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AIM: Inflammatory bowel diseases (IBD) are common chronic gastrointestinal diseases characterized by mucosal damage in the gastrointestinal tract and impaired immune response. 2,4,6-trinitrobenzenesulfonic (TNBS) induced colitis model has the ability to mimic IBD pathology. Docosahexaenoic acid (DHA) is a long chain omega 3-fatty acid (n-3 PUFA) with an anti-inflammatory effect. The aim of the study is to investigate anti-inflammatory effect of DHA in TNBS induced colitis model.

METHODS: Female Wistar Albino rats were divided into 3 (n=10/per group) groups: Control, colitis and colitis+DHA. Groups were treated with saline and DHA (600 mg/kg/day) via gavage for 6 weeks. At the end of 6th week, TNBS was administered to colitis and colitis+DHA groups intrarectally and rats were sacrificed three days later. Colon tissues were collected for macroscopic and microscopic evaluation. Myeloperoxidase (MPO) activity, malondialdehyde (MDA) and glutathione (GSH) levels, total antioxidant (TAS) and total oxidant status (TOS). IL-6, NF-κB, TNF-α levels were measured. All experimental procedures were approved by Committee for Animal Research of Acibadem University

RESULTS: The macroscopic damage score of the colitis group was significantly higher than the DHA group ($p<0.05$). MPO levels, MDA levels and TNF-α cytokine levels of DHA group decreased significantly compared to colitis group ($p<0.05$). There was no significant difference between GSH and IL-6 levels between colitis and DHA groups and no significant difference were observed in NF-κB levels between the groups. One-way ANOVA test was used for statistical analysis (SPSS 23 version).

CONCLUSION: No significant difference were found between the groups in terms of cytokine levels, however biochemical and histological analysis revealed that DHA has a protective effect on the intestinal epithelium. This anti-inflammatory effect is thought to be achieved by increasing the durability of the membrane. DHA may be used as a complementary/preventive option in combination with drug therapy for IBD patients.

Keywords: Experimental colitis, TNBS, DHA, inflammation

PC127

Coriandrum Sativum Effect on Liver Ischemia Reperfusion Injury

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AIM: Liver ischemia/reperfusion (IR) injury is a clinical condition that increases morbidity and mortality after trauma, hepatectomy and liver transplantation. In reperfusion, as a result of various inflammatory mediators secreted from Kupffer and other liver cells, neutrophils pass from sinusoidal endothelial cells into tissue, and causes tissue damage. There are many studies carried on for prevention of damage. Coriandrum sativum has been shown effective in experimentally generated brain, kidney ischemia reperfusion injuries. The aim of this study was to investigate the effect of Coriandrum sativum (kişniş-golyandro) from North Cyprus-Nicosia, which has anti-inflammatory and antioxidant effects, in liver IR damage with light microscopy and biochemical levels.

METHODS: Experimental protocol were performed according to the guideline approved by Animal Care and Use Local Ethics Committee of Near East University (2019/01-57). Overall, 6-7 months old (450-500gr) 32 female Wistar Albino rats are grouped as sham, ischemia/reperfusion, ischemia/reperfusion+Coriandrum sativum and Coriandrum sativum. Sixty minutes of ischemia and 60 minutes of reperfusion were performed. In the treatment group, 300 mg/kg/day Coriandrum sativum was given 3 days before ischemia and 1 hour before ischemia by gavage. At the end of the reperfusion period, liver tissues were fixed in 4% paraformaldehyde. Serum ALP, ALT and ALP enzymes were measured. Microscopic scoring was performed in terms of sinusoidal congestion, vacuolization and necrosis. Statistical analysis were performed with SPSS 17.0 program and Kruskal Wallis test and Mann-Whitney U tests were applied.

RESULTS: Histologically, sinusoidal enlargement and diffuse congestion, Kupffer cell activation, neutrophil increase in necrotic areas, and vacuolization in hepatocytes were observed in ischemic liver tissue. No necrotic areas were observed in the treatment group and congestion was decreased compared to the ischemic group. AST and ALT values were significantly increased in the ischemic group and decreased significantly in the treatment group.

CONCLUSION: Coriandrum sativum decreased liver ischemia reperfusion injury.

Keywords: Liver, Ischemia/Reperfusion, Coriandrum sativum

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Protective Effects of Neuropeptide W against Sepsis-Induced Hepatorenal Injury in Rats

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AIM: Sepsis, a serious clinical syndrome characterized by a dysregulated host response to invading pathogens, results in multiple life-threatening organ dysfunctions or even death. We aimed to investigate possible protective effects of NPW, a novel peptide regulating neuroendocrine functions, against oxidative hepatorenal damage in an experimental sepsis model.

METHODS: Under anesthesia, sepsis was induced in male Sprague-Dawley rats by cecal ligation and puncture method (n=32). Either saline or tumor necrosis factor-alpha inhibitor (etanercept; 1 mg/kg) +antibiotics (ceftriaxon;100 mg/kg) or NPW (0.1 and 0.3 µg/kg) was given subcutaneously in repetitive three doses: immediately after operation, at postoperative 12th and 24th hours. In control group (n=8), sham-operation was performed and subcutaneous three saline injections were given within twenty-four hours. The rats were decapitated at 25th hour of sepsis induction. Kidney and liver samples were obtained for measurement of myeloperoxidase activity, malondialdehyde and antioxidant glutathione levels. Histopathological evaluations were performed. ANOVA and Student's t-test were used for data analysis.

RESULTS: Malondialdehyde levels and myeloperoxidase activity in liver and kidney tissues were increased in saline-treated sepsis group as compared with control group ($p<0.05$-$p<0.001$), while in liver of etanercept+antibiotics-treated group (positive-treatment) these elevations were suppressed ($p<0.01$-$p<0.001$), but no difference was observed in renal tissues. The 0.3 µg/kg NPW dose decreased hepatic myeloperoxidase activity and suppressed malondialdehyde levels in both tissues ($p<0.05$-$p<0.001$), while 0.1 µg/kg NPW dose only reduced hepatic myeloperoxidase activity ($p<0.01$). No differences in glutathione levels were observed among groups. High damage scores (severe hepatocyte degeneration, sinusoidal congestion and Kupffer cell activation) in sepsis were reduced by etanercept+antibiotics and NPW (0.1 and 0.3 µg/kg), demonstrating a nearly normal hepatic structure.

CONCLUSION: When applied during first 24 hours of sepsis, NPW dose-dependently alleviated hepatorenal damage. The protective effect of NPW specifically against oxidative liver damage is associated with its inhibitory effect on neutrophil migration.

Keywords: NPW, ulcer, stress, oxidative damage

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Protective Effects of Neuropeptide-W on Stress-Induced Gastric Ulcer in Rats

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AIM: Stress has an important role in etiopathogenesis of gastric ulcer, and causes gastric mucosal lesions, inflammation and oxidative damage. Neuropeptide-W (NPW), present in hypothalamus and in many peripheral tissues including stomach, contributes to central regulation of neuroendocrine functions, regulation of food intake, anxiety and fear, energy homeostasis and activation of stress axis. The possible protective effects of NPW in ameliorating oxidative gastric damage were elucidated in stress-induced rats.

METHODS: To establish water-immersion restraint stress (WIRS) model, Sprague-Dawley male rats (n=30) were fasted for 24 hours before experiment, but had free access to water. Rats were then restrained in wire-cages and immersed in 20-25 °C water-bath down to their xiphoid processes for 6 hours. Before WIRS, a single dose of saline or NPW (0.1; 0.3; 1 or 5 µg/kg) was subcutaneously injected. Following decapitation, macroscopic/microscopic scorings were made, and oxidant and antioxidant parameters, including myeloperoxidase activity, malondialdehyde and glutathione levels were measured in gastric samples. ANOVA and Student's t-test were used for statistical analysis.

RESULTS: Compared with saline-treated ulcer group, macroscopic damage score was significantly decreased in 0.3 and 5 µg/kg NPW-treated groups ($p<0.05$), and a tendency to decrease was observed at 0.1 µg/kg dose ($p>0.05$). No significant differences were observed in glutathione levels of experimental groups. Malondialdehyde level, showing lipid peroxidation, and myeloperoxidase activity, indicating neutrophil infiltration into tissue, were suppressed at 0.1 µg/kg NPW dose ($p<0.01$ and $p<0.05$). At 5 µg/kg dose of NPW, myeloperoxidase activity and malondialdehyde were decreased, but did not reach to statistical significance. Blinded histological examination of stomach revealed that damage in ulcer group was reduced especially at 5 µg/kg NPW dose. The medium NPW dose (1 µg/kg) was found ineffective in all parameters.

CONCLUSION: Our results revealed that NPW has a dose-dependent and an inverse-U-shaped protective effect in stress-induced oxidative gastric injury.

Keywords: NPW, ulcer, water-immersion restraint stress, oxidative damage

PC130

The Effect of Yarrow Extracts on Uterine Contractions Isolated from Non-pregnant Rats

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AIM: In recent years, there has been a rise in the number of applications in medical schools for complementary medicine. Phytotherapy specifically has been receiving attention. While yarrow is one of many potential plants, its effects in uterus contractions are not well known. This study aims to determine the effects of the yarrow (Achillea Millefolium) extracts on uterus contractions isolated from non-pregnant rats.

METHODS: In this study, Wistar-type female albino rats, weighing 200-250 grams, were divided into 4 groups (n=8): Group I – Control; Group II – CPE; Group III – Oxytocin; Group IV – Oxytocin+CPE. The uteri were dissected into 1.2x2x1cm longitudinal strips. The strips were hung on a bath to record contractions. Group I was the control group. Once the contractions stabilized, doses of CPE (0.125, 0.25, 0.5, 1.0, 2.0mg/ml) were cumulatively applied to Group II within 10-minute intervals. For Group III, further contractions were induced by applying 0.0004IU/mL oxytocin. For Group IV, contractions were induced with oxytocin and subsequently, doses of CPE (0.125, 0.25, 0.5, 1.0, 2.0 mg/ml) were cumulatively applied group within 10-minute intervals.

RESULTS: After analyzing the frequency parameters; an inhibition was observed in spontaneous uterus rectus contractions ($p<0.05$) when 2mg/ml of CPE was applied to Group II and no inhibition was observed ($p>0.05$) in Group IV. After analyzing the amplitude parameters; an inhibition was observed in Group II at every dose of CPE for the spontaneous uterus rectus contractions ($p<0.05$) and an inhabitation was only observed when 2.0mg/ml of CPE was applied to Group IV ($p<0.05$).

CONCLUSION: In conclusion, CPE decreased the contractions in both spontaneous uterus rectus contractions and those which were induced with oxytocin. Accordingly, there may be possibility in using CPE when there is a risk of miscarriage.

Keywords: Yarrow, Uterus, Smooth Muscle, Oxytocin.

PC131

Effect of PACAP (Pituitary Adenylate Cyclase Activating Polypeptide) and Its Receptor on Oocyte in Vitro Maturation

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AIM: The aim of this study is to investigate the role of PACAP (pituitary adenylate cyclase-activating peptide), which has an important role on oocyte development, in vitro maturation.

METHODS; In our study we injected i.p (intraperitoneal) with 5 i.u. PMSG (pregnant mare serum gonadotropin) to 21-24 days old female mice to enhance multiple follicular development. The ovaries of mice were collected after sacrifice by cervical dislocation. Immature oocytes (GV) were separated from granulosa cells and cultured separately in DMEM medium, a commercial IVM medium and with 450 ng solution with PACAP. Genetic analysis is achieved by flourization of PACAP and receptors (PAC1, VPAC2 and VIP) with whole mount immunofluorescence and qRT-PCR on Metafase II oocytes.

RESULTS: After culturized 24 hours maturation averages are as follow: on DMEM group %57, IVM group %53 and IVM with PACAP group is %57. After whole mount immunofluorescence PAC1, VPAC1 and VIP showed different immunoreactivitiy.

CONCLUSION: Addition of PACAP supplementation to IVM medium enhances the maturation. However, to analyze the effects on receptors which are vital for maturation and other side effects we need to increase the numbers of oocytes and more advanced techniques.

Keywords: Oocyte, PACAP, qRT-PCR, whole mounth immunohistochemistry, cell culture

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Effect of Salermide on Young and Aged Testicular Tissue

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AIM: Aging is associated with increased oxidative stress, atrophy and decreased antioxidant defense in testicular tissue. Salermide (SLM) was shown to be protective against oxidant stress in aged rat brain in our previous study. Our aim is to investigate the oxidant stress levels and histological changes of SLM application in testicular tissue in aging.

METHODS: Four groups were formed using aged (22 months, n=12) and young (3 months, n=12) Wistar albino rats. Rats; 1-Young Control (YC), 2-Young Salermide (Y-SLM: 1mM SLM, 25 µl/100 g, ip), 3-Aged Control (AC: Dimethyl sulfoxide (DMSO: 100 µl/bw, ip)), 4-Aged Salermide (A-SLM: 1mM SLM, 25 µl/100 g, ip). Malondialdehyde (MDA), with TBARS formation, Glutathione (GSH) modified Ellman, total oxidant level (TOS) and total antioxidant level (TAS) with commercial kits, oxidative stress index (OSI) was calculated. Histologically, light microscope examination was performed with Hematoxylin-Eosin (HE) staining. ANOVA, LSD and Pearson r were used for statistical analysis ($p < 0.05$).

RESULTS: Aging increased TOS, OSI and MDA and decreased GSH levels. While the application of SLM decreased OSI in the aged; TAS has increased. In young, SLM application increased MDA; reduced GSH. OSI showed negative correlation with TAS and positive with TOS. Aging testicular tissue is associated with atrophy in some seminiferous tubules and deterioration in spermatogenic cell lines compared with the young control. While the application of SLM to young rats did not change compared with the control group, it was observed that germinal epithelial irregularity persisted in the seminiferous tubules with the application of SLM in aged rats, whereas in some areas the cells of the spermatogenic series were in normal arrangement and interstitial connective tissue integrity was preserved.

CONCLUSION: SLM application in testicular tissue in aging may be protective with increased antioxidant defense, decreased atrophy and improvement in spermatogenic structure.

Keywords: Aging, Salermide, Testis, Oxidan-Antioxidant System

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The Effect of Systemic Adropin Administration on MDA and GSH Levels in Testicular Tissues of Diabetic Rats

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AIM: Long-term hyperglycemia in diabetes causes infertility as well as microvascular and macrovascular complications. Free radicals attack spermatozoa cell membranes because of their richly polyunsaturated fatty acids contents. Diabetic free radicals decrease sperm count, antioxidant capacities and increase lipid peroxidation. Adropin is a peptide which is synthesized from liver via ENHO gene and improves insulin resistance and glucose homeostasis. Low adropin level has a relationship with endothelial dysfunction in diabetes and cardiovascular diseases. The purpose of our study was to investigate the effect of systemic adropin treatment on oxidant-antioxidant systems in testis of diabetic rats.

METHODS: 28-male wistar-albino rats divided into four groups: 1. Control, 2. Control+Adropin, 3. Diabetes, 4. Diabetes+Adropin. 65mg/kg/i.p./single dose Streptozotocin was given for diabetes. After 72 hours, rats with blood glucose levels above 250mg/dL were considered diabetes. Following 10 weeks, 450nmol/kg/i.p. adropin was injected twice a day for 10 days. Rats were sacrificed by intracardiac blood collection with anesthesia. MDA, TOS and GSH levels were measured in testis tissues. Statistical analysis was performed with Kruskal-Wallis and Mann-Whitney-U tests. $p<0.05$ was considered statistically significant. The study was approved by G.U. Local Ethics Committee.

RESULTS: MDA levels of diabetic group were higher than control ($p<0.05$). Adropin treatment didn't change MDA values compared with diabetic group. However, TOS values significantly decreased in adropin treatment group ($p<0.05$). There weren't significant changes in GSH levels.

CONCLUSION: 10-day Adropin treatment decreased oxidative stress related with diabetes but did not affect GSH levels. Further studies are needed to reveal relationship with adropin and oxidative stress on testis tissues.

Keywords: Antioxidative, Diabetes, Oxidative Stress, Rat, Testis

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Effectiveness of Syringic Acid Aganist Reproductive Organ Damage in Rats

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AIM: The aim of this study is to investigate the possible beneficial role of syringic acid aganist reproductive organ damage induced by bilateral ovarian torsion/detorsion (T/D) model in female rats.

METHODS: In this study, thirty-two Sprague-Dawley female rats were randomly divided into 4 groups. Groups were desingned as group I (sham), group II (T/D), group III (10 mg/kg dose of syringic acid+T/D), and group IV (50 mg/kg dose of syringic acid+T/D). In group I, the abdomen was opened and closed again without T/D model. In group II, 3 hours of torsion followed 3 hours of detorsion were applied. In the group III and group IV, syringic acid was given intraperitoneally at 10 and 50 mg/kg doses 30 minutes before detorsion and then T/D was made as announced in group II. At the end of detorsion, rats were sacrificed and the ovarian tissues removed.

RESULTS: Malondialdehyde (MDA) level, myeloperoxidase (MPO) activity, tumor necrosis factor-alpha (TNF-α), interleukin-1beta (IL-1β), total oxidant status (TOS) and oxidative stress index (OSI) values increased significantly in group II compared with group I. However, superoxide dismutase (SOD) and total antioxidant status (TAS) values decreased in group II. Conversely, the antioxidant enzyme activity increased, while TOS, OSI value, MPO activity and TNF-α, IL-1β, MDA levels decreased significantly via syringic acid in the group III and group IV.

CONCLUSION: As a conclusion, syringic acid was shown to be effective in protection against the ovary damage that induced by T/D model in rats.

Keywords: Syringic acid, reproductive organ, torsion/detorsion, rat.

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The Therapeutic Efficacy of Gentisic Acid in Torsion-Detorsion Model of the Ovarian Tissue in Rats

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AIM: The aim of this study was to evaluate the therapeutic efficacy of gentisic acid against ovarian damage due to torsion detorsion that is frequently encountered in the clinic.

METHODS: This experimental study was performed on thirty- two female wistar rats obtained from Atatürk University Experimental Animals Research Center. Our experimental groups were arranged as sham, torsion detorsion (TD), TD+Low dose of gentisic acid and TD+High dose of gentisic acid. In our TD group, the artery and colleterals feeding the ovary were rotated 720 ° clockwise and clamped for 3 hours. At the end of this period, the clamp was opened and the ovary was allowed to re-blood for 3 hours. In our TD + Low and TD + High dose treatment groups, genticic aist was administered orally at doses of 100 and 200 mg / kg for 1 week and then torsion detorsion was performed in the TD group. All procedures were completed under anesthesia.

RESULTS: It was determined that myeloperoxidase (MPO), malondialdehyde (MDA), total oxidant status (TOS), oxidative stress index (OSI), tumor necrosis factor-alpha (TNF-alpha), interleukin-1beta (IL-1beta) levels increased and superoxide dismutase (SOD) and total antioxidant status (TAS) levels decreased significantly in TD group compared to sham group but in TD+Low dose and TD+High dose groups, MPO, MDA, TOS, OSI, TNF-alpha, IL-1beta levels decreased and SOD, TAS levels increased due to gentisic acid treatments.

CONCLUSION: When our current results were evaluated, it was thought that ovarian tissue damage induced by torsion detorsion could be alleviated via low and high dose treatments of gentisic acid.

Keywords: Gentisic acid, torsion detorsion, ovarian tissue, rat

PC136

The Effects of Electromagnetic Field Exposure in Prenatal and Postnatal Periods on Ovarian Tissue in Rats

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AIM: Exposure to electromagnetic field (EMF) can have adverse effects on many organs and tissues, including the reproductive system. The aim of this study was to investigate the effects of EMF exposure in prenatal and postnatal periods on ovarian development in female offspring.

METHODS: In this study, rat pups born from 8 pregnant rats were used. Pregnant rats were randomly divided into two groups; Sham group (EMF -) and EMF group (EMF +, 5 days / hf, 4 hours / day, 50 Hz-3 mT EMF exposure was applied). EMF exposure was initiated on the first day of pregnancy and continued until the 28th postnatal day. At the end of the exposure, blood and ovarian tissue samples of female offspring (Sham; n = 10, EMF; n = 12) were taken. Blood FSH, LH, estradiol levels, iNOS and eNOS levels in tissue were measured by ELISA. Expressions of iNOS and eNOS in ovaries were evaluated by immunohistochemical method. Ovarian structure was evaluated by routine histological examination. Results were evaluated by independent samples t-test in SPSS.22 program.

RESULTS: FSH levels were significantly higher in the EMF group than in the Sham group (p=0.028). No significant difference was found in LH levels. Estrogen levels were significantly lower in the EMF group than in the Sham group (p=0.008). Tissue iNOS levels and expression were significantly higher in the EMF group than in the Sham group (p=0.024). There was no significant difference in tissue eNOS levels. In the EMF group, congestion, bleeding areas and degeneration of follicle structures were observed in ovarian tissue.

CONCLUSION: Exposure to 50 Hz, 3 mT EMF used in this study during prenatal and postnatal lactation periods may lead to impaired ovarian structure and function in female rats. EMF may affect ovarian physiology by increasing iNOS levels and may lead to fertility disorders.

Keywords: Electromagnetic Field, iNOS, Ovarium, Rat, Sex Hormones

PC137

Investigation of the Role of Irisin and Adropin in Physiopathology of Experimental Renal Ischemia/Reperfusion Injury

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AIM: Ischemia reperfusion (IR) is one of the most common cause of acute kidney injury (AKI). The new polypeptide hormones adropine and irisin play an important role in metabolism and energy homeostasis. In this study, we aimed to determine the relationship between irisin and adropin levels and renal function and to investigate the usefulness of these agents as biomarkers in the early diagnosis of ischemic AKI.

METHODS: Male Spraque-Dawley rats weighing 270-320 grams were divided into Control, IR24 and IR48 groups (n = 7). Kidney vessels of IR24 and IR48 groups were clamped for 60 min to create ischemia under anesthesia. The IR24 group was reperfused for 24 hours and the IR48 group for 48 hours. IR24 rats were placed in metabolic cages immediately after ischemia, IR48 rats were collected in metabolic cages 24 hours after ischemia, and blood and kidney tissues were euthanized under anesthesia. Mann-Whitney U test was used for statistical comparisons. $p<0.05$ was considered significant. Ethics committee approval was received.

RESULTS: Serum urea and creatinine levels and Fractional Na+ and K+ excretion were increased in IR groups ($p<0.05$). Creatinine clearance decreased ($p<0.05$). Serum adropine levels decreased in IR48 group ($p<0.05$). Urine irisin and adropine levels were increased in IR24 and IR48 groups ($p<0.05$). There was no significant difference in renal irisin and adropine levels.

CONCLUSION: In our study, urine irisin and adropine levels were negatively correlated with creatine clearance and positively correlated with fractional Na+ and K+ excretions. Increased urinary irisin and adropine excretion in IR groups may suggest a role in the pathophysiology of impaired renal function. These two hormones; should be investigated as potential biomarkers in AKI due to renal ischemia reperfusion injury.

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Keywords: Acute kidney injury, ischemia-reperfusion, irisin, adropin

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The Effect of Salermide Administration on the Oxidative Stress in the Kidney Tissue During Aging

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AIM: Aging is associated with increased oxidative stress. During the aging process, while the oxidant stress increase in the kidneys increases, the antioxidant capacity decreases. Salermide administration has been shown to reduce oxidative stress in the cerebral cortex and hippocampus of elderly rats. The aim of this study was to investigate the effect of administration of salermide (SLM) in young and elderly rat kidney tissue on the oxidative stress parameters TOS (total oxidant status), OSI (oxidative stress index), MDA (malondialdehyde) and on the antioxidant parameters TAS (total antioxidant status) and GSH (glutathione).

METHODS: A total of 24 male Wistar type rats (young: 3 months of age, elderly: 22 months of age) were used: Young-Control (n = 6), Young-Salermide (n = 6), Elder-Control (n = 6), Elder - Salermide (n = 6) groups were formed. Intraperitoneal injections of 4% DMSO-PBS to the control 1mM salermide; 25 µl / 100g bw to the salermide groups were performed for 21 days in a row and tissues were isolated. MDA and GSH levels were measured by spectrophotometer. TAS and TOS were viewed with commercial kit. The ratio to each other was calculated as OSI value. ANOVA, Pearson r was used for statistical analysis ($p<0.05$).

RESULTS: Aging significantly increased TOS, GSH and OSI values in renal tissue and decreased paired total kidney weight / body weight ratio, but did not change MDA in the renal tissue. Administration of salermide in renal tissue significantly increased TAS and significantly reduced OSI in elderly rats compared with the control group. There was a negative correlation between renal TAS levels and OSI and a positive correlation between TOS and OSI. Paired total kidney weight / body weight ratio was negatively correlated with TOS and OSI in elderly rats.

CONCLUSION: Our results showed that salermide is a protective agent during the aging process by increasing antioxidant defense against oxidative damage in the kidney tissue.

Keywords: Aging, kidney, salermide, TAS, TOS, OSI

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Investigation of the Effects of Oxytocin on Experimental Myoglobinuric Acute Kidney Injury

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AIM: It has been reported that nitric oxide and free radicals damage play an important role in the pathophysiology of myoglobinuric acute kidney injury (MAKI). We aimed to investigate the role of oxytocin (OT) against kidney damage, renal function in the experimental MAKI model, which is reported to be antioxidant and has therapeutic effects in different renal injury models.

METHODS: 32 male Spraque Dawley rats weighing 190-230 gr were used (n=8). Rats that dehydrated for 24 hours, were treated with physiological serum (FS) in the Control and Control+OT groups, 50% glycerol at the dose of 8 ml/kg intramuscularly to the MAKI and MAKI+OT groups. 1 and 24 hours after glycerol injection, Control and MAKI groups were injected intraperitoneally with FS, Control+OT and MAKI+OT groups with ip 40 IU / kg OT. Rats were taken to metabolic cages after ip injection at 24 hours and had their urines collected. 48 hours after glycerol injection, the rats were sacrificed under anesthesia by taking their blood and kidneys. Student t and Mann Whitney U test were used according to distribution of variables. $p<0.05$ was considered significant. Ethics committee approval was received.

RESULTS: When the Control and MAKI groups were compared; serum urea, creatinine, Na+, K+, malondialdehyde, glutathione levels, fractional Na+ and K+ excretion were increased ($p<0.05$). Urine urea, creatinine, Na+, K+, creatine clearance, oxytocin, urinary and renal NO levels were decreased ($p<0.05$). A significant increase in kidney NO level was observed in the MAKI+OT group ($p<0.05$).

CONCLUSION: There was no therapeutic effect of oxytocin although there was increase in renal NO level. However, due to the very short half-life of oxytocin; We think that the therapeutic effects of oxytocin should be investigated in more detail by making adjustments in the dose, frequency, route and hours of administration after kidney damage.

Keywords: Oxytocin, Myoglobinuric Acute Kidney Injury, Free Radicals, Nitric Oxide, Antioxidant

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Toxic Effects of Methotrexate on Rat Kidney Tissue and Protective Role of Agomelatine

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AIM: Methotrexate (MTX) is an anti-inflammatory and antineoplastic drug which is frequently used in clinical practice and acts as a folic acid antimetabolite. Both the efficacy in the treatment and toxic effects of MTX may vary from patient to patient. This study was planned to determine the possible renal damage caused by MTX and to investigate as to whether agomelatine (AGO) has a protective effect.

METHODS: In this study, 24 Wistar Albino male rats (3-4 months) have been examined and randomly divided into three groups. Group I: Control group (0.1 mL saline, gavage and intraperitoneal; ip), Group II: MTX (20 mg/kg MTX, single-dose, ip) applied group, Group III: MTX (20 mg/kg, single-dose, ip) + AGO (40 mg/kg, gavage, 7 days) applied group. The rats were sacrificed after 24 hours the last AGO administration. Kidneys were extracted for histopathological/immunohistochemical (CGSF, HSP-70, iNOS, OPN) analyzes. Evaluation of the findings was performed with ANOVA and Bonferroni Dunn tests in SPPS 15 packaged software. $p<0.05$ values were considered significant. Histopathological changes were graded in a blinded manner.

RESULTS: Normal kidney architecture was observed in Group I and III. The kidneys of the rats in Group II were slightly swollen and pale. At the histopathological examination; marked hyperemia, slight hemorrhages, tubular cell necrosis and expansion of Bowman spaces were observed ($p<0.05$). Immunohistochemically increase in CGSF ($p<0.01$), iNOS ($p<0.05$), OPN ($p<0.05$) immunoreactions in both epithelial and mesenchymal cells of the kidneys were observed in Group II. Also, mild expression in HSP-70 immunoreaction in the proximal tubule epithelium was found. Both histological and immunohistochemical findings were significantly reduced in AGO treated group ($p<0.05$) compared to group II.

CONCLUSION: The lesions were attributed to MTX toxicity since there were no pathological findings in groups except MTX treated group. Also, the results obtained from AGO treated group suggest that this toxicity can be reduced with AGO treatment.

Keywords: Agomelatin, kidney, methotrexate

PC141

Determination of Serum Glutathione Reductase Activity in Pregnant Women

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AIM: Pregnancy is a physiological process in which the need for oxygen increases to perform many body functions requiring high energy. The aim of this study was to determine the activity level of glutathione reductase (GR), the enzyme that determines the level of glutathione, the most important antioxidant substance in the organism, during pregnancy, where many body functions are affected.

METHODS: Our study consisted of 35 pregnant women (1st and 2nd trimester n=12, 3rd trimester n=11) and 54 female students who accepted to participate in the study. 2 cc blood samples were taken from the forearm or hand vein of individuals. After the serum samples were obtained, GR activity level was measured by Beutler method for spectrophotometric measurements. Our study was conducted with permission from A.I.C.U Science Ethics Committee with the letter numbered 29513 dated 26/12/2018.

RESULTS: In our study, the mean age was 25 in pregnant women and 22 in non-pregnant university students. As a result of the analysis of the blood samples in the spectrophotometer, the GR activity level was 1.65±0.15 U/L in pregnant women and 1.97±0.17 U/L in pregnant women. It was determined that GR activity level was 16.24% lower in pregnant individuals.

CONCLUSION: In our study, the level of glutathione reductase enzyme activity, which plays an important role in biological activity, was examined in pregnant individuals who are important for both mother and child health. When the enzyme activities of the samples taken from pregnant individuals and non-pregnant students were compared, it was determined that enzyme activity decreased in pregnant individuals. The decrease in the activity of GR in pregnant women is indicative of a decrease in the level of glutathione. This is important in terms of showing that antioxidant load of pregnant women is less than non-pregnant ones.

Keywords: Pregnant women, glutathione reductase, serum.

PC142

Determination of in Vitro and in Silico Effects of Some Uracil Derivatives on Carbonic Anhydrase I Isoenzyme

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AIM: Carbonic anhydrase (CA) is a metalloenzyme that catalyzes the rapid conversion of carbon dioxide to bicarbonate. It is involved in important physiological processes such as respiration, carbon dioxide and ion transport, bone resorption, urogenesis, gluconeogenesis, lipogenesis and electrolyte secretion. The CA enzyme involved in these processes are important therapeutic targets that have the potential to be inhibited for disorders such as edema, glaucoma, obesity, cancer, epilepsy and osteoporosis. Uracil is one of four nucleobases located in the structure of ribonucleic acids. Uracil derivatives have been identified as having many biological and chemotherapeutic sites. In this study, carbonic anhydrase (CA) I isoenzyme from human erythrocytes was purified by affinity gel. The aim of this study was to investigate the inhibition effect of some uracil derivatives such as 5-carboxyuracil, 6- carboxyuracil, 6-methyl uracil and 1,3-dimethyl uracil on CA I isoenzyme.

METHODS: CA I isoenzyme was isolated using the Sepharose-L-tyrosine-sulfanilamide affinity column. To determine CA activity, esterase method based on spectrophotometric measurement based on conversion of 4-nitrophenyl acetate to 4-nitrophenol at 348 nm was used as substrate. In this study, %Activity- [Inhibitor] plots were plotted for uracil derivatives tested on purified CA isoenzymes. IC50 values were calculated.

RESULTS: IC50 values were calculated for human CA I and 5-carboxyuracil, 6- carboxyuracil, 6-methyl uracil and 1,3-dimethyl uracil 0.92, 1.46, 115.52 and 632.4 µM. In silico data were found between -4.232 and -6.446 kcal / mol.

CONCLUSION: Inhibition effects of four different uracil derivatives on purified human CA I enzyme were investigated. 5-carboxyuracil showed the strongest inhibitory effect on CA I enzyme and 1,3-dimethyl uracil showed the weakest effect. According to these results, it was determined that uracil derivatives tested were potent CA I inhibitors and could be used in the treatment of many diseases such as glaucoma, obesity, cancer, epilepsy and osteoporosis.

Keywords: Carbonic Anhydrase I, In silico, Uracil.

PC143

The Effect of Exenatide on Adipogenic Differentiation of Dental Pulp Stem Cells

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AIM: Stem cells are pluripotent cells that have the self-renewal and differentiation capability. Dental pulp mesenchymal stem cells are among of several stem cell sources. Exenatide is a glucagon-like peptide-1 receptor agonist used in the treatment of type 2 diabetes mellitus. It potentiates glucose-mediated insulin secretion and reduces glucagon secretion. By activating adenylate cyclase, it increases the formation of cAMP, stimulates several second messenger systems such as protein kinase A, Epac and produces various effects on the body. It also protects cells from cytokine-related cell death by blocking the JAK-STAT pathway. In this study, we aimed to investigate the effects of exenatide on adipogenic differentiation of dental pulp stem cells due to their effects on cells.

METHOD: Eight dental pulps were used in the study (n=4). Dental pulp stem cells were isolated, cultured and treated with exenatide. Experiments were performed in 1000000 cells. Cell viability was tested with the Muse Count & Viability Kit. 97% viability was determined. Cells were identified by flow cytometry, differentiated into adipogenic cells. StemPro differentiation kit was used to induce differentiation. Cells were stained with oil red o.

RESULTS: When the control and exenatide treated groups were differentiated into adipogenic cells, adipogenic differentiation started 3 days earlier in the exenatide treated group. However, there was no statistically significant difference between the control group and the drug treated group with the Spearman rank differences correlation coefficient ($p>.05$).

CONCLUSION: Although it is found that the exenatide accelerated adipogenic differentiation, there was no difference in the number of differentiated cells. These findings suggest that the exenatide is effective on adipogenic differentiation of dental pulp stem cells, but it is thought that this effect is controlled by different mechanisms since the number of adipogenic cells obtained is not different.

Keywords: Dental pulp stem cells, exenatide, adipogenic differentiation

PC144

Investigation of Anti-Inflammatory Effects of Boric Acid: Experimental Knee Osteoarthritis induced with Monosodium Iodoacetate in Rats

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AIM: Osteoarthritis (OA) is a chronic degenerative joint disease that most commonly seen in the knee joint. Boron is an essential element and known to have antioxidant, hepatoprotective, anti-genotoxic and anti-inflammatory effects in addition to bone growth and alleviation of arthritic symptoms. In this study; it was aimed to investigate the anti-inflammatory efficacy of boric acid (H3BO3) in the elimination / reduction and amelioration of inflammation which plays an important role in the pathogenesis of OA on rats with knee osteoarthritis (KOA) induced with monosodium iodoacetate (MIA).

METHODS: Experimental KOA model was induced by intraarticular (i.a) MIA injection to the right patellar ligament of rats and H3BO3 were administered to these rats 100 µL i.a. at 1st, 7th, 14th, 21st days or 1 mL orally once daily for 4 weeks (5 days/week). The groups were randomly assigned, and healthy control was selected as the first group. The 2nd, 3rd, 4th, 5th and 6th groups were determined as deceased control, 4 mg/kg H3BO3 i.a., 10 mg/kg H3BO3 i.a., 4 mg/kg H3BO3 oral and 10 mg/kg H3BO3 oral, respectively. Rats were sacrificed under general anesthesia and blood samples were taken. Serum TNFα, IL1-β and MMP13 levels were determined by using commercial kit with ELISA method. The study was approved by Ataturk University Local Ethics Committee for Experimental Animals.

RESULTS: TNFα, IL1-β and MMP13 levels were significantly increased in Group 2 compared with Group 1($p<0.05$); According to the Group 2, there was a decrease in the Groups 5 ($p\geq0.05$) and a statistically significant decrease in the Group 3, 4 and 5 ($p<0.05$).

CONCLUSION: In this study, it was concluded that H3BO3 has anti-inflammatory effect in the treatment of DOA and may be a new therapeutic agent alone and/or in combination

Keywords: Osteoarthritis, Boric Acid, Inflammation parameters

PC145

A Correlational Study on Itching and Quality of Life in Patients with Dermatosis

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AIM: Itching is one of the most common symptoms in dermatoses. Itching can continue throughout the day or at different time periods throughout the day. The duration and severity of the itching may disrupt the adaptation of patients to their daily work and the quality of life is adversely affected at the end of the process. In this study, the effect of itching on quality of life was investigated in the group of patients with dermatosis.

METHODS: Dermatology Quality of Life Index and Modified Itching Severity Scores were performed in 64 dermatosis patients (28 male,36 female) in Ankara University Medical Faculty Dermatology Clinic. Spearman Correlation Test was used to examine the correlation between the two tests. T-test is used when comparing scale scores with gender. Statistical significance level was admitted as $p<0.05$. The analyzing was conducted in SPSS20.0 program. (For this study, the permission of the Ethics Committee numbered 9586 was obtained from Ankara University.)

RESULTS: Dermatology Quality of Life Index and Modified Itching Severity Scores of correlation was found to be significant and positive correlation ($r = 0.605$, $p <0.001$). As for the correlation between patient age and Dermatology Quality of Life Index score in the same test, the result was found to be significant and negative correlation ($r = -0.185$, $p < 0.001$). There was no difference between gender independent variable and dermatology quality of life index score ($p = 0.232$).

CONCLUSION: In this study, itching was found to decrease the quality of life. The negative effect of itching on quality of life decreased as the patient age increased. This suggests that elderly patients have higher adaptation ability in the disease process. Collaboration with Liaison Psychiatry in the treatment of these patients may be positive on patient quality of life. Dermatology rehabilitation units can be established by providing support from different branches.

Keywords: Dermatosis, Dermarehabilitation, Itching, Quality of Life

PC146

Diagnostic Value of Gait Analysis in Patients with Lumbar Disc Herniation

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AIM: Although diagnosis of lumbar disc herniation (LDH) is based on clinical examination and imaging, the diagnostic criteria are contentious. The gait analysis has been used previously for diagnosis of other spinal diseases. In this study, we aimed to investigate the diagnostic value of gait analysis in LDH patients.

METHODS: Nine patients with LDH (M/F, 7/2; mean age 50.8±11.0 years) and six healthy controls (M/F, 3/3; mean age 50.2±8.0 years) were included. Gait analyses of the participants were performed by FMD-System-Gait-Analysis (Zebris © Medical GmbH, Germany) device in Anatomy Department. Between-group comparisons were made by t-test and Mann Whitney U-test. This study was approved by the ethic board of Trakya University (TÜTF-BAEK 2019/153).

RESULTS: Both study groups were comparable in terms of demographic characteristics such as mean age and gender distribution. Gait analysis showed that swing width ($p=0.01$), stance phase ($p=0.005$ for left; $p=0.019$ for right), load response ($p=0.001$ for left; $p=0.032$ for right) were increased in LDH patients compared to controls. Step length ($p=0.003$ for left; $p=0.001$ for right), single support ($p=0.011$ for left; $p=0.004$ for right) and swing phase ($p=0.005$ for left; $p=0.019$ for right) were reduced in LDH patients. Overall, our results suggest that gait was impaired in patients with LDH.

CONCLUSION: Gait analysis may be used as an adjunct method in diagnosis and follow up of patients with LDH.

Keywords: Diagnostic value, gait analysis, stance phase, swing phase

PC147

How Do Curcumin and Rutin Affect Locomotor Activity in Lipopolysaccharide Administered Rats?

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AIM: Lipopolysaccharide (LPS) triggers the innate immune system to release pro-inflammatory cytokines. Curcumin and rutin are the flavonoids with well-established anti-inflammatory properties. The locomotor activity was investigated in the animals which curcumin, rutin and/or LPS were administered.

METHODS: Adult male Wistar albino rats received curcumin (50 mg/kg/day, n=7) or rutin (50 mg/kg/day, n=7) or vehicle (control [n=7] and LPS [n=6] groups) for 14 days. Except for the controls, LPS (0.47 mg/kg) was intraperitoneally injected at 13th and 14th days. After 24-h, the open-field test was conducted in a cube-shaped apparatus which was divided into central and peripheral zones (3:2 of total area). Total distance moved (cm), distance moved in the zones (cm) and time spent in the zones (s) were estimated. Kruskal-Wallis test and post-hoc Dunn's test were used for the statistical analyses Ethical approval was acquired (2017/3-2).

RESULTS: There was a significance in the total distance moved was significant between (p=0.033) which was resulted from the difference between the control and LPS groups (p=0.004). Although it didn't reach to the significance level, Curcumin and Rutin animals travelled more than the LPS group (respectively, p=0.157 and p=0.055). The distance moved in the peripheral zone was significant (p=0.036) whereas no significance was found in the central zone (p=0.458). The travelled distance in the peripheral zone was lowest in LPS animals which was not statistically significant versus the Curcumin and Rutin groups (respectively, p=0.078 and p=0.058), but the controls (p=0.004). The time spent in the central zone was similar among the groups (p=0.432).

CONCLUSION: LPS resulted in decreased locomotor activity. The administration of curcumin and rutin led to an increase in locomotion even though the significance level wasn't attained. None of the animals displayed an anxiety-like behavior as seen by the time spent in the central zone. Supported by Hatay Mustafa Kemal University (BAP #16741).

Keywords: Sickness behavior, rutin, curcumin, lipopolysaccharide

PC148

Investigation of the Effect of Some Natural Phenolic Substances on Bovine Liver Carbonic Anhydrase 5A Enzyme

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AIM: Carbonic anhydrase (CA) reversibly catalyze the fundamental reaction of carbondyoxide hydration to bicarbonate and protons in all living organisms, being actively involved in the regulation of patho/physiological processes. Physiological and pharmacological studies with CA inhibitors have led to an understanding of the importance of mitochondrial carbonic anhydrases (CA 5A and CA VB) in various metabolic pathways including gluconeogenesis, urogenesis and lipogenesis. CA 5A and 5B have been found to be necessary to convert carbon dioxide to bicarbonate at a rate sufficient to support metabolic needs for these three major pathways. In this study, it was aimed to purify CA 5A enzyme from bovine liver with newly synthesized affinity gel and to investigate the inhibition effect of natural phenolic substances such as catechol, resorcinol, resveratrol and tyrosine on CA 5A we obtained pure.

METHODS: Healthy bovine liver CA 5A was isolated using a cellulose – phenyl - sulfanilamide affinity column. Spectrophotometric esterase method was used to determine the activity of CA 5A based on the conversion of 4-nitrophenyl acetate to 4-nitrophenol at 348 nm as substrate. In this study, % Activity-[Inhibitor] plots were plotted for the substances tested on purified CA 5A. IC50 values were calculated.

RESULTS: The CA 5A enzyme was purified from bovine liver mitochondria using affinity chromatography in 124,8 fold, approximately 27.5% yield. IC50 values of catechol, resorcinol and resveratrol on the purified enzyme were determined as 72.5, 61.8 and 35.6 µM, respectively.

CONCLUSIONS: It was determined that tyrosine showed no significant inhibitory effect on CA 5A which is one of the natural phenolic substances, whereas catechol, resorcinol and resveratrol showed strong inhibitory effect. Three natural CA 5A inhibitors identified in this study can be used in the treatment of many diseases, especially obesity. This study was financed by Turkish Research Council-TÜBİTAK (KBAG 114Z731). We are thankfull to TÜBİTAK for financial support.

Keywords: Carbonic anhydrase, enzyme, phenolic compound, inhibition

PC149

Robotic Modeling of Direct and Indirect Light Reflex by Arduino Uno

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AIM: According to the theories of Jean Piaget and Jerome Bruner, education is an active, dynamic process and strengthened by the interactive participation of learners. In medical education, animation and 3D modeling are preferred all over the world because of their contribution to permanent learning. For this purpose, a "direct and indirect light reflex model, which works with 3-D, mobile, robotic coding which provides the explanation of physiological mechanisms was established.

METHODS: According to this model, 24 plexiglass scissors were used to represent the pupil sphincter muscles, which represent the Hoberman circle and the radial muscles surrounding it, to show the direct and indirect myosis response of the pupil to light stimulation. The iris is made of colored silicone material and mounted to the front to show myosis and mydriasis by servo and DC motors to which the mechanisms behind it are connected. The LDR sensor module for retinal representation is integrated with the code written into the Arduino Uno for the detection of the captured light. Servo and DC motors, which are provided to be opened according to the measured light value, activate various mechanical structures that represent radial and circular muscles and provide various degrees of reversible myosis response. Arduno Uno coding and connections are designed to cover representative double-sided retina, Edinger Westphal nuclei and N. Oculomotorius, allowing observation of the bilateral response by shedding light on any eye. Connectors are designed to be plugged and detached so that learners can monitor changes in light reflex caused by various pathologies.
CONCLUSION: As a result, this modeling, which has been made to make the theoretical knowledge more permanent with interactive experiences, provides a valuable basis for the insertion of ciliary muscles, lenses and optical devices for further development in the future.

Keywords: Arduino Uno, Light refleks, Modeling

PC150

Rethinking Large Group Lectures: How Far in This Format?

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AIM: Large group teaching is the most widely applied and discussed learning method of higher education in Turkey. In this study, experiences of students and teachers in classroom and lecture presentations were evaluated.

METHODS: Third year students and teachers at Marmara University School of Medicine, where language of teaching is English, have participated in study. In 3rd year curriculum, two courses (116 lectures) out of five courses were chosen for evaluation. Using "Lecture Observation/Checklist Form", one or two observers/researchers observed ambiance and activities in 76 lectures. Three other researchers evaluated 43 presentations of those observed lectures by "Presentation Evaluation Form." Evaluations were made using variance analysis.

RESULTS: In 218-student class, average of students who attended lectures were 51.21 (min.=12, max.=107). Eighty percent of teachers did not make any activities to attract attention and prepare students for lesson. Only 12% of lectures were taught interactively (cases, videos, etc.), but 88 % were given without any interaction. The mean number of questions per lecture asked by students was 1.96 (min.=0, max.=10) and questions asked by teachers to students was 5.13 (min.=0, max.=20). Of evaluated 43 slide-presentations, 79.1% was clinical and 20.9% was basic-science lectures. Number of slides per 50-min lecture was 35.28 (min.=25, max.=64). While quality of slide content and methodology was "improvable" in 27.9% of presentations," others were "acceptable" or "adequate". In only 39.5% of presentations, learning objectives/contents were shared. In 62.8% of presentations, the contents were presented without any cases, videos or patient histories. In 65.1% of presentations, a sufficient association or integration was not made between clinical/basic sciences.

CONCLUSION: These results indicated that intense content of basic/clinical sciences given as direct lecturing with minimum interaction, and problems as inadequate preparation of presentations, insufficient integration of basic/clinical sciences raise the question: how long can lectures continue in this format?

Keywords: Integration, lectures, medical education, undergraduate

PC151

Quality of Life in International Students; the Case of Suleyman Demirel University

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AIM: The quality of life of foreign students studying at Süleyman Demirel University was investigated.

METHODS: Personal information form with Sirgy et al. (2007) was used in the questionnaire. Our study was approved by the Clinical Studies Ethics Committee

RESULTS: The study included 38 foreign students; 13(34.2%) Health Sciences, 8(21.1%) Engineering 15(39.5%) Faculty of Economics and Administrative Sciences participated. On the basis of their country of origin, Europe 3(8.3%), Africa 10 (27.8%), Asia 22 (61.1%), America 1(2.6%) frequency was found. General language levels were 22 (57.9%) for reading, 22 (57.9%) for writing, 17 (44.7%) for understanding, 18 (47.4%) for speaking. On the basis of the problems they experienced, housing comes first with a rate of 11 (28.9%). 20 (52.6%) of the teaching at the university, 18(47.4%) on the basis of class, 13 (26.3%) of course load, 14 (36.8%) of reputation, 11 (26.3%) of health services, telecommunications and technology 14 (36.8%), security and transportation 16 (42.1%), overall quality of life 19 (50.0%), sports facilities 17(44.7%), environment 15 (39%) 5) The level of satisfaction with the Rectorate International Relations Unit 18 (47.4%) was determined. Library services 14 (36.8%), nutrition services 18(47.4%), housing services 16(42.1%), social life 18(47.4%), their thoughts on cultural centers on campus 12 (31%) 6), club studies with 17 (44.7%) were found to be moderately satisfied. There was a significant correlation between gender and exposure to race, skin and gender, and male exposure was higher (p=0.022, r=- 0.370). There was a significant correlation between gender and achievement, and women's course achievement was higher (p=0.005, r=0.448). There was a significant correlation between language levels and success (p=0.022, r=0.370). There was a significant correlation between students' accommodation and their responses in the comparison of housing service satisfaction (p=0.001, r=0.539). There was a significant correlation between general quality of life and housing (p=0.006, r=0.436).

CONCLUSION: Language levels, psychological satisfaction and housing problems of foreign students with dissolution and their quality of life and academic achievement can be reached to higher levels.

Keywords: Foreign Students, Quality of Life, Education.

PC152

Investigation of Odor-Sleep Relationship among Suleyman Demirel University Medical Faculty Students

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AIM: Odor is one of the chemical substances which can be detected by the sense of smell and dissolved in air in small concentrations. The smell is related to one's feelings, mental state and behavior. The relationship between various odors and sleep quality was investigated in medical students.

METHODS: In our cross-sectional study, socio-demographic characteristics, Pittsburg Sleep Quality Index (PSQI) and odor questionnaire developed according to literature were used for medical students of our university. During the survey application, the participants were not informed about the smell. Data were analyzed with descriptive statistics and ANOVA test. Our study was approved by the Clinical Studies Ethics Committee.

RESULTS: 103 (53.1%) male students and 91 (46.9%) female students were included. The mean age of the students was 21.91±1.94. 45 (23.2%) of the students were smoking and 50 (25.8%) were drinking alcohol. In our study, the mean total PSQI score was 12.88±5.60. 106 (54.9%) of the students who participated in the study think that the bad smell of the environment affects sleep quality. 60 (36.1%) of the participants stated that the smell of lavender, 40 (24.1%) of the mint and 27 (16.3%) of the fragrance of rose gave peace and rest. Statistically significant difference was found between the duration of falling asleep of the students and the quality of sleep in the bedroom smells (p=0.30) and increase. One-night sleep duration of the participants was found to be statistically significant (p=0.43) and increased between the odors they used in the bedroom and the sleep quality.

CONCLUSION: In our study, it was found that the use of fragrances that were good for the person had a positive effect on improving sleep quality. Further studies are needed to investigate the mechanism of the relationship between odor and sleep quality.

Keywords: Sleep, Sleep quality, Odor.

PC153

The Awareness of the Students of the Faculty of Medicine about Food Additives and Their Effects on Health

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AIM: The aim of this study was to determine knowledge, attitudes and awareness of food additives and their effects on health in medical students.

METHODS: Personal information form and questionnaire developed in accordance with the literature were used to determine the level of knowledge, attitude and awareness of the students about the effects of food additives and their effects on health. Our study was approved by the Ethics Committee of Clinical Studies (26/10/2017-198).

RESULTS: 115 students with a mean age of 22.03±2.05, F: 70 (60.9%) and M:45 (39.1%) participated in the study. The distribution of grades in the Faculty of Medicine Term 1–16(13.9%), Term 2–20(17.4%), Term 3-18(15.7%), Term 4–15 (13.0%), Term 5-21(18.3%), Term 6-25 (21.7%) students participated in this study. 41.7% (48) of the mothers and 62.6% (72) of the fathers had undergraduate education. 55.3% (63) of the mothers were housewives; 22.6% (26) of the fathers were educators. Among the participants, the rate of carrying the idea of homemade natural food was 85.2% (98) high. Homemade natural foods were generally found to be yoghurt, bread, tomato paste, pickles and jam. Homemade food sensitivity of the parents was found to be high (80.9%). The sensitivity to not using food additives was also 66.1% (76). Considering the sensitivity of food additive product use, the rate was lower with 48.7% (56). Answers to the questions posed to look at their knowledge and attitudes towards the use of additives; shelf life extension 111 (96.5%), taste enhancement 101 (87.8%), color enhancement 93 (80.9%), consistency 93 (80.9%), bacterial reproduction 88 (76.5%), clumping was 80 (69.6%). There was a significant correlation with the tendency towards natural nutrients and the sensitivity of not using additives, hesitant use against additives, avoidance and desire not to consume (p=0.001, r=0.693; p=0.001, r=0.305; p= 0.001, r=0.302; p=0.006, r=0.257).

CONCLUSION: Healthy nutrition of medical students is important both for their own health and for gaining these habits for their patients
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Keywords: Food Additives, Additives Awareness, Health

PC154

The Relationship between Healthy Lifestyle Behaviors and Sleep Quality

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AIM: In this study, we investigated the relationship between healthy lifestyle behaviors and sleep quality in Süleyman Demirel University students.

METHODS: In this cross-sectional study, socio-demographic characteristics, Pittsburg Sleep Quality Index (PSQI) and Healthy Lifestyle Behavior Scale II questionnaire were used to assess the sleep quality of Suleyman Demirel University students. Sleep quality as dependent variable and healthy lifestyle behaviors as independent variable were evaluated. Our study was approved by the Clinical Studies Ethics Committee.

RESULTS: 37 (69.8%) female and 16 (30.2%) male students participated in the study. The mean age of the students was 21.67±1.95. The students who participated in the study; 31 (64.6%) of them were Faculty of Health Sciences, 4 (8.3%) were Faculty of Arts and Sciences, 9 (18.8%) were Faculty of Economics and Administrative Sciences and 4 (8.3%) were included. The students who participated in the study; 33 (63.5%) people live between 500 and 1000 TL, 32 (61.5%) people live in the apartment, 24 (45.3%) people smoke and drink alcohol. In our study, the total PSQI mean score was 15.0±8.22 and the mean score of the Health Lifestyle Behavior II scale was 132.52±20.28. There was a correlation between healthy lifestyle behavior score and the number of people staying (p =0.36). There was a statistically significant difference between the departments in PSQI score and it was higher in the Faculty of Arts and Sciences compared to other faculties.

CONCLUSION: We found that there was a significant relationship between healthy living behaviors and sleep quality of the participants. For healthy sleep, we anticipate that we should put healthy lifestyle behaviors at the center of our lives.

Keywords: Sleep, Sleep quality, Healthy life.

PC155

Fatigue and Sleep Quality of Pre-Clinic Students in the Faculty of Medicine

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AIM: The aim of this study is to determine the relationship between sleep quality and fatigue seen in preclinical medical students.

METHODS: In this cross-sectional study, socio-demographic characteristics questionnaire, Pittsburg Sleep Quality Index (PSQI) and Piper Fatigue Scale questionnaires were used to assess sleep quality in the first, second and third grade students of the medical faculty of our university. Our study was approved by the clinical studies ethics committee.

RESULTS: The students who participated in the study; Term I 43 students (31.9%), Term II 52 students (38.5%) and Term III 40 students (29.6%) were included in the study. 76(56.3%) female students and 59(43.7%) male students participated in the study. In order to stay awake, the use of nutrient-drug supplements was found in 29 (21.5%) people, alcohol use in 35 (25.9%) people and smoking 29 (21.5%) people. Study hours of the students are 87 hours (64.4%), 1-2 hours 42 (31.1%), 5-8 hours 3 (2.2%) and 9 hours and more 3 hours (2.2%) person. Of the participants,113 (83.7%) preferred sleeping in the dark, while 62 (45.9%) thought that beverages consumed before bedtime did not affect sleep quality. The mean age of the students was 20.31±0.12. In our study, total PSQI mean was 12.6±0.49 and PIPER mean was 5±0.15. There was a statistically significant difference (p=0.038) between the time to fall asleep between the term II and III students and decreased. There was a statistically significant difference (p=0.01) in the PSQI of the students in term I and III (p=0.01) and decreased. There was a statistically significant difference (p=0.39) in PIPER between the students in term I and term II and decreased.

CONCLUSION: The fatigue levels of the students who participated in our study increased in Term I and II and decreased in Term III. Sleep quality of the students decreased in Term I and II and increased in Term III.

Keywords: Sleep, Fatigue, Sleep quality, Pre-clinical period.

PC156

Measurement and Analysis of Electromagnetic Fields of Mobile Communication Antennas in Turkish Republic of Northern Cyprus

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AIM: Public concerns about base stations and adverse health effects have been raised with extensive use of mobile phones. Radiofrequency electromagnetic field (RF-EMF) measurements are done for various reasons such as to define safety hygiene standard or regulatory documents; to identify RF-EMF sources; to obtain data to be used for epidemiologic studies to observe long term exposure results. The multiple factors affecting reliability of the measurements can be categorized with measurement device specifications and measurement conditions.

METHODS: In this study, five measurement reports published by the Information Technologies and Communication Authority (ITCA) in North Cyprus between 2009-2018 were reviewed, the change in the RF-EMF public exposure caused by base stations were analyzed and adverse health effects comparing the results with national and international guidelines were defined.

RESULTS: The limitation of this study is that data extracted from various reports having gaps about the measurement criteria during RF-EMF measurement. So that it is difficult to define adverse health effects across the years. Further limitation, the points such as measurement time and duration, near field/far field issues, weather conditions, technical specification of base stations, selection criteria of base station that should be taken into consideration while performing the RF measurements should be clearly reflected in the reports, so that there should be no gap in informing the public about their health effects.

CONCLUSION: The present data along with current scientific evidence let to the conclusion that short-term RF-EMF exposure from mobile phone technology is not related to levels of well-being or physical symptoms in individuals having EMF hypersensitivity. Furthermore, those individuals are unable to detect the presence of RF-EMF and present with a range of serious symptoms and often have a very poor quality of life. Therefore, EMF measurement should be done by considering short and long term adverse effects.

Keywords: Radiofrequency, Electromagnetic fields, Measurement, Health effects.