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05-08 September 2016

Düzce University, Turkey

Turkish Society of Physiological Sciences

42nd National Physiology Congress

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Düzce University, Convention Center, Düzce - TURKEY

05 September Monday	06 September Tuesday	07 September Wednesday	08 September Thursday
	08.45 – 10.15 Symposium 1: Cafer Marangoz, Erdal Ağar, Mehmet Yıldırım Panel 1: Narin Derin, Sezen Milli Avtan, Fatih Karaaslan A & B Lecture Theatres	08.45 – 10.15 Oral Presentations – II A & B & C Lecture Theatres	08.45 – 10.15 Symposium 2: Deniz Atasoy, Bilal Kerman, Yasemin Gürsoy Özdemir Symposium 3: Sadi Kurdak, Kerem Tuncay Özgünen A & B Lecture Theatres
10.00 – 14.30 Workshops	10.15 – 10.45 Coffee Break	10.15 – 10.45 Coffee Break	10.15 – 10.45 Coffee Break
12.30 – 13.00 Lunch for Workshop Participants	10.45 – 11.35 Conference 2 Cenk Ayata	10.45 – 11.35 Conference 5 (Markus Hecker)	10.45 – 11.35 Conference 8 Richard Vaughn-Jones
14.45 – 15.30 Data Blitz-I A & B Lecture Theatres	11.40 - 12.30 Data Blitz-II A & B Lecture Theatres	11.40 - 12.25 Data Blitz-III A & B & C Lecture Theatres	11.35 – 12.10 Awards & Closing Session
15.30 – 15.45 Photograph Presentation & Exhibition Gürkan Öztürk	12.30 – 14.00 Poster Presentations & Lunch	12.25 - 13.45 Poster Presentations & Lunch	12.10 – 13.10 Annual General Meeting Turkish Society of Physiological Sciences
15.45 – 16.30 Poster Presentations & Coffee Break	14.00 – 14.45 Conference 3 Ahmet Gül	13.45 / 14.00 – 15.00 Oral Presentations – III A & B & C Lecture Theatres	13.10 – 19.00 Excursion to waterfalls
16.30 – 17.00 Opening Session	14.45 – 15.00 Oral Presentations Dr. Banu Ocakçıoğlu memorial program Metin Baştuğ	15.05 – 15.50 Conference 6 Tayfun Uzbay	
17.00 – 18.00 Respect to Masters	15.00 – 16.15 Oral Presentations – I A & B & C Lecture Theatres	15.50 – 16. 20 Coffee Break	
18.00 – 19.00 Conference 1 M. Gazi Yaşargil	16.15 – 16. 45 Coffee Break	16.20 – 17.10 Conference 7 Jens Leipziger	
19.00 – 19.20 Opening Resital Piano: Ayşe Kaptan Flute: Eda Özdiş	16.45 – 17.30 Conference 4 Kemal Türker	17.10 – 18.40 Panel 3 Cafer Marangoz, Şeref Erdoğan, Gürkan Öztürk, Elif Şen	
19.30 - 21.00 Reception (Düzce University, Convention Center)	17.30 – 18.15 Panel 2: Europhysiology Bayram Yılmaz, Richard Vaughn-Jones, Jens Leipziger, Markus Hecker	20.00 – 24.00 Gala Dinner (Turkuaz Beach Hotel, Akçakoca)	

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All abstracts have been reviewed by the following list of referees.

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ACTA PHYSIOLOGICA

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Conferences

Conference 1
The Impact of Scientific Evolution on the Neurosciences
M. Gazi Yaşargil
Yeditepe University, Medical School Hospital, Department of Brain Surgery, İstanbul

It is not surprising that the invention of motor cars and airplanes was not considered 2000 or even 200 years ago, due to the abscence of their socio-economic necessity. However, it is surprising that inventions for optic glasses and microscopes remained fairly delayed, not only to advance scientific research, but also to help those people with inherited or acquired weakness of their visual functions.
It is indeed astonishing that Ibn al-Haytham (Alhazen 915-1039), astronomer and mathematician, initially an engineer for hydraulics, who examined such phenomena as the rainbow, atmospheric refraction, mirror and lentiform crystals, and, notably, the anatomy and physiology of the eye, and wrote the famous book on optics (Kitab el-Menazir), which became widely influential in Europe, but he failed to consider developing an optical aid. The first single lens "spectacles" were manufactured in Florence, Italy (1303-1313), but the demand for them remained low until the invention of cheap books in the 17th century. The manufacture of sophisticated eye glasses with individual diopters, the availability of contact lenses, and finally laser surgery of the cornea, required 600 years of diligent research.At the end of the 16th century and beginning of the 17th century simple microscopes and telescopes were constructed in the Netherlands and Italy. Interestingly, periods of devastating epidemics and several wars in Europe did not inhibit the incessant endeavors of manufacturers, glass grinders, mathematicians, astronomers, scientists, and even philosophers (Descartes, Spinoza). The upheaval of the industrial revolution in England between 1770 and 1825 culminated in the production of achromatic microscopes without spherical aberration. The formulation of the equation "angular aperture" in 1880 by Ernst Abbe at Zeiss Company in Jena, Germany, allowed the serial production of high quality microscopes and telescopes. Advances in the entire field of neurosciences, particularly in integral neurophysiology, EEG, MEG, angiography, CT, MRI and ultrasound technologies constitute today the prime and essential components of neuro-diagnosis and neuro-therapies. Within the past 50 years, neurosurgery has experienced a great number of technological innovations, such as the introduction of stereotactic technology, operating microscope, bipolar coagulation technology, bipolar forceps, different sizes and shapes of temporary and permanent vessel and aneurysm clips, microsutures, ultrasound devices to identify the deep localized lesions, ultrasound microflowmeter, ultrasonic suction, ultrasonic microdrill apparatus, high speed drill apparatus, flexible and rigid endoscopy technology, intraoperative stimulation and monitoring technology, intraoperative tractography using diffusion tensor mapping, and anisotropic diffusion weighted MRI which provides spatial and directional information of the neuronal fibers, gradient respondent gamma surgery, and intensity modulated radiation therapy. Modern operating rooms offer hitherto unimagined technologies for the accurate targeting of the lesions, and their complete elimination without endangering adjacent normal structures and functions. A great number of lesions localized in so-called eloquent areas of the CNS, and defined as inoperable, are, at the present time, explored on a routine basis and successfully treated in many centers. The above qualification of a fully equipped department with a team of expert personnel represent ideal working conditions.One of the axioms guiding open societies is the issue of ethics, desiring us to respect the rights, freedom and dignity of each individual and, in cases of illness, requiring us to fulfill each patient's claim to equal benefit from advances in medicine and surgery. Our professional goal is to further improve diagnostic and therapeutic procedures, and to ensure their availability globally to each and every individual.

Conference 2
Spreading Depolarization Waves in Injured Brain
Cenk Ayata
Harvard Medical School, Massachusetts General Hospital, Neurovascular Research Lab &Department of Neurology, Boston, MA, USA

Spreading depolarization are intense, slowly propagating waves of neuronal and glial pandepolarization that emerge in an apparently spontaneous fashion in injured brain regardless of the mode of injury (ischemic, hemorrhagic, traumatic). Starting at the onset of injury, recurrent spreading depolarizations continue to occur for many days after injury with very high frequency. They worsen the oxygen supply-demand mismatch by increasing the metabolic demand and decreasing the blood flow. Therefore, spreading depolarizations are considered a clinically relevant therapeutic target in various types of brain injury. However, pharmacological inhibition of spreading depolarizations has clinically proven to be difficult to achieve without unwanted side effects. Instead, recent efforts have turned to the origins of spreading depolarizations. If we develop a better understanding of how and why spreading depolarizations are triggered in the first place, we can perhaps implement measures in neurocritical care that might minimize their occurrence. In my talk, I will present data showing that oxygen supply-demand mismatch transients trigger spreading depolarizations in susceptible peri-infarct "hot zones." Such supply-demand mismatch transients can be precipitated by transient reduction in oxygen supply, such as during brief hypoxic or hypotensive events that are clinically exceedingly common, or by transient increase in oxygen demand, such as during functional activation, which is part of life. In addition, I will present data showing that brief intracranial pressure spikes, which are also very common in neurocritical care, are also capable of triggering spreading depolarizations. I will finish by summarizing the clinical implications of the data, and how it can be tested clinically.

Conference 3

Asia Minor, Genes, and Fever

Ahmet Gül
İstanbul University, İstanbul Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İstanbul, Turkey

Interaction with environment plays a critical role in shaping our genetic variations. Especially, polymorphisms in the genes involved in inflammatory response show regional variations and affect our adaptation to the local environment by protecting integrity of our body. Fever is one of the most important components of inflammatory response, and it is usually induced by pathogen- or danger-associated danger signals during microbial infections. However, mutations in some innate immune response genes are also responsible for hereditary fever syndromes, which are characterized by recurrent and self-limited inflammatory episodes without an obvious trigger. These conditions are now known as autoinflammatorydisorders. Familial Mediterranean fever is the most common form of autoinflammatory disorders. It is associated with autosomal recessively inherited MEFV gene variations, and prevalence of the carriers of these variations is quite high in Eastern Mediterranean populations, including those living in Asia Minor, reaching 20%. MEFV gene exon 10 variations result in increased activation of interleukin-1 beta (IL-1β) in inflammatory cells by proteolytic cleavage of its precursor by caspase 1 enzyme following triggers. IL-1β is known as the strongest endogenous pyrogen and responsible for fever and inflammatory response. Increased prevalence of MEFV mutation carriers in the Eastern Mediterranean may result from its accumulation through ages because of a selective heterozygous advantage. Higher frequency of sickle cell anemia mutations in certain regions of Africa is considered to be associated with a heterozygous advantage against malaria. Similarly, the MEFV variants might have provided a selective advantage to populations living in Asia Minor and neighboring regions by protecting them against pandemic infections with high mortalitysuch as smallpox through overcoming specific immune evasion ways of microbes with a higher inflammasome activity and IL-1 production.

Conference 4

How Do We Masticate Without Eating Our Own Tongue?

Kemal S. Türker
Koç University School of Medicine, Department of Physiology, İstanbul, Turkey

Mastication has two fundamental control mechanisms: the central pattern generator (CPG) that sets the pattern of mastication by alternately sending action potentials to jaw opening and closing muscles; and the peripheral controller that modulates the output of the CPG and jaw muscle motoneurons so that optimum bite forces are developed between the jaws. The peripheral control mechanism includes the cutaneous and mucosal receptors that innervate the lips and the oral mucosa, periodontal mechanoreceptors that innervate the support tissues of the tooth root, and muscle spindles in the jaw muscles. These receptors monitor chewing forces and modify the activity of muscles in the jaw, tongue and cheeks in order to facilitate mastication and prevent damage to oral tissues. To investigate their connections to motoneurons that innervate jaw muscles, we stimulate these receptors electrically and/or mechanically in consenting adult volunteers. The responses of the jaw muscles to the stimuli are recorded using intramuscular fine wire and surface electromyography (EMG) electrodes. These studies contribute to a better understanding of the neuronal circuitry of the masticatory system and provide a scientific baseline from where the neurophysiological consequences of interventions that change the physical relationship of the masticatory elementscan be investigated.

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Conference 5

Epigenetic Control of Endothelial Nitric Oxide Synthase Expression and Its Role in Coronary Heart Disease

Markus Hecker
Department of Cardiovascular Physiology, Heidelberg University, Germany

A single nucleotide polymorphism (SNP) within the promoter of the endothelial nitric oxide (NO) synthase (NOS3) gene (T-786C, rs2070744) adversely affects the response of endothelial cells fromCC-genotypeindividuals to shear stressor the prototypic antitype 1 T-helper (Th1) cell cytokine interleukin-10. Homozygosity for the C-allele, whichoccurs in about 12% of Caucasians, is a strong predictor for coronary heart disease (CHD), polymyalgia rheumatica or rheumatoid arthritis (RA).We have previously identified a compensatory mechanisminvolving manganese-dependent superoxide dismutase that helps to maintain the bioavailability of endothelial cell-derived NO. With the shear stress-dependent increased release of 15-deoxy-$\Delta^{12,14}$-prostaglandin J_2 (15d-PGJ_2) from CC- but not TT-genotype endothelial cells, we have characterised anothercompensatory mechanism that may not only support the anti-inflammatory capacity of the CC-genotype endothelial cells but also act as a novel general defence mechanism against chronic inflammation. Correlating plasma 15d-PGJ_2 levels with the severity of the disease in patients with CHD or RA support this notion.

Moreover, data acquired quite recently point to a possible epigenetic control of *NOS3* expression through chromatin remodelling that may differ in at least two aspects between CC- and TT-genotype endothelial cells. Having generated knock-in mice harbouring the human C- or T-type *NOS3* promoteron a disease-susceptible genetic background, we will verify that the T-786C SNP of the human *NOS3* gene, if present,boosts the development of arteriosclerosis and/or arthritis in these animals. The reason for this complex experimental approach is that instead of the 5'-GGC(TŽC)GG-3' motif found in humans the murine *Nos3*promoter contains a 5'-GGCCAT-3'motif so that the suspected critical CpG-dinucleotide cannot form. Finally, we have begun to corroborate in an *in vitro* transmigration model mimicking shear stress conditions at arteriosclerosis predilection sites that the T-786C SNP of the human *NOS3* gene not only differentially affects monocyte-endothelial cell but also Th1 and Th17 cell-endothelial cell interaction, respectively, through 15d-PGJ_2. In a nutshell, due to the acquired compensatory mechanisms the formerly adverse SNP in the promoter of the human *NOS3* gene may be viewed as a largely neutral mutation.

Conference 6

Neuroplasticity in Substance Addiction

Tayfun Uzbay
Üsküdar University, Neuropsychopharmacology Application and Research Center (NPARC), İstanbul, Turkey

Substance abuse and addiction is increasingly understood as a neurobiological disorder where continuously abuse of addictive substances corrupts the normal circuitry of rewarding and adaptive behaviors generating fromadaptive changes in central nervous system (CNS) induced by these substances.Neuroplasticity can briefly be defined as adaptive changes against internal and external stimuli in the brain's neurons, and structural and functional alterations in synapses formed by these neurons.If the changes are not confined to a single neuron but reach the level of a synapse, the adaptive response formed may also be called "synaptic plasticity" (1). Finally, neuroplasticity is a flexible re-organization, adaptation or remodeling of mammalian brain carried out by changes in synapticformation and elements. It is affected by endogenous, exogenous and environmental stressful factors. While normal synaptic plasticity is involved in several vital functions such as mind, memory, learning, psychomotor performance and healthy behaviors, abnormal neuroplasticity may cause some serious CNS disorders such as addiction, depression, autism and schizophrenia. Long term potentiation (LTP) formation in neurons is necessary for learning and it is an adaptive response associated with synaptic plasticity. Because learning and memory is an important part of brain neuroplasticity, we can interpret the addiction as a negative neuroplasticity or a negative neuronal adaptation appearing under a heavy stress depending on toxic effects of continuously abused drugs in brain.In a molecular and cellular level, addiction is a negative neuroadaptation in some specific structures or pathways such as dopaminergic system in brain (2). This statement may be related to neurodegeneration or generates unusual, mutant or zombie (terrorist) neurons or both of themin these specific brain regions (3). The process is directly generated and/or supported by chronic use of addictive agents.A treatment that inhibits neurodegeneration andstimulates healthy neurogenesis in damaged areas, and/or prevents to generate the zombie/terrorist neurons or convertingthem to normal neuronsmay provide a radical solution for this serious public health problem.

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Conference 7

Extracellular ATP Signaling in Kidney Functions MAKE SENSE

Jens Leipziger
Institute of Biomedicine, Physiology, Aarhus University, Denmark

I will take you along a trail of own discoveries that have outlined an auto- and paracrine signaling system that is necessary for proper renal function. This system uses extracellular ATP, which is released from renal epithelia to then stimulate membrane receptors (purinergic P2X and P2Y). Multiple physiological stimuli exist that lead to cellular ATP release and these will be discussed. Most intriguingly, the flow of pre-urine along the renal tubule can be sensed by the primary cilium. Its bending causes an increase of $[Ca^{2+}]_i$ and activates ATP secretion. Stimulation of purinergic receptors has pronounced effects on the ability to transport ions and water along the entire renal tubule. These intra-renal purinergic signals work as endogenous "diuretics", i.e. they favor the excretion of urine. Importantly, the tubular lumen, i.e. the urinary space is an active signaling compartment, from which renal functions are regulated. Eventually, evidence accumulates indicating that aberrant activation of intra-renal purinergic signals are danger signals for the activation of immune responses and are involved in renal damage, fibrosis and loss of organ function.

Conference 8

Ca^{2+}-H^+ Coupling in the Heart: A Driver of Contractility, Arrhythmia and Nuclear Signalling

Richard D Vaughan Jones
Burdon Sanderson Cardiac Science Centre, Department of Physiology Anatomy & Genetics, Oxford, UK

H^+ ions are universal products of metabolism. In myocytes of the heart, the intracellular H^+ concentration ($[H^+]_i$) is kept close to 60nM (pHi 7.20) by means of sarcolemmal H^+ extrusion on Na^+-coupled transporters such as Na/H exchange (NHE1). Extrusion is essential because of the H^+ ion's high chemical reactivity, although significant fluctuations in $[H^+]_i$do occur physiologically, and during clinical events such as myocardial ischaemia/reperfusion. In the ventricular myocyte, there is an intimate positive coupling between Ca^{2+} signalling and $[H^+]_I$, which can help to protect contractility during periods of intracellular acidosis. If pronounced, acidosis can also drive intracellular Ca^{2+} overload, triggering pro-arrhythmogenic Ca^{2+} waves. I will describe how myocardial $[H^+]_i$ is regulated, emphasising the importance of cytoplasmic histidyl dipeptides (HDPs) for diffusively shuttling H^+ ions within individual cells. I will then focus on three distinct mechanisms of myocardial Ca^{2+}-H^+ coupling. One mechanism, relies upon a rise of intracellular Na^+, driven by $[H^+]_i$ stimulation of NHE1. This rise modulates sarcoplasmic reticulum (SR) Ca^{2+}-loading, thereby regulating Ca^{2+} signalling and the triggering ofCa^{2+} waves. A second mechanism relies upon the exchange of $H^+$for Ca^{2+} ions at intracellular buffers, particularly the HDPs. This second mechanismmay be important for maintaining Ca^{2+}-activated processes in the face of competitive inhibition by H^+ ions. A third mechanism is associated with the counter transport by HDPs of Ca^{2+} and H^+ ions through nuclear pores, resulting in a coupling between nuclear Ca^{2+} signalling and nuclear pH, a phenomenon that may be important for modulating gene transcription. Overall, the combination of NHE1 activity andthe diffusive transport of intracellular Ca^{2+} and H^+on HDPs, forms a fundamental system in ventricular myocytes that controls the amplitude and spatial distribution of Ca^{2+} within the SR and cytoplasm, and helps to determine the pH of the nucleus.I will speculate on how this system may become distorted in disease processes such as myocardial ischaemia and heart failure.

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Symposia

Symposium 1: Current Studies in Experimental Epilepsy

S1.1 The Kindling Model of Epilepsy

Cafer Marangoz
Retired from the Department of Physiology, Medical Faculty, Ondokuz Mayis University, Samsun, Turkey

Epilepsy is a very important disease manifested by recurrent paroxysmal bursts of abnormal electrical brain activity. More than 50 million people worldwide suffer from epilepsy, and about 30% of those affected have seizures that are resistant to treatment with the currently available antiepileptic drugs. For development of new and more effective drugs, and the study of mechanisms of the epilepsies requires appropriate experimental models. A good model for epilepsy should have certain features. Kindling has been extensively studied as an epilepsy model of complex partial seizures with secondary generalization. Kindling model of epilepsy iscreated by the repeated subthreshold electrical stimuli or repeated subthreshold chemical stimuli. The aim one of the studies in our laboratory was to reveal the effects of nitrendipine, levetiracetam and phenobarbital on kindling model. In order to induce kindling, three days of the week (Mondays, Wednesdays and Fridays)35 mg/kg pentylenetetrazole was administered intra¬peritoneally (i.p) until theanimals kindled. Electrocorticographic activities were obtained from awake animals and their convulsive behaviors were classified. Nitrendipine (5 mg/kg), 20 mg/kg levetiracetam and 10 mg/kg phenobarbital significantly suppressed spike frequency in fully kindled rats ($p<0.05$). Coadministrationof effective doses of 5 mg/kg nitrendipine and 20 mg/kg levetiracetam reduced epileptiform activityeffectively ($p<0.05$). Our aim in the second study was to investigate the effect of carbenoxolone, a gap junction blocker, on the anticonvulsant effect of phenytoin in pentylenetetrazole kindled rats. Phenytoin decreased generalized seizure duration, total spike number and seizure severity score ($p<0.05$). Carbenoxolone and phenytoin have antiseizure effects in PTZ kindled rats. There was no significant difference between the carbenoxolone + phenytoin combination and phenytoin in terms of generalized seizure duration,total spike number and seizure stage ($p>0.05$). Our third study showed a decrease in the CA1 hippocampal pyramidal neurons numberof kindled rats ($p<0.05$).

S1.2 The Effects of Cannabinoids on Epileptiform Activity

Erdal Ağar
Department of Physiology Faculty of Medicine University of Ondokuz Mayis, Samsun, Turkey

Cannabinoids are a heterogeneous group of compounds, which can be separated into three different groups: phytocannabinoids, endogenous compounds known as endocannabinoids and synthetic compounds. Cannabinoids involve many physiological and pathological conditions in mammals. Cannabinoids exert protective effects in different neurodegenerative disorders, including epilepsy. The cannabinoid system also plays a key role in regulating seizure activity in brain through the activation of cannabinoid CB1 receptors.Epilepsies are the most prevalent neurological disorder; they are characterized by recurrent, unprovoked seizures. Epilepsies are complex syndromes due to their multifactorial origins and manifestations. An abundant series of cannabinoid agonists and antagonists has been tested in in vivo and in vitro experimental models of epileptic activity. Δ9tetrahydrocannabinoid (THC) andcannabimimetic compounds are anticonvulsant in various experimental models of epilepsy. Cannabidiol (CBD) inhibited epileptiform activity in vitro and reduced the severity and lethality of seizures in a pentylenetetrazole model of generalized seizures in vivo and tonic–clonic seizures in acute pilocarpine and penicillin models of temporal lobe and partial seizures. CBD, even at high doses, did not induce excitatory effects or convulsions in rats. Despite the extensive accounts of the antiepileptic effects of CBD, the mechanisms underlying these effects are not well understood. The CB1receptor antagonist AM251 disrupts the endocannabinoid tone by blocking CB1receptor activation, which caused development of status epilepticus in populations of epileptic neurons in the hippocampal neuronal culture and penicilinin duced epilepsy models whereas the CB1 receptor agonist, ACEA exhibits antiepileptic activity in the most of experimental model of epilepsy. There are a few reports on the clinical use of cannabinoid extracts as antiepileptics have been published; it is unclear whether cannabinoids might be efficacious and safe in the treatment of epilepsy.

S1.3 The Effect of Adenosine on Epileptiform Activity

Mehmet Yıldırım
Department of Medical Physiology, Faculty of Medicine, Health Sciences University,İstanbul, Turkey

Adenosine is an inhibitory neuromodulator that suppress excitatory synaptic communication between neurons. Because it is not a classical neurotransmitter, adenosine is neither stored in presynaptic vesicles nor it affects only on synaptic area. It controls neuronal activity through activation of A_1, A_{2A}, A_{2B} and A_3 receptors. Adenosine and its receptors are involved in different diseases and disorders such as hypoxia, ischemia, inflammation, pain, Parkinson and epilepsy.Epilepsy is a major public health problem affecting at about 1% of the population. At the basis of epileptic seizures, there is a loss of balance in neuronal excitability. It has been reported that many neurotransmitters and neuromodulators can be associated with this change in the neuronal excitability. In this context, it has been suggested that adenosine may act as an endogenous anticonvulsant. Many studies have reported a protective effect of adenosine against epileptic seizure and epileptiform activity. For examples, the daily systemic administration of adenosine prevents the epileptic behavioral induced by pentylenetetrazole. Adenosine also inhibits epileptiform activity induced by bicuculline in the rat hippocampus. In our laboratory, we have compared the effects of focal and intracerebroventricular (i.c.v.) administered adenosine (1, 10 and 100 µg/rat) on the penicillin-induced epileptiform activity in rats. Our findings suggest that focal adenosine is more effective than i.c.v. adenosine. In another study, we also found that adenosine (100 µg/rat, i.c.) and nitric oxide may decrease penicillin-induced epileptiform activity in rats and that nitric oxide, at least in part, may mediate the anticonvulsant effect of adenosine.Consistent with the literature, our results indicate that adenosine has an inhibitory effect on epileptiform activity.

Symposium 2: Role of Neuronal and Non-neuronal Cell Types in CNS Function in Health and Disease

S2.1 Optogenetic Manipulation of Neuronal Circuits Regulating Feeding Behavior

Deniz Atasoy
İstanbul Medipol University, Medical School, Department of Physiology, İstanbul, Turkey

New tools for mapping and manipulating molecularly defined neural circuits have improved the understanding of how the central nervous system regulates appetite.tion of starvation-sensitive agouti-related peptide (AGRP) neurons can rapidly elicit behavioral state similar to food deprivation, which present an entry point for reverse-engineering neural circuits for hunger. We mapped functional synaptic interactions of AGRP neurons with multiple cell populations in mice and probed the contribution of these distinct circuits to feeding behaviour using optogenetic and pharmacogenetic techniques. We have also developed tools for detailed structural analysis of AGRP neuronal connections using serial-section electron microscopy. Our results characterized some basic features of functional and anatomical circuit organization for AGRP axon projections.

S2.2 Comparison of Central and Peripheral Myelination Dynamics

Bilal Ersen Kerman
Istanbul Medipol University, REMER, İstanbul, Turkey

Myelin is an insulating material that accelerates the electrical impulse propagation along axons and that provides trophic support to neurons.Dysmyelination or demyelination (improper development or loss of myelin, respectively) occurs in many neurological disorders, such as multiple sclerosis, Pelizaeus–Merzbacher disease and other leukodystrophies leading to disruption of electrical impulse conductivity, atrophy of neurons, and permanent functional deficits.Myelin is produced by specialized glial cells: oligodendrocytes and Schwann cells. In the peripheral nervous system, Schwann cells myelinate axons in one internode (myelinated region) and cell ratio. Conversely, in the central nervous system, oligodendrocytes send out processes to myelinate several internodes. Common molecular pathways and mechanical properties as well as significant differences are observed for myelination within both systems. In order to study myelin formation in detail, we are observing wrapping of axons by both oligodendrocytes and Schwann cells in vitro through live imaging.We observed that at the early stages of myelination, oligodendrocytes surveyed the environment and their processes anchored on the axons. Next, these processes wrapped around the axons and expanded to cover the entire internode. These findings lead us to propose a novel myelination model, which was named SARAPE. Previously, it was proposed that Schwann cells wrapped the axons like a rolling carpet. In our initial observations, Schwann cells interacted with axons in a dynamic fashion. We believe that comparing and contrasting myelination processes in both systems will lead to better understanding of basic mechanisms of myelination. We believe that this information will aid in development of novel therapies against myelin disorders.

S2.3 The Role of Pericytes in Central Nervous System and Neurodegenerative Diseases

Yasemin Gürsoy-Özdemir
Koç University, Medical School, Department of Neurology and Neuroscience, İstanbul, Turkey

Pericytes are the cells of the blood brain barrier. They are localized especially in the precapillar arterioles, capillaries and post capillary venous system. They function in brain activity dependent bloodstream regulation (neurovascular coupling), maintenance of the blood brain barrier integrity and angiogenesis. These cells express genes associated with contractility similar to the smooth muscle cells and have a role in the regulation of bloodstream in the vascular bed. They prevent full reperfusion in ischemic strokes (especially in the case of reperfusion insult) by disrupting microcirculation as a result of oxydative-nitrative effect. Their role in neurodegenerative diseases like Alzheimer's disease is well documented with recent studies. Especially, loss of pericytes and increment of PDGF which is a downstream product of pericytes in cerebrospinal fluid and blood implies pericytes are involved in the development of neurodegenerative diseases. In this talk, pathophysiology of pericytes in central nervous system and neurodegenerative diseases will be discussed.

Symposium 3: Thermal Stress and Physical Activity

S3.1 Thermal Stress and Physical Activity

Sanlı Sadi Kurdak
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It'sknown that in today's world there are very serious campaigns that inspire an active life style. Additionally, due to their intense competitive calendar, athletes are obliged to train and compete at all times throughout the year. During physical activity, approximately 25% of the energy released with metabolic reactions is used to do active work. The remaining 75% is released as heat and this energy causes the body temperature to increase. Because of this, body temperature tends to proportionally increase with respect to the type and intensity of the exercise during various types of physical activity. In warm blooded organisms that are programmed to maintain life at around 37°C, the stability of the body temperature is sustained through activation of some unique physiological mechanisms. Beside the changes in skin blood flow and sweating rate, the entirety of the defense mechanisms that orient towards maintaining body water electrolyte balance force the organ systems that play a part in this process to work actively. The increase in metabolic need during physical activity creates a significant stress foremost on the cardiovascular, respiratory and skeletal, but also on all other organ systems. Besides the uncontrolled increase of body temperature and the water-electrolyte imbalance, the addition of problems in blood flow makes the maintenance of homeostatic conditions harder during physical activity in high temperatures. Any type of problem that may occur in this fragile balance, in the most optimistic case, will decrease athletic performance and in some cases cause life threatening issues. Deriving from this point, researchers conducted studies to assess different strategies to over-

come the problem of hyperthermia during physical activity. Among these, active cooling strategies, sweating and proper hydration methods and studies that address the treatment of problems that arise after instances of hyperthermia and acclimatization are the ones that stand out. The importance of having fundamental knowledge on hyperthermia, exercise and thermoregulation mechanisms to all bodies that participate in sportive activities in different scales in maintaining athletic performance as well as protecting human health, should not be forgotten.

S3.2 Football in Hot and Humid Conditions - Potential Threats and Precautions

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In the world different sports are is played regardless of age, gender and physical capacity. Even though most people perform sports for recreational purposes, it can really be physically demanding at the professional level. When we make a worldwide list of sports according to their popularity, 8 of 10 post popular sports are played outdoor and most of them are played either whole year or between spring and autumn. Most popular sport of the list football, is generally played in hot seasons when the preseason preparation period is included.Most energy liberated during physical activity appear as heat and must be dissipated from body surface to prevent thermal damage to homeostasis. Even though under mild environmental conditions excess heat can be liberated via evaporation, a drastic increase in surrounding environmental temperature and especially humidity causes the body to gain heat instead of losing. It is well known that the sweating rate almost increase instantaneously following the initiation of physical activity. It is important to remember that there is a positive correlation between the sweating rate and the intensity of the physical activity. Both information lead to a simple conclusion that throughout a high level physical activity just as in a professional football match, fluid loss by evaporation is inevitable. One of the threats to player's health is if the surrounding environment is humid enough then evaporation might lead to vastly fluid loss rather than excess heat dissipation which in turn causes an extra increase in body core temperature.It is known that in hot and humid environments during a football match, some players' body core temperature might increase to levels that is defined as profound hyperthermia. Such high values definitely raise concerns for the well-being of the players. To minimize the adverse effects of hot and humid conditions some preventive measures must be taken. Proper hydration of the player, acclimation to environment and cooling interventions before and during exercise are some of the topics that will be discussed as prophylactic interventions.

Panels

Panel 1: Medical Simulation and Mathematical Modelling

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Mathematical models in physiology are used to test hypothesis, to understand any system as a whole and to predict/estimate the values of variables cannot be measured technically. Besides scientific studies, mathematical models and simulators built by using these models are also performed for medical education. The history of medical simulation, the first medical simulation center in our country (Simmerk), contribution of simulation to medical education and use of mathematical modelling in physiology will be discussed in Medical Simulation and Mathematical Modelling titled panel in 42nd National Physiology Congress.

Panel 2: Europhysiology
Biennial Joint Physiology Meetings in Europe

Bayram Yılmaz[1], Richard Vaughan-Jones[2], Jens Leipziger[3] and Markus Hecker[4]
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Earlier this year, the Physiological Society, the Scandinavian Physiological Society, the Deutsche Physiologische Gesellschaft and the Federation of European Physiological Societies (FEPS) initiated an agreement to co-host a series of biennial joint meetings. The series will begin in London, UK in 2018 and will subsequently be organised in Berlin, Germany (2020) and Copenhagen, Denmark in 2022. The Europhysiology meetings will replace the national meetings of the respective societies. FEPS will always be a joint organiser of these biennial meetings.The aim of the Europhysiology meetings is to bring together the broader European physiology community and promote collaboration among scientists. In the last two decades physiology meetings have been challenged by evolving sub-disciplinary and thematic meetings. In this exciting initiative, it is hoped that participation of large numbers of physiologists accross Europe will enable organizers to hold specific sessions and thematic symposia to represent all aspects of physiology. It is also expected that these joint biennial meetings will attract scientists from other parts of the world.In this panel, former President of the Physiological Society (Richard Vaughan-Jones), Representative of the Scandinavian Physiological Society (Jens Leipziger) and President (Markus Hecker) and Secretary General (Bayram Yılmaz) of FEPS will discuss perspectives, challenges and opportunities of the Europhysiology meetings with the Turkish physiologists.

Panel 3: Research University Identity, Quality Problems in PhD and Residency Education and Search of Contemporary University in Turkey

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In the last 20 years, several countries have restructured their higher education system and made new university legislation. European Union member countries are continuing their efforts to increase their number of world-class universities and to compete with the best universities in the United States for global higher education. In the process of restructuring higher education in Europe, there are five main factors. They are autonomy, expansion of higher education, market sensitivity (entrepreneurial and innovative university),harmony and quality control. There have been a dramatic increase in the number of new state and foundation universities in Turkey in order to meet the increasing demand for higher education, and this process is ongoing. Most of the newly established universities prioritize education, while setting infrastructure for scientific research becoming a second priority. In addition, need and employment of high profile researchers appears to be an important problem. There has long been a quality concern in PhD education. Residency training and education is usually programmed to educate specialist doctors, and yet the efficiency of residency training towards fostering research scientists is discussed. Particularly, there have been problems in employment of residency trained doctors in basic medical sciences. In this panel, problems and reorganization of Turkish higher education system in line with trends in developed countries and suggestions for improvement will be discussed.

ACTA PHYSIOLOGICA

Turkish Society of Physiological Sciences
42nd National Physiology Congress

Oral Communications

OC01

The Effect of Coenzyme Q10 on Absence Seizures and the Role of Nitric Oxide Pathway in this Effect

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AIM: It is thought that, a dietary supplement Coenzyme Q10 (CoQ10) influence the nitric oxide pathway and decreased generalized epileptic seizures. In this study, we have investigated effects of CoQ10's role on absence seizures and the role of nitric oxide pathway in this disorder.
METHODS: Six months old WAG/Rij male rats with spontaneous seizure activities were randomly divided into 12 groups (n=72). One week after placing the electrodes for EEG recording, animals were connected to the Powerlab data acquisition unit for observing the spontaneous seizure activities. Three hours after the EEG recording, the solvent of CoQ10 soybean oil (control group), CoQ10 (25, 50, 100 ve 200 mg/kg), L-arginine (500 ve 1000 mg/kg), 7-Nitroindazole (25 ve 50 mg/kg) and combination of these drugs were applied intraperitoneally (i.p.). EEG recording was started again after 15 min and three more hours of recording was obtained. Seizure activities recorded (total number of seizures, total seizure duration, total number of spikes, the number of spikes per seizure, the average duration per seizure) after the drugs were analyzed by comparison with the pre-drug seizure activities.
RESULTS: CoQ10 (50 mg/kg and higher doses) and nitric oxide precursor L-arginine (500 ve 1000 mg/kg) increased the absence seizures compared with the control group ($p<0.05$). On the other hand, neuronal nitric oxide synthase inhibitor 7-Nitroindazole (25 and 50 mg/kg) reduced the seizures ($p<0.01$). The combination of CoQ10 (200 mg/kg) + L-arginine (1000 mg/kg) was not significant in comparison with the L-arginine which was administered alone ($p>0.05$). CoQ10 repressed the effect of 7-Nitroindazole and was brought closer to the control group values in the combination of CoQ10 (200 mg/kg) + 7-nitroindazole (50 mg/kg) group.
CONCLUSIONS: We suggest that absence epileptic patients should avoid the use of food supplements that have CoQ10 and/or cause nitric oxide release.

OC02

The Role of T-Type Calcium Channels in Proconvulsant Effect of Apelin-13 on Penicillin-Induced Epileptiform Activity

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AIM: Epilepsy is characterized by recurrent seizures that involves abnormal, excessive and hypersynchronized electrical discharges of neurons. It has been shown that the endogenous neuropeptide, apelin-13 affect intracellular calcium level, suggesting apelin-13 may act as a partial/weak agonist of Ca^{2+} influx. The aim of this study was to investigate the interaction of apelin-13 and a selective T-type calcium channel blocker NNC 55-0396inpenicillin-induced epileptiformactivity.
METHODS: 35 male albino Wistar rats (180-240 g) were divided into 5 groups. Groups: 1-Control, 2-Apelin-13 (15 µg, i.c.v.), 3-NNC 55-0396 (30 µg, i.c.), 4-Apelin-13 (15 µg, i.c.v.) + NNC 55-0396 (30 µg, i.c.), and 5-NNC 55-0396 (30 µg, i.c.) + apelin-13 (15 µg, i.c.v.) (n=7 per group). Rats were placed in the stereotaxic frame after anesthetized by 1.25 g/kg urethane (i.p.). After drilling two holes on the skull using a hand drill, the recording electrode were placed into the holes and connected to the PowerLab data acquisition system. Substances were applied 30 min after penicillin (500 IU, 2.5 µl, i.c.) injection. The data obtained were compared by One-Way ANOVA with Post-Hoc Tukey test. $p\leq0.05$ was considered statistically significant.
RESULTS: Apelin-13 increased the mean frequency of epileptiform activity in 20th minuntil theend of theexperiments. NNC 55-0396 decreased the spike frequency in the 40th minute. The administration of NNC 55-0396 after apelin-13 reversed the proconvulsant effect of apelin-13 and caused a decrease in the spike frequency in 140th min. Interestingly, when apelin-13 was administrated 10 minutes after NNC 55-0396 injection, the proconvulsant effect of apelin-13 was not observed. Even though, the mean spike frequency was significantly decreased in the 60th min.
CONCLUSIONS: The proconvulsant effect of apelin-13 was blocked by NNC 55-0396. Therefore, it is assumed that the proconvulsant action of apelin-13 might be mediated by T-type calcium channels in the experimental penicillin model of epilepsy.

OC03

Effects of Agomelatineon Penicillin-Induced Epilepsy with Electrocorticogram and Blood Pressure

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AIM: Agomelatine is an antidepressant which has been in use since 2009. It is a synthetic analog of melatonin, so it binds to melatonin receptors MT1 and MT2. In addition, agomelatine is an antagonist of serotonin receptor 5-HT2c. Thus, it causes antidepressant effects by increasing noradrenalin and dopamine concentrations. In this study, we investigated the effects of agomelatine on epileptic activity and blood pressure changes in penicilin- induced experimental epilepsy model.
METHODS: Forty adult male Spraque-Dawley rats were used in four groups (n=10 /group). Control (tap water), 10 mg/kg Agomelatine, 50 mg/kg Agomelatine and 100 mg/kg Agomelatine (n=10). Agomelatine was administered by oral gavage for 14 days. After administration of the last dose, animals were anesthesized with

urethane (1,25 g/kg). Femoral artery was catheterized for blood pressure measurement. Then, penicillin (500IU/2,5µl) was applied intracortically to induce epileptic seizures. Electrocorticography was recorded for 90 min through electrodes located on the somotomotor cortex. Spike frequencies and amplitudes recorded were analyzed by One-Way ANOVA with LSD. P<0.05 was considered to be statistically significant. RESULTS: Agomelatine at 50 mg/kg dose significantly decreased spike fequency (p<0.001) at the end of 14 day application period. On the other hand, amplitudes of spikes did not significantly differ in any of the groups. Agomelatine administration had no significant effect on mean blood pressure values recorded from the femoral artery.
CONCLUSIONS: The most important finding of the present study is that agomelatine (50 mg/kg) treatment for 14 days can have anticonvulsant effects. These result suggest that Agomelatine may also be used as an important antidepressant in epilepsy patients.This project was supported by Necmettin Erbakan University Research Fund (BAP #141318006).

OC04

The Combination of Nesfatin-1 and Phenytoin Has a Synergistic Effect in Improving Seizure-induced Neuronal Damage and Memory Dysfunction in Rats

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AIM: Based on anti-inflammatory and anti-apoptotic effects of nesfatin-1 (NES) reported in several inflammatory models, we aimed to investigate neuroprotective effects of nesfatin-1 on seizure-induced neuronal injury.
METHODS: Following passive avoidance test (PAT), male Wistar albino rats were divided into control (n=12) and pentylenetetrazole (PTZ)-induced seizure (n=72) groups. Thirty minutes prior to PTZ (45 mg/kg; intraperitoneal, i.p.), NES (0.3, 1 or 3µg/kg/day), phenytoin (PH, 40 mg/kg/day), PH + NES (0.3µg/kg/day) or saline was injected i.p, and seizures were scored using Racine's scale. Treatments were repeated at 24th and 48th h of seizures. At 72nd hour, PAT was repeated to evaluate memory function, and rats were decapitated. Oxidative parameters, histological and immunohistochemical evaluations were determined in brain tissues. Statistical analysis was performed by ANOVA and Student's t tests.
RESULTS: Among PTZ groups, high percentage of rats with tonic-clonic seizures and high average seizure-scores were reduced only in PH+NES-treated group (p<0.05). Control rats avoided entrance to dark-chamber in 5 min, while rats in PTZ groups entered in shorter times, indicating memory dysfunction. NES (3 µg/kg/day) increased delay in entrance (p<0.05). Seizure-induced elevations in malondialdehyde, nitric oxide and chemiluminescence levels were depressed by NES- (0.3 µg/kg), and PH+NES-treated groups, while all doses of NES, but not PH, elevated depleted glutathione level (p<0.001). Neuronal degeneration in cerebral cortex, hippocampal CA3 and dentate gyrus of saline-treated PTZ group (p<0.001) was reduced in NES- (0.3 µg/kg), PH- and PH+NES-treated rats. Increased TUNEL-positive cells were determined in cortices of PTZ-administered rats, but no significant difference was observed among treatments. Increased glial fibrillary acidic protein immunolabelling determined in cortex and hippocampal CA3 of PTZ-administered group was reduced in NES- (0.3 µg/kg) and PH+NES-treated groups (p<0.05).
CONCLUSIONS: Nesfatin-1 has a synergistic effect with phenytoin, potentiating its anti-seizure effect along with an additional neuroprotection on seizure-induced oxidative brain injury.

OC05

The Connection Between Sleep Spindles and Seizures in Schizencephaly: A Case Report

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AIM: The aim of this case report is to define the interaction between sleep and epilepsy (and, sleep spindles and seizures), also the importance of electrophysiological follow up in sleep laboratory and correct diagnostic approach.
CASE: Sleep spindles are generated from the thalamus. Sleep spindles and seizures originate from the same type of dynamical system. It has been shown that antagonizing manipulations made on sleep spindles had the same effect on seizures. Schizencephaly is a rare congenital disorder of cell migration with defect in sulcation. It is characterized by gray matter lined clefts.
RESULTS: 23 years old male patient was a student attending university. He had complaints of short-term paresthesia in right arm at daytime and morning. Brain MRI showed us "Cortical Heterotopia" at left temporoparietal area. In polisomnography (PSG) analysis, there were no sleep spindles, mostly there were delta wave oscillations together with repeated seizures.
CONCLUSIONS: The absence of sleep spindles in PSG, presence of epileptic seizures and somatic complaints of the patient together with the appearance of heterotopic area on brain MRI led us to think about the influenced of associative thalamocortical tracts. Subcortical heterotopic neurons due to schizencephaly may be shown by MR tractography. As a result; this case is believed to be of importance with regard to understand the physiopathological basis of the relationship between sleep spindle and epilepsy.

OC06

Effects of Cannabinoid Receptor Blockers on Serum Nesfatin-1/Nucb2 Levels in REM sleep Deprived Mice

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AIM: Recently, the effects of both nesfatin-1 and cannabinoid receptors on sleep, metabolism, and control of food intake have been demonstrated (1,2). No previous study investigated the relationship between cannabinoid receptor blockers and nesfatin-1 levels. In this study, nesfatin-1, insulin and glucose levels were investigated in 72-hour REM sleep deprived balb/c mice after intraperitoneal administration of a cannabinoid, WIN55,212,2 and cannabinoid receptor blockers (CB1 blocker AM251 and CB2 blocker SR144528).
METHODS: In total, 60 balb/c mice were exposed to 72 hours sleep deprivation on modified flowerpot method. Groups and intraperitoneal drug administrations were as follows: Group 1 (control) received injection of vehicle (78% saline+1% Ethanol+1% Tween 80+20% DMSO). Group 2 received WIN 55,212,2, Group 3 received AM251 followed by WIN 55,212,2. Group 4 received SR144528 followed by WIN 55,212,2 injection. Group 5 received only AM251. Group 6 received only SR144528. Blood samples were collected 1 h after drug administrations and prepared for biochemical measurements. Glucose levels were measured by glucometer, whereas insulin and nesfatin-1 levels were measured by ELISA.
RESULTS: There was no significant (>10%) weight change after 72-hour REM sleep deprivation. Glucose and insulin levels were higher in CB2 receptor antagonist groups compared to controls. Nesfatin-1 levels were comparable among the groups.
CONCLUSIONS: We suggest that CB2 receptor antagonist led to increase in blood glucose and insulin levels. Nesfatin-1 levels were not affected from administration of cannabinoid agonist or antagonists. This study was supported by TUBAP (2015/230).

OC07

Effect of Resveratrol on Diabetic Nephropathy

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AIM: Resveratrol is known with its anticancer, anti-inflammatory, antioxidative effects. The aim of present study was to investigate morphologic, biochemical and functional effects of resveratrol on diabetic nephropathy in streptozotocin diabetic rat model.
METHODS: Ethical Committee for the Use and Care of Laboratory Animals of Gazi University approved the procedures used in this study. 30 adult male Wistar albino rats weighing 250-300 g were used in experiments. The rats were divided into 4 groups as follows: 1.Control, 2.Resveratrol, 3.Diabetes, 4.Diabetes+Resveratrol. Streptozotocin(65 mg/kg in 0,1M in citrate buffer)was administered to diabetes groups, citrate buffer was administered to control groups intraperitoneally as a single dose. Two weeks after streptozotocin administration, a basal blood glucose level above 250 mg/dl were considered diabetic. Application of resveratrol (10/mg/kg/day dose dissolved in 0.1M ethanol) or vehicle wasstarted 2 weeks after diabetes formation and continued through 8 weeks by using oral gavage. At the end of experiments, rats were anaesthetized with Rompun+ketamine(50+60-100mg/kg), and sacrificed by cardiac puncture. During the study: Fasting blood glucose levels, renal functions were analyzed and renal vascular responses and immunohistochemically, morphological research performed by TEM, proinflammatory cytokines TGF-β, iNOS, eNOS, fibronectin levels were measured. Kidney tissue oxidant (malondialdehyde,MDA) and antioxidants (glutathione, GSH) parameters were studied, total nitric oxide (NOx)levels were also determined. Results were statistically analyzed by using Kruskal-Wallis and Mann-Whitney tests. $P<0.05$ was considered to be statistically significant.
RESULTS: Fasting blood glucose, fluid intake, urine volume, ALP, ALT, BUN and creatinine levels in blood were determined to increase in diabetic groups and diminution in sodium level ($p<0.05$). But, application of resveratrol did not have any significant effect on these parameters. In diabetic and resveratrol applied groups; Angiotensin II and Phenilephrine on perfussion pressure were not significant when compared with the control. However both Angiotensin II and Phenilephrine effects were significantly decreased in Diabetes+Resveratrol($p<0.05$). In the same group, vasodilator responses of acetylcholine were found to significantly decreased ($p<0.05$). By resveratrol treatment, diabetes induced increased kidney MDA levels were decreased ($p<0.01$) and GSH levels were increased ($p<0.01$), but NOx levels were not significantly changed. Examination of TEM: application of resveratrol significantly preserved diabetes-related deteriorating renal tissue.
CONCLUSIONS: Increment of TGFβ,fibronectin and iNOS immunreactivity were partially decreased; however, decreased eNOS level is increased with treatment of resveratrol.
This study was supported by Gazi University Scientific Research Projects Unit (01/2011-75).

OC08

Investigation of Possible Effects of Exendine During Exposure to Moderate Chronic Stress in Dehydroepiandrosterone-induced Polycystic Ovary Syndrome in Rats

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AIM: Polycystic ovary syndrome (PCOS) is a disease leading to endocrine, metabolic and reproductive problems. Chronic stress in women with PCOS causes to increase insulin resistance by affecting hypothalamic-pituatary-gonadal and hypothalamic-pituatary-adrenal axises. Nowadays insulin hormone analogs (Glucagon-like peptide 1 (GLP) agonists) are investigated to decrease insulin resistance. Exenatide (Exe-4) molecule is the best natural GLP-1 agonist

and its affinity to GLP-1 receptors is high. It contributes to decrease insulin resistance associated with PCOS by increasing pancreatic cell mass, feeling of fullness and loss of weight. Despite the fact that target of PCOS cure is to decrease insuline resistance and to adjust androgen levels, stress situation of women with PCOS is not considered during the cure. For contributing to this problem and investigating effects of stress on PCOS, possible effects of Exe in moderate chronic stress on cure of rats with PCOS induced by DHEA was investigated.
METHODS: PCOS model; DHEA (6mg/100 g) in 0.2ml sesame oil was applied subcutaneously to 21-days Sprague-Dawley rats until their vaginal opening was observed. 0.2 ml sesame oil was injected subcutaneously to rats in solution groups. Then vaginal smear was taken from rats having vaginal opening and their cycles were observed to check PCOS. Blood samples from tails of rats having cycle deficits were taken and HOMA-IR values was calculated.Restricted movement field for stress was applied to the rats with insulin resistance during one hour in each day of 4 weeks. Exe-4 (10µg/kg/day) was applied intraperitoneally to the rats in stress medium for four weeks. Effects of Exe-4 and chronic mild stress application on HOMA-IR, LH, FSH and corticosterone were investigated after taking blood samples from the rats at the end of the applications. Moreover ovariums werehistologically investigated.
RESULTS: Administration of Exe-4 in stress situation increased HOMA-IR, corticosterone level and duration of completing eustrus cycle but it decreased number of total healthy folicules. Normal Exe-4 dose in PCOS treatment during moderate chronic stress did not have significant effect on insulin resistance and ovarium deficits.
CONCLUSIONS: Chronic stress has harmful effects on metabolic diseases like PCOS and limits effects of treatment agents in PCOS.

OC09

The Effect of Tadalafil on Renal Fibrosis Induced by Ureteral Obstruction

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AIM: It has been reported that the cGMP increasing approaches may improve kidney functions during acute and chronic renal failure. This study aimed to evaluate the possible therapeutic effects of tadalafil, a specific inhibitor of cGMP degrading phosphodiesterase-5 (PDE5) enzyme on renal fibrosis induced by unilateral ureteral obstruction(UO).
METHODS: Male Sprague-Dawley rats (277.6±9.7 g) were divided into sham-operated, UO, and tadalafil treated (10 mg/72 h, ig) (UO+T). UO was induced by complete ligation of left urether and the animals were sacrificed 14 days after the surgery. The kidney samples were stained with hematoxylin-eosin and Masson's trichrome stains. Both alpha-sma (smooth muscle actin) and TGF-Beta (Transforming growth factor-beta) levels in kidney were determined by ELISA in addition to urinary cGMP level. Serum and urinary creatinine were determined and creatinine clearance was calculated. Data were expressed as mean ± SD and the statistical comparisons were performed by one-way ANOVA and Newman Keuls as a post-hoc test.
RESULTS: An increased collagen deposition, tubular dilation, lymphocyte infiltration and necrosis was observed in UO group in addition to increased alpha-sma level (from 0.41±0.06 to 1.21±0.12 mg/g protein; $p<0.001$). Tadalafil treatment decreased the collagen deposition and alpha-sma level when compared to UO ($p<0.05$). Tissue TGF-Beta content increased from 0.16±0.01 to 0.42 ±0.02 ng/mg protein in UO group ($p<0.01$) and significantly decreased in UO+T group ($p<0.01$). Urinary cGMP levels decreased in UO group ($p<0.05$) and tadalafil treatment restored it to the range of controls. Creatinine clearance decreased in UO group ($p<0.001$) and did not change in treated animals.
CONCLUSIONS: Our results suggest that tadalafil treatment ameliorates renal fibrosis in UO by reducing TGF-Beta expression. Since fibrosis was not completely prevented, no significant improvements in kidney function were observed. However, tadalafil may have a clinical importance to treat fibrosis induced by urinary stones.

OC10

8-br cADPR Suppresses the Renal Ischemia-Reperfusion Injury

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AIM: Renal ischemia-reperfusion (I/R) injury is a significant clinical problem resulting in acute renal insufficiency. During I/R, increased cytokines, reactive oxygen types and calcium accumulating causes kidney injury. In this study, we examined the effects of nifedipine, non-specific calcium channelantagonist, and 8-br-cADPR, TRPM2 ion channel antagonist, on renal I/R injury by using biochemical and histopathological methods.
METHODS: A total of 60 Wistar albino rats were used in the study. Group 1 is the control group. Group 2 sham; right kidney has been dissected. Group 3 I/R; right kidney has been dissected, ischemia for 1 hour and reperfusion for 24 hours was applied to the left kidney. The surgical processes in the 3rd group were applied to the animals in Group 4, 5 and 6,respectively 4 mg/kg nifedipine, 4 mg/kg nifedipine+40 µg/kg 8-br-cADPR and 4 mg/kg nifedipine+400 µg/kg 8-br-cADPR were applied intraperitoneally before the commencement of reperfusion. The differences were compared with the Tukey Post Hoc Analysis following the OneWayANOVA test ($P<0.05$).
RESULTS: When compared to the control group; the levels of CD38, cADPR, TNF-α, IL-1β, MPO and MDA increasing in I/R group have significantly decreased in the groups to which especially 8-br cADPR was applied. The rennin level decreasing when compared to the control group has meaningfully increased with the application of high dosage 8-br cADPR. Significant changes did not occur in EPO levels. In the histological examinations; the renal injury increasing with I/R, caspase-3 expression and
TRPM2 ion canal distribution were decreased with the application of calcium channel antagonists.
CONCLUSIONS: The oxidative injury, cytokine levels, caspase-3, TRPM2 ion channel distribution and TRPM2 ion channelantagonist increasing in I/R were suppressed with the application of 8-br cADPR.
This study has been supported by Ataturk University BAP (2014/146).

OC11

Individual Variation of Leptin, Nesfatin-1 and Irisin Levels During Aerobic Exercise Performed Morning and Night in Trained and Untrained Male Subjects

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AIM: Exercise is an important factor to regulate energy homeostasis. However, it is unclear if exercise modify or have an effect on energy homeostasis via stimulating energy-related hormones. Skeletal muscle and fat tissue are endocrine acting organs that produced leptin, nesfatin-1 and irisin hormones which regulate vital physiological processes in energy-metabolic systems. We have investigated effects of acute aerobic exercise performed morning and night on leptin, nesfatin-1 and irisin levels in trained and untrained subjects.
METHODS: Thirty trained (18.3±0.1 years) and 30 untrained (18.6±0.1 years) male subjects performed two aerobic running exercise (3 days between test) to subjects' 50-85% of maximal heart rate for 30 min. The written informed consent approved by the institutional ethics committee were taken. Pre-post exercise venous blood samples were taken and analyzed for leptin, nesfatin-1 and irisin using a ELISA. Paired and unpaired t-tests used to analyse data
RESULTS: We observed increase in irisin levels in all subjects ($p<0.001$). Significant increases observed in nesfatin-1 levels in night exercise in both groups ($p<0.05$). Importantly, leptin and nesfatin-1 levels varied among subjects. In trained and untrained groups, leptin and nesfatin-1 levels increased in 4 (13%) vs 12 (40%) subjects in morning and 9 (30%) vs 10 (33%) subjects in night exercise, while they decreased in 5 (16%) vs 7 (23%) subjects in morning and 6 (20%) vs 3 (10%) subjects in night exercise, respectively.
CONCLUSIONS: Exercise may provide additional effects on increase energy consumption via alteration of irisin levels. However, increase in leptin and nesfatin-1 levels on reduction of food intake may not be applicable due to individual variation. Interestingly, exercise-induced energy imbalance was caused to be a decrease leptin and nesfatin-1 levels that may increase in food intake in some subjects. Consequently, exercise has strong beneficial effects on increased energy consumption but not on appetite regulation.

OC12

Investigation of Hemorheological Parameters and Response to Oxidative Stress Before and After the Treatment in Newly-Diagnosed Patients with Chronic Obstructive Pulmonary Disease

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AIM: Chronic obstructive pulmonary disease (COPD) is characterized by progressive airflow limitation associated with increased inflammatory response. Lungs are highly susceptible to oxidative damage because of rich vascular bed and large surface area. The aim of the current study was to determine alterations in hemorheology (erythrocyte aggregation and deformability) and oxidative stress (total oxidant/antioxidant status [TOS/TAS], oxidative stress index [OSI]) in response to treatment in newly-diagnosed COPD patients.
METHODS: The study comprised 13 newly-diagnosed COPD patients (58.46±2.69 years), 12 controls (54.16±3.29 years). The severity of COPD was determined as stage I (n=3), stage II (n=10) according to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. Short-acting beta-2 agonists was applied to stage I COPD patients, stage II patients were treated with long-acting anticholinergics for 1 month. Hemorheological parameters were measured by an ektacytometer. TOS and TAS were determined using a kit andOSI was calculated.
RESULTS: FEV1 and MEF 25/75 were increased after treatment ($p=0.046$, $p=0.045$, respectively). TOS (30.67±3.84) and OSI of COPD patients (2.25±0.29) were higher than controls (8.84±1.69, 0.58±0.13, respectively). TAS decreased after treatment. Differences were statistically significant ($p=0.0001$, $p=0.033$, respectively). No alteration was observed in erythrocyte aggregation and deformability.
CONCLUSIONS: According to the current treatment protocol for stage I-II COPD, only symptomatic treatment is applied and steroids are not used for suppressing the inflammation. This treatment does not seem to provide adequate contribution to the reduction of oxidative stress and further decreases antioxidant status as well. Based on the results of our study, it can be speculated that usage of treatment methods which will decrease oxidative stress and improve hemorheology might be a suitable approach in patients with COPD.

OC13

Investigation of Protective Effects of Alpha Crystallin Against Ischemia-Reperfusion Induced Acute Lung Injury

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AIM: This study aimed to investigate the protective effect of α-crystallin against acute lung injury via oxidative stress parameters. Antioxidant capacity of alpha crystallin, which is one of the main lens proteins in vertebrates has shown in previous studies.THODS: In our study, 24 Sprague-Dawley male rats were divided into three groups: control, ischemia-reperfusion (IR), and alpha-crystalline+IR. After anesthesia, infrarenal abdominal aorta (IAA) of control group animals was dissected by closing incision and ischemia-reperfusion was not applied. IAA of IR group animals were clamped for 90 minto induce ischemia. Then, clamp was removed for 180 min of reperfusion. IR protocol was administered by giving alpha-crystalline(50 mg/100 g body weight) one hour before IR. To obtain bronchoalveolar lavage fluid (BALF), 5 ml physiological saline was administered intratracheally. The liquid was withdrawn from the trachea until 90% or more of the given amount of saline solution was obtained. This was applied three times. Extracted lung samples, blood, and BALF were stored in -80˚C for biochemical analysis. The findings ob-

tained from biochemical studies were analyzed using GraphPad Prism version 5.0 for Windows statistical software package. One-Way ANOVA test followed by Bonferroni post hoc tests was used.
RESULTS: When we examined the ELISA analysis of lung tissues,blood and BALF, oxidative parameters TOC and MDA of IR group increased whereas SOD and TAC decreased. When alpha-crystalline + IR was compared with the IR, MDA and TOC levels of alpha crystalline+IR group decreased, SOD and TAC levels increased.When we compared lung tissues of IR group to alpha- crystalline+IR group, MDA (26.12±1.39 nm/100 mg protein; 18.54±0.71 nm/100 mg protein, p<0.001) and TOS levels (7.70±0.34 nm/ 100 mg protein, 5.62±0.30 nm/100 mg protein, p0,01) decreased significantly while SOD (20 25±1.55 ng/100 mg protein; 26.66 ± 0.73 ng/100 mg protein, p<0.01) and TAC levels (14.91± 1.46 U/100 mg protein; 17.31±0.73 U/100 mg protein, p<0.01) increased significantly.
CONCLUSIONS: All in all, our biochemical results concluded that alpha crystalline may prevent acute lung injury induced by IR.

OC14

The Effects of Exercise on Vascular Responses in Type I Diabetic Rats

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AIM: Diabetes Mellitus (DM) is a metabolic disorder with multiethiologic nature characterized by the defects in insulin production and the effects of insulin or both, leading disorders in carbohydrate, fat, and protein metabolism. In the long-term, diabetes causes dysfunctions and damages in different tissues. It is known that exercise has beneficial effects on the pathologies associated with DM. This study aims to evaluate the effects of moderate swimming exercise on vascular responses in type-1 diabetic rats.
METHODS: The totally 36 male adult Wistar Albino rats were used in this study. The groups in the experiment were generated as diabetes, diabetes + exercise, exercise and control. Streptozotocin (STZ) (50 mg/kg, intraperitoneally) was given to induce T1D. The rats in group diabetes + exercise and exercise only were subjected to 1 h swimming exercise for 4 weeks after STZ injection. The initial and final blood glucose levels and weekly body weight were measured. In vitro thoracic aorta responses were recorded at the end of the experiment.
RESULTS: A reduction in body weight of type-1 diabetic rats was determined from week 1 to week 4 (p<0.001). Blood glucose levels were significantly (p<0.001) greater in both type-1 diabetic groups than in controls and group exercise, but swimming exercise did not affect blood glucose levels of type-1 diabetic rats. No differences between groups were found in the response of thoracic aorta to norepinephrine and sodium nitroprusside. It was determined that highest relaxation response to acetylcholine was observed in control and this response gradually decreased in group diabetes + exercise, group exercise, and group diabetes. These differences were significant in the concentration of 10^{-7}, 10^{-6} and 10^{-5} mmol of acetylcholine (p=0.003, p<0.001, p=0.001, respectively).
CONCLUSIONS: It was observed that 4-week moderate swimming exercise regimen corrected endothelium-dependent relaxation responses in type-1 diabetic rats.

OC15

What are the Mechanisms Mediating the Neuroprotective Effects of Ozone in Diabetic Neuropathy?

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AIM: Ozone, which has therapeutic effect in many pathologies, partially prevented diabetic neuropathy in rats in our previous study. In the present study, it was investigated that the mechanisms mediating the neuroprotective effects of ozone in diabetic neuropathy.mly divided into 6 groups (n=7): control (C), ozone (O), diabetic (D), ozone-treated diabetic (DO), insulin-treated diabetic (DI), and ozone- and insulin-treated diabetic (DOI). Diabetes was induced by a single injection of streptozotocin (60 mg/kg, i.p.), after which insulin was administered (3 IU, i.p., once a day) to the DI and DOI groups for 6 weeks, and 1.1 mg/kg (50 µg/ml, i.p., once a day) ozone was given to the O, DO, and DOI groups for 6 weeks. 6 weeks after the induction of diabetes, the electrophysiological, biochemical and histopathological tests were made. Data were analysed using the one way ANOVA and post hoc Tukey tests. p<0.05 was considered statistically significant.
RESULTS: While the blood glucose, HbA1c, plasma total oxidant status, oxidative stress index and apoptotic cell number of the D group were significantly higher than the C and O groups, the same values of DO, DI and DOI groups were significantly lower than the D group. While the nerve conduction velocity, amplitude of compound action potential, axon number and endoneural capillary number of the D group were significantly lower than the C and O groups, the same values of DO, DI and DOI groups were significantly higher than the D group.
CONCLUSIONS: Consistent with previous studies, ozone reduced the blood glucose and HbA1c levels, and partially prevented diabetic neuropathy in this study. These findings indicate that the neuroprotective effect of ozone in diabetic neuropathy are mediated through oxidative stress, vascular and apoptotic mechanisms. We believe that ozone, as a potential therapeutic agent for diabetic neuropathy, a focus on ozone and a molecule to be investigated in detail.

OC16

Silencing HMGB1 Expression Inhibits Myocardial Apoptosis-induced by Doxorubicin via TLR4 Dependent Manner Through MAPK Signal Transduction

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AIM: Doxorubisin (DOX) istoxic on many tissuesincluding the heart, but is an anticancer drug widely used for cancer treatment. It is not still completely understood the mechanism of DOX-induced heart failure. It, therefore, has not been developed a treatment for DOX-induced heart failure. High mobility group box 1 (HMGB1) which is a chromatin protein highly conservative among the species and AMP-activated kinase (AMPK) have connection between cell's survival and death pathways. The aim of the study was to investigate whether DOX -induced heart failure mediates HMGB1 to initiate the apoptosis through (AMPK-α1) or not.

METHODS: It was created 4 groups as a control, HMGB1 inhibition (HMGB1), DOX, HMGB1+DOX by using H9c2 cell line. Silencing HMGB1 expression was performed by using spesific small interfering RNA (10 nM). DOX was used at 2 μM concentration for 36 and 48 hours. The silencing HMGB1 and DOX were performed cotreatment. Western blot and qRT-PCR identify protein and genes expressions related to apoptosis. Apoptosis was determined by TUNEL and FITC-IETD-FMK. Statistical analysis was performed by one-way-ANOVA.

RESULTS: ERK1/2 and AMPK gene expressions were down by DOX, although P38 expression was high by DOX. HMGB1+DOX inhibition caused to low expression of ERK1/2, AMPK but not P38 gene expression. Although DOX gave rise to decrease AMPK, P-AMPK, ERK1/2, PERK1/2, P38, JNK protein expressions, increase caspase-3 protein expression, HMGB1+DOX inhibition led to increase AMPK, P-AMPK, ERK1/2, PERK1/2, P38, JNK and decrease caspase-3 protein expression. The number of TUNEL positive and active caspase 8 cells at ADR group was higher than control and HMGB1 ($p<0.01$). However, the number of TUNEL positive and active caspase-8 cells at HMGB1+DOX was lower vs DOX group ($p<0.01$).

CONCLUSIONS: HMGB1 plays important role as amplifying on DOX toxicity on heart by TLR4 via MAPK signal transduction.

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OC17

The Effect of Resveratrol and Glibenclamide on Ischemia/ Reperfusion Induced Arrhythmias in STZ-induced Diabetic Rats

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AIM: Diabetes mellitus is highly associated with cardiovascular complications, which is one of the major causes of morbidity and mortality in developing countries.The present study was aimed to investigate the effect of resveratrol alone and its combination with glibenclamide on ischemia and reperfusion induced arrhythmias in STZ-induced diabetic rats.

METHODS: In this study, 37 male Sprague Dawley rats, 4-5 months of age, were used. Diabetes mellitus was induced by intraperitoneal injection of STZ (65 mg/kg). Blood glucose levels above 250 mg/dl were accepted as diabetic. Resveratrol (5 mg/kg, ip) and glibenclamide (5 mg/kg, ip) were freshly prepared and daily administrated for 6 week. Heart rate, blood pressure incidence of arrhythmias and arrhythmias score were determined. The arrhythmias was identified in accordance with the Lambeth Conventions (3). Data was analyzed by one-way ANOVA with LSD post hoc test.

RESULTS: Resveratrol and its combination with glibenclamide resulted in significantly decreased arrhythmia score at reperfusion ($p<0.05$). Arrhythmic period, duration of other types of arrhythmia and incidence of other types of arrhythmias during reperfusion were found to be significantly decreased in diabetic rats treated with resveratrol and its combination with glibenclamide ($p< 0.05$).

CONCLUSIONS: Arrhythmia score and incidence of arrhythmias during reperfusion were decreased in diabetic rats receiving resveratrol and its combination with glibenclamide. Further studies are needed to understand the underlying mechanism of cardio protective effect of resveratrol in diabetes mellitus. This study was supported by the Abant İzzet Baysal University Research Fund.

OC18

Effects of Quercetin on Cyclophosphamide-induced Cardiotoxicity in Rats

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AIM: Cyclophosphamide (CYP) is an anti-carcinogenic substance and causes cardiotoxicity and disorders of vascular contraction-relaxation mechanism. The study aimed to investigate protective effects of Quercetin(Q) on cardiac injury and thoracic aorta smooth muscle contraction-relaxation responses in the CYP-induced rat model.

METHODS: In our study, we used 40-male Sprague-Dawley rats (200-250g).Rats were assigned to five groups(8 each group): Control, CYP, Q50+CYP, Q100+CYP and Q100. For seven days, the control group was given intragastric(i.g.) the cornoil(1ml) as solvent of Q. CYP group was given cornoil for seven days and given intraperitoneal(i.p.) single-dose of CYP(200mg/kg) on the seventh day. Rats in groups Q50+CYP and Q100+CYP were given 50 and 100mg/kg dose of Q(i.g.) dissolved in cornoil for 7 days. These two groups rats were given a single dose of

CYP(200mg/kg,i.p.) on the seventh day. Rats in Q100 group was given 100mg/kg dose of Q for seven days. On the eighth day of experiment, blood and tissue samples were collected from all groups of rats after sacrification. In blood samples, the levels of Troponin-

I, CK and CK-MB were measured.Heart tissues were used for biochemical and histopathological evaluation. Aortic tissues were used in the isolated-organ bath system to examinephenylephrine(PH)-induced contraction and acetylcholine(ACh)-induced relaxation. Collected data were analyzed using Tukey Test in ANOVA. RESULTS: Level of MDA in CYP and Q100+CYP groups were significantly increased compared with control group($p<0.0001$). SOD activity and GSH levels were significantly decreased in CYP group compared to control and Q100+CYP groups($p<0.0001$). In isolated-organbath system, the contraction and relaxation responses of aortic tissue were evaluated according to PH(10^{-9}-10-5M) and ACh(10-6M) doses of and inducing sequences. Responses coming from CYP group were decreased significantly compared to other groups($p<0.05$). Serum Troponin-I, CK-MB and CK levels significantly increased in CYP group compared to other groups($p<0.05$). The histopathological examination of cardiac tissue showed that CYP group has considerably myositis and myofibril degeneration in addition to dramatically increasing apoptotic cell density compared to other groups ($p<0.05$).
CONCLUSIONS: The present findings revealed that especially higher dose of Q has preventive effect on degenerative and toxic effects of CYP of the heart and thoracic aorta tissues.

OC19

The Effect of Phenoxybenzamine to Decreased Heart Muscle Contractility After *in vitro* Constituted Ischemia

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AIM: An ischemia-reperfusion injury may occur in heart myocardium following open heart surgery. This may cause mortality after cardiac surgery due to diminished contractility of the heart. Phenoxybenzamine is an agent causing vascular dilatation and has positive inotropic and chronotropic effects. In this study effects of phenoxybenzamineon heart muscle has been investigated by an *in vitro* study designed with ischemia-reperfusion injury model on human atrium.
METHODS: Patients were divided into 4 groups: Phenoxybenzamine control, ischemia hypotermia control, ischemia-hypotermia phenoxybenzamine (treatment), phenoxybenzamine ischemia-hypotermia (prophylactic). In all groups atrium tissues are placed into isolated organ bath and washed for 3 hto diminish the anaesthetic agents. Cumulative dose of H2O2 was introduced to establish ischemia. Adrenaline 0.5mg/ml was put in tissue cabs for producing isovolumetric contractions. Contraction width measurements were used as contraction parameters. Friedman and Kruskal Wallis tests were used for statistical evaluation.RESULTS: Inhibition of contraction was statistically significant at the first dose of Phenoxybenzamine following the initial administration of adrenaline in control group. In ischemia hypotermia control group H2O2 diminished the contractions occured by administration of first dose adrenaline which was aggravated by second adrenaline. In treatment group diminished atrium contractions caused by ischemia-hypotermia was significantly elevated after phenoxybenzamine. In prophylactic group contractions were almost normal and statistically meaningful after initial phenoxybenzamine administration beyond cooling and ischemia caused by all doses of H2O2. Adrenaline induced contractions were also elevated after ischemia-hypotermia.
CONCLUSIONS: Results of this study showed that preoperative administration of phenoxybenzamine may prevent negative inotropic effect of ischemia induced injury in human heart. By the help of additional vasodilator effect at splanchnic vasculature phenoxybenzamine may be useful in patients with low cardiac output after cardiac surgery.

OC20

The Effect of an Angiotensin II AT1 Receptor Antagonist, L-158,809, on Baroreflex Sensitivity in Conscious Two-kidney, One-clip Hypertensive Rats

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AIM: The mechanism by which baroreflex sensitivity decreases in 2K1C hypertensive rats is not clear. In this study, we aimed to determine if angiotensin II (ANG II) contributes to decrease the baroreflex sensitivity in 2K1C hypertension, by using L-158,809, an ANG II type 1 (AT1) receptor antagonist.
METHODS: 2K1C rats or their sham operated (SO) controls were given L-158,809 (0.3 mg/kg/d, oral gavage) or vehicle for 7 days, two weeks after clipping or sham operation. Then, baseline blood pressure was measured and the last dose of L-158,809 or vehicle was given (i.v.) one day after femoral artery and vein cannulation. Later, baroreflex sensitivity was measured by pharmacological (Oxford) method before and after β1 blockade by atenolol (1 mg/kg). Statistical analysis was performed by using either two-way ANOVA or Mann-Whitney U test with alpha correction. The significance level was considered as $p<0.05$.
RESULTS: L-158,809 decreased blood pressure in 2K1C rats ($p<0.05$). 1) The baroreflex sensitivity before β1 blockade: L-158,809 increased bradycardic response of baroreflex in the rats [$F(1,38)=5.166$, $p<0.05$]. There was an interaction between clipping and L-158,809 for their effects on tachycardic response of baroreflex [for the interaction $F(1,42)=11.870$, $p=0.001$)]. Tachycardic response was greater in 2K1C rats than in SO rats under L-158,809 treatment ($p<0.05$). 2) The baroreflex sensitivity after β1 blockade: Clipping decreased parasympathetic bradycardic response of baroreflex ($p<0.05$). L-158,809 increased this bradycardic response in 2K1C rats ($p<0.05$).
CONCLUSIONS: Our findings show that ANG II contributes to decrease the baroreflex sensitivity in 2K1C hypertensive rats by type 1 (AT1) receptors. This is because an ANG II AT1 antagonist L-158,809 increased the tachycardic response of baroreflex by inverting the decreasing tendency of the response and the bradycardic response of parasympathetic baroreflex in clipped rats.
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OC21

Effect of Caffeine on Vascular Smooth Muscle Cell Proliferation and Calcium Level

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AIM: Caffeine has been reported to reduce vascular smooth muscle cell proliferation. Increasing intracellular calcium suggests the role of vascular smooth muscle cell proliferation. In this study, we aimed to investigate caffeine's effects of the vascular smooth muscle cell proliferation and intracellular calcium levels.
METHODS: In our study, Wistar male rats (180-200 g) were used for animal experiments. Primary culture cells were obtained from aortic smooth muscle tissue of rats. The number of cells per milliliter was determined by counting the cells obtained on thoma counting chamber. The cultivation was homogeneously made into ninety-six culture vessels in equal numbers. After 24 h of incubation, the cells were treated with 10 µM, 100 µM and 1000 µM caffeine. At the end of 24 h of incubation period, cell proliferation and viability were assessed spectrophotometrically by MTT (tetrazolium salt 3-[4,5-dimethythiazol-2-yl]-2,5-diphenyltetrazolium bromide). Intracellular calcium level was measured by cell microspectroflorometric method. Before measurement the cells were plated on coverslips of 24 mm diameter. Calcium indicator Fura 2- AM was incubated for 1 h at 37 °C. The cells were administered 1000 µM caffeine during measurement. The data which were analyzed by ANOVA and paired t-tests were handled with SPSS.
RESULTS: Caffeine administered in 100 µM ($p<0.001$) and 1000 µM ($p<0.01$) concentrations caused a significant reduction in cell proliferation when compared to the control group. Caffeine with 1000 µM concentration caused higher reduction in the cell proliferation, when compared to the concentrations of 10 µM ($p<0.05$) and of 100 µM ($p<0.001$). Intracellular calcium level significantly decreased with 1000 µM caffeine administration ($p<0.001$).
CONCLUSIONS: According to these findings, caffeine causes a reduction in cell proliferation and this reduction depends on the dose. This finding can be considered to be associated with reduced intracellular calcium reduction.

OC22

The Effects of Reactive Oxygen Species and TRPA1 Receptors on Nociceptive Firing and Calcitonin Gene-related Peptide Release in Rat Meninges

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AIM:It was shown that oxidative stress was increased in migraine patients in clinical studies. In studies with experimental migraine models were reported that migraine is associated with oxidative stress in trigeminal nociceptive system. Migraine headache likely involves redox sensitive TRPA1 receptor ion channels in sensory neurons. Pro-calcitonin has a function as partial agonist for calcitonin gene-related peptide(CGRP) receptor and reactive oxygen species can activate pro-calcitonin expression from the CGRP gene. In the present study, we aimed to investigate the actions of redox active TRPA1 specific agonists including acrolein, methylglyoxal and H2O2 on nociceptive firing and CGRP release in rat meninges.
METHODS: ecorded,for this, redox agents methylglyoxal(300 µM,n=8) or acrolein(300 µM,n=6) was applied. In different experiments, using ELISA assay, we tested the action of redox agents acrolein(300 µM,n=4), methylglyoxal(300 µM, n=8) and H2O2(300 µM,n=8) on release of the main migraine mediator CGRP from meningeal preparation. Data were analyzed with paired t-test using Origin 8.5 software.
RESULTS: Both methylglyoxal and acrolein from redox active TRPA1 specific agonists induced nociceptive firing in rat meninges which are very sensitive to pain, respectively($p<0.05$). Moreover, acrolein from these specific agonists increased significantly release of CGRP which is established as main mediator of migraine in meningeal nerves where is considered to be onset of migraine pain($p<0.05$), but both methylglyoxal and H2O2 didn't change CGRP release($p>0.05$).
CONCLUSIONS: Methylglyoxal and acrolein increased the nociceptive firing and moreover acrolein increased CGRP release in meningeal nerves showing that redox active agents cause migraine headache by inducing oxidative stress. Our findings suggest that oxidative stress caused by redox active agents show its the effect via TRPA1 receptors in meningeal nerves.
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OC23

Role of Normobaric Oxygen Treatment on Newborn Hypoxia-Ischemia

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AIM: Hypoxic-ischemia (HI) is a widely used animal model to mimic the preterm or perinatal sublethal hypoxia. It causes diffuse neurodegeneration in the brain and results in mental retardation, cerebral palsy and epilepsy. Normobaric oxygen (NBO) enhances post-ischemic tissue re-oxygenation and promotes neuronal survival. However, its therapeutic effect is compromised byreactive oxygen species which are formed in response to oxygen.
METHODS: In this contex, we investigated effects of NBO combined with free radical scavenger melatonin after newborn hypoxic-ischemia. For this aim we anesthetized 7 days old rat with 1% isoflurane (30% O2; reminder N2O) and exposed to 8% oxygen for 2 hours after right carotid artery ligation, evaluated effects of normobaric oxygen (70% or 100% over 120 min), administered either alone or in combination with melatonin (4 mg/kg, i.p.) on apoptotic cell death, neuronal survival, infarct volume, brain swelling and cell signalling. One-way ANOVA was used for statistical analysis.
RESULTS: Combination of oxygen and melatonin treatment decreased infarct volume, neuronal injury, brain swelling more strongly than oxygen or melatonin alone. As compared with oxygen and me-

latonin treatment, phosphorylation of SAPK/JNK-1/2 was reduced and ERK-1/2, CREB phosphorylation were increased in NBO/melatonin combined animals.
CONCLUSIONS: Here, we provided evidence that NBO treatment is beneficial after newborn HI, which was associate with improved neuronal survival and ERK-1/2 and CREB activities. This data encourages proof-of- concept studies in human hypoxia-ischemiatreatment.

OC24

Anti-obesity and Anti-diabetic Effects of Ifenprodil, a Selective NMDA-GluN2B Receptor Antagonist

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AIM: N-methyl-D-aspartate receptors (NMDARs) play critical roles in the regulation of neuronal development and survival, and are amongst the most important proteins in the post-synaptic density of excitatory synapses. NMDARs also have effects on energy balance. Deletion of NMDA-GluN1 receptors from agouti-related peptide (AgRP) neurons leads to a reduction in body weight and food intake. We have recently shown that genetic loss of NMDA-GluN2B receptors specifically in AgRP neurons reduces body weight, food intake, neuronal development, and dendritic plasticity. We have also shown that the deletion of NMDA-GluN2B receptors from AgRP neurons prevents the development of diabetes in ob/ob mice. Therefore, we hypothesized that the administration of ifenprodil, a highly selective NMDA-GluN2B receptor antagonist, into the arcuate nucleus of the hypothalamus will correct the metabolic phenotype of diabetic ob/ob mice.
METHODS: We injected ifenprodil (25 nM/day) into the arcuate nucleus by stereotaxically implanting a guide cannula for 5 days. The changes in body weight, food intake, and blood glucose levels were monitored daily for 10 days. At the end of the experiment, a green fluorescent protein (GFP) marker (AAVeGFP) was injected to verify the accuracy of the injection sites under a confocal fluorescence microscope. Data were evaluated by repeated measures 2-way analysis of variance.
RESULTS: Here we show that administration of ifenprodil into the arcuate nucleus markedly ($P<0.001$) reduces food intake and body weight within 3 days and this rebounds quickly after ifenprodil injection ceases. In addition, the administration of ifenprodil leads to normalization of hyperglycemia in diabetic ob/ob mice ($P<0.001$). Of note, the normalization of hyperglycemia is dependent on the reduction in food intake.
CONCLUSIONS: NMDA-GluN2B receptor action in the central nervous system plays an important role in regulating fuel homeostasis and ifenprodil may have a therapeutic potential for treatment/prevention of diabetes and obesity.

OC25

The Therapeutic Effects of Catalase-PEG on the Disrupted Blood-brain Barrier Integrity by Hyperosmolar Mannitol Infusion in Rats

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AIM: Several methodological approaches including the administration of hyperosmolar solutions have been described to temporarily increase paracellular permeability of theraupetic drugs into the brain in pathological conditions such as epilepsy and brain tumors. The limitations of this methodological approach include certain side effects sourced by the inevitable exposure of the brain tissue to potentially neurotoxic circulatory substances. Therefore, defining means of modulation of hyperosmolar blood-brain barrier (BBB) opening may serve both to elucidate the mechanisms of BBB disruption and to reduce the potential brain damage in this setting. In this context, the aim of this study was to explore whether catalase-polyethylene glycol (PEG) as an antioxidant agent may exert protection against BBB disruption induced by hyperosmolar mannitol in rats.
METHODS: In this study, 84 adult male Wistar albino rats (10-12 weeks) weighing 230-280 g were used. In order to open the BBB, a hyperosmolar mannitol solution (25%; 1.6 M) was infused through a catheter inserted into the right internal carotid artery for 30 s at a rate of 0.25 mL, kg−1 s−1. Catalase-PEG (2.500 IU/0.2 mL) was administered intravenously 2 min before mannitol treatment. Evans blue (EB) dye and horseradish peroxidase (HRP) were used as marker of BBB disruption.
RESULTS: A significant increase of EB extravasation was observed unilaterally in the right cerebral cortex, right hippocampus and cerebellum by mannitol infusion compared with sham animals ($p<0.01$), and preconditioning with catalase-PEG significantly reduced the increased EB extravasation in these regions ($p<0.01$). Similarly, a significant coloration of HRP extravasation was observed unilaterally in the right cerebral cortex, right hippocampus and cerebellum by mannitol infusion compared with sham animals, and preconditioning with catalase-PEG significantly reduced the HRP extravasation in these regions.
CONCLUSIONS: Our results indicate that regulation of oxidant/antioxidant status modulates the barrier function in brain microvessels and catalase-PEG could be useful for the improvement of BBB integrity against hyperosmolar BBB disruption.

OC26

TRPM2 Antagonist ACA Ameliorates Okadaic Acid-induced Oxidative Stress and Neuroinflammation in Rats

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AIM: Okadaic acid (OKA) is a specific protein phosphatases inhibitor and induced impairments in cognitive function and free radical homeostasis. Transient receptor potential melastatin 2 (TRPM2) is an oxidative stress sensing calcium-permeable channel that is thought to contribute to calcium dysregulation associated with neurodegenerative diseases, including Alzheimer's disease. This study aimed to investigate the oxidative stress and neuroinflammation effect of TRPM2 inhibitor N-(p-Amylcinnamoyl) anthranilic acid (ACA) in a neurodegenerative model induced by OKA.
METHODS: Male Sprague-Dawley rats (n=50) were randomly divided into five groups; i) control, ii) sham: rats were injected icv with artificial cerebrospinal fluid-(aCSF) and treated with vehicle for 13 days, iii) ACA: rats were treated with ACA intraperitoneally (ip) 25 mg/kg/day for 13 days, iv)OKA: OKA was dissolved in aCSF and injected icv (200 ng) in a volume of 10 µl bilaterally and v) OKA+ACA: rats were injected icv with OKA (200 ng) and treated with ACA ip 25 mg/kg/day for 13 days.At the end of the experiment, the rats were sacrificed by taking blood of their hearts, then the hippocampus and cerebral cortex of rats were removed. SOD, GSH-PX enzyme activation, and MDA and GSH, TNF-α, IL-1β levels in tissues were measured.
RESULTS: While the MDA, IL-1β, TNF-α levels of tissues were significantly increased in OKA group, SOD, GSH-PX enzyme activation and GSH levels were decreased compared to all other groups (P< 0.05). OKA+ACA treatment increased SOD and GSH-PX enzyme activation and GSH levels, and conversely decreased the levels of MDA, TNF-α and IL-1β in comparison to OKA group.
CONCLUSIONS: Our results suggested that ACA supplementation prevented oxidative stress and neuroinflammation in OKA-induced neurodegeneration.This study was supported İnönü University BAP (2015/105).

OC27

The Effects of Caffeine Application Before Psychological Stress on Anxiety Level and Cognitive Functions

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AIM: Caffeine is an addictive substance which is found in food and drinks. Psychological stress affects cognitive functions negatively. Caffeine can be protective in stressful conditions; but there is no clear information about that. This study aimed to investigate the effects of acute and chronic coffee application before acute and chronic stress on anxiety-like behaviour and working memory.
METHODS: Acute and chronic stress were applied to male Sprague Dawley rats (200-250 g, n=42). Acute and chronic caffeine (3 mg/kg) were given rats intraperitonaelly 5 min before stress. Anxiety was evaluated with Holeboard and cognitive functions was evaluated by Object Recognition Test. The measurements of glutathione (GSH), malondialdehide (MDA), nitric oxide (NO), myeloperoxidase (MPO), superoxide dismutase and catalase, luminol and lucigenin chemiluminescence in brain tissue and histological evaluations were done. Statistical analyses were done with GraphPad prism Program by t-test, ANOVA and Tukey test. p<0.05 is accepted as significant.
RESULTS: Caffeine increased cognitive function in chronic stress (p<0.05-0.01) Anxiety increased in stress groups. Caffeine decreased anxiety (p<0.05-0.01). Chronic caffeine decreased MPO (p<0.05) which was increased by acute stress (p<0.05). Caffeine blocked the increase which was done by chronic stress (p<0.05-0.01) Acute stress increased MDA (p<0.001) and lucigenin (p<0.001). Chronic caffeine decreased them (p<0.01). Acute caffeine decreased MDA (p<0.01). Acute stress increased NO (p<0.05) and caffeine applications decreased them p<0.05-0.001). Acute caffeine decreased SOD (p<0.001) which was increased by acute stress (p<0.001). Acute caffeine increased GSH(p<0.001) and decreased luminol(p<0.05). Neuronal injury which was increased in stress histologically was decreased by caffeine. It is more prominant in chronic caffeine.
CONCLUSIONS: It is seen that acute and chronic caffeine decreased anxiety and increased cognitive function which was decreased especially by chronic stress. It is thought that caffeine decreased the oxidative injury which was increased by stress in brain tissue.

OC28

Investigation of the Anti-inflammatory and Anti-oxidant Effects of Phosphodiesterase-5 Inhibitor Tadalafil on Rat Adjuvant-induced Model of Arthritis

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AIM: Rheumatoid arthritis is a chronic, progressive, inflammatory autoimmune disease associated with articular, extra-articular and systemic effects. Inflammation and altered oxidant/antioxidant balance influence the prognosis of the disease. There are numerous experimental studies which studied the anti-inflammatory and antioxidant effects of phosphodiesterase-5 inhibitors.This study aimed to investigate the anti-inflammatory and anti-oxidant effects of phosphodiesterase-5 inhibitor tadalafil on rat adjuvant- induced arthritis model.
METHODS: 56 Male Sprague-Dawley rats (300-450g) were included in the study. Arthritis was induced by intradermal injection of Complete Freud's adjuvant(0.1ml) into the plantar surface of right hand pawwhile control groups received the vehicle (paraffin oil;0.1 ml). Beginning from the 5th day, groups were treatedwith tadalafil or saline (10 mg/kg/per oral) for 11 days. On day-15, rats with arthritis received soluble guanylylcyclase inhibitor ODQ (10mg/kg), non-selective nitric oxide inhibitor L-NAME (25 mg/kg) or non-selective

cyclooxygenase inhibitor indomethacin (10mg/kg). Animals were depitated on day-16, Metatarsophalangeal joint,gastrocnemius muscle, liver and trunk blood were sampled.Joint and muscle samples were evaluated histolopathologically and scored.Malondialdehyde (MDA) level, glutathione content, myeloperoxidase (MPO) activity and chemiluminesce levels were measured in muscle and liver. Trunkblood was usedfor total oxidant status (TOC) and total antioxidant capacity (TAC) assays...Statistical analysis was performed by ANOVA and Student's t-tests.
RESULTS: Arthritis group revealed markedly increased paw edema (34.76±0.93 mm2, p<0.01), increased muscle MDA (6.60±1.26 nmol/g, p<0.01) and glutathione levels (0.75±0.08 mmol/g; p<0.001) compared to control. High microscopic score showing joint injury and increased muscle luminolandlucigenin-enhanced chemiluminesce levels in the arthritis group were attenuated by tadalafil (4.00±0.69; 13.17±2.47 rlu/mg and 10.69±1.43 rlu/mg, p<0,01-0,001). ODQ, L-NAME and indomethacin did not change the effects of tadalafil on these parameters.
CONCLUSIONS: Inhibition of PDE-5 enzyme by tadalafil decreases the extent of the histopathological damage in joints and generation of reactive oxygen metabolites in the muscle in a rat model of experimental rheumatoid artritis via mechanisms that do not seem to interfere with guanlyl cyclase, nitric oxide or cyclooxygenase.

OC29

The Effects of Dental Bleaching Agent and α-Tocopherol on Dental Pulp Stem Cell

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AIM: Tooth bleaching agents contain peroxide and lead to cellular damage. Therefore, our study aims to find the effects of application of hydrogen peroxide (HP) on dental pulp stem cell (DPSC) cultures and whether vitaminE has any protective effects against the potential damage to occur.
METHODS: Study groups were: Control (C), 2Hydrogen Peroxide (2HP) (2 µg/ml), 6Hydrogen Peroxide (6HP) (6 µg/ml), vitaminE (100 µM)+2HP (E2HP), vitaminE (100 µM)+6HP (E6HP) groups. DPSC treated according to assigned groups, the cells were removed from their media at 0, 24, 72 hours. DNA damage was measured using comet assay. TNF-alpha, IL-6, TOS, TAS levels were measured using ELISA method. Kruskal -Wallis variance of analysis and Mann Whitney-U Test with Bonferroni correction were used for the analysis of the data.
RESULTS: Tail intensity was observed to significantly increase in only HP groups compared to control group at all time points (p=0.000). Analyses performed at 24 h showed significant decrease in vitaminE groups compared to 2HP group (p=0.000). Tail intensity showed significant decreases in vitaminE groups compared to 6HP group at 0 h and 72 h (p=0.000). Tail moments increased significantly in 2HP and 6HP groups at all time points compared to control group (p=0.000). Measurements performed at 24 h showed significant decreases in averages of vitamin E groups compared to 2HP group (p=0.000). Tail moment was found significantly decreased in vitamin E groups compared to 6HP group at 0 h and 72 h, respectively (p=0.015 and p=0.000). A comparison of TNF-alpha, IL-6, TAS, TOS and OSI levels of the study groups didnot reveal significant differences at all time points.
CONCLUSIONS: As a result, we suggest that HP dosages used leads to genotoxicity and vitamin E decreases HP-induced DNA damage. Our results indicate that the HP dosages used had no effect on the oxidative and inflammatory processes.

OC30

Effects of Alpha-Lipoic Acid on Urotensin II and TGF-β1 on Steroid-induced Osteonecrosis in Rats

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AIM: It was known that systemic glucocorticoids which are using in variety immunological, inflammatory and rheumatological diseases, cause oxidative stress and also osteonecrosis. In our study, we investigated effects of alpha lipoic acid (ALA) in glucocorticoid-induced osteonecrosis in rats.
METHODS: Totally 40 male Wistar rats were equally divided into 4 groups which were control (C; n=10), Metilprednisolon Asetat (MPA; 15 mg/kg/twice a week for 2 weeks, n=10), Alfa Lipoic Acid (ALA; 100 mg/kg/per day for 4 weeks, n=10), ALA and MPA (n=10) groups. While ALA was administered intraperitoneally to rats from the age of 13 weeks, MPA was administered subcutaneously from age of 15 weeks. Animals were sacrificed and their femur and blood samples were collected for biochemical and histopathological analysis. Osteonecrosis model was diagnosed with histopathological examination. Urotensin-II (U-II) and transforming growth factor (TGF-β1) were assayed. The data were analyzed by one-way ANOVA followed by post hoc Bonferroni multiple comparison test and expressed as mean ± standard error of the mean.
RESULTS: In histopathological evaluation, it was determined that fatty degeneration and osteonecrosis significantly decreased in treatment group (ALA+MPA) when compared to MPA group (p<0.05). It was observed that myeloid necrosis and osteocyte necrosis increased in MPA group but these were not observed in other groups. As compared to the controls, both U-II and TGF-β1 levels significantly increased in MPA group (p<0.05). U-II and TGF-β1 levels significantly decreased in treatment group (ALA+MPA) as comparison with MPA group (p<0.05).
CONCLUSIONS: Previous studies showed that osteonecrosis could be induced with administration of a single dose of glucocorticoid andnecrotic lesions could be seen after administration of MPA for two weeks. Therefore, the results of our study with administration of MPA for 2 weeks showed that ALA treatment which started before 2 weeks of glucocorticoid injection, ameliorated the experimental glucocorticoid-induced osteonecrosis.

OC31

Antioxidant Effects of Melatonin on Ovarian Ischemia-Reperfusion Injury of Rats

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AIM: Ovarian torsion is a rare gynecological emergency that can lead to serious problems as infertility. In this study, we aimed to investigate the possible beneficial effects of melatonin on oxidative stress injury in ovarian ischemia-reperfusion model.
METHODS: A total of 35 female Wistar-Albino rats in 5 groups (n=7) was presented. First two groups constituted sham (Group I) and detorsion control groups (Group II). Group III: the rats received 10 mg/kg melatonin 30 minutes before torsion; Group IV: melatonin was injected 30 minutes before detorsion; Group V: melatonin was injected twice, before torsion and detorsion. As markers of oxidative stress, the total antioxidant status (TAS), total oxidant status (TOS), oxidative stress index (OSI), myeloperoxidase (MPO), interleukin 1beta (IL1β) and malondialdehyde (MDA) levels were investigated. Tissue samples were stained with hematoxylin-eosin and histopathological changes (edema, hemorrhage, inflammation, necrosis) were scored; and the tissue inducible nitric oxide synthase (iNOS) expressions were also assessed by immunohistochemistry. The Kruskal-Wallis and the Mann-Whitney U tests were used for the statistical analysis.
RESULTS: When compared to control group, in all treatment groups (Group III, IV, V) the TAS levels were increased, whereas TOS and MDA were decreased statistically significant ($p<0.05$). In addition, in Group V, when compared to controls, OSI and MPO levels were also decreased significantly ($p<0.05$). The scores of histopathological changes were increased in Group II; decreased in Group III and V significantly ($p<0.05$). iNOS staining results were also supportive of these findings.
CONCLUSIONS: Melatonin reduced the severe oxidative stress and increased antioxidant capacity in the ovarian ischemia-reperfusion model. In addition, reduction of OSI levels especially in Group V supports the opinion that melatonin injection may has a prophylactic and therapeutic importance in ovarian torsion. However, further studies are needed to understand the underlying mechanism of melatonin administration in ovarian torsion.

OC32

Effects of Circadian Rhythm on Brain Injury and Related Molecular Mechanisims

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AIM: In addition to daily physiological functions circadian rhythm can also affect pathophysiological processes. Various studies, especially clinical ones have been showing the probable relationship between ischemia and circadian rhythm since 1970s. However, as most of those studies remained restricted with clinical observations, current experimental researches focusing on molecular mechanisms are insufficient. This investigation aimed to find out effects of circadian rhythm on ischemia induced neuronal damage at molecular level after middle cerebral artery occlusion (MCAO).
METHODS: Male Balb/c mice (8-10 weeks) were exposed to 30 minof MCAO following 72 h ofreperfusion at four distinct time points (06:00 a.m., 12:00 a.m., 06:00 p.m. and 12:00 p.m.) selected according to their circadian rhythms. Post-ischemic lesion, neuronal survival, apoptotic cell death and activation of intracellular signaling molecules were analyzed at each time point for investigating the role of biological clock on the pathophysiology of stroke.
RESULTS: Neuronal survival was increased significantly in ischemic mice operated at 00:00 a.m. time point, compared to 06:00 a.m. while apoptotic cell death was decreased. Protein levels of stress kinases JNK, GSK-3, PTEN and iNOS also showed a decline in 00:00 a.m. group. However, expression of circadian rhythm related proteins, BMAL-1, Clock, PerI and PerII, and eNOS were increased at the same time point.
CONCLUSIONS: In conclusion, activational changes of proteins by circadian rhythm regulations directly influence brain injury following ischemia. Depending on circadian rhythm, protein expression at 12 p.m. especially BMAL-1, Clock, PerI, PerII and eNOS, increased neuronal survival and decreased apoptotic cell death after MCAO. These results contribute to identification of new pharmacological therapeutic target molecules after neuronal injury.

OC33

Induction of Behavioral and Histological Alterations in Rats by Chronic Consuming of Artificial Sweeteners: A Comparative Study

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AIM: Previous studies have reported the negative health outcomes (obesity, type 2 diabetes mellitus and metabolic syndrome) of sugar-sweetened beverages. Therefore, many people turned to artificial sweeteners to lessen the risk of these diseases. However, it has been suggested that artificial sweeteners may also have harmful or unclear effects with regard to regulation of energy balance or other metabolic activities. In our study, we aimed to compare the neurobehavioral effects of most widely used artificial sweeteners including aspartame, sucralose, and saccharin in rats.
METHODS: Twenty-four adult male Sprague-Dawley rats were included in the study. All animals were housed with unlimited access to regular chow. Control group (n=6) received regular tap water while other groups received aspartame (3 mg/kg/day, n=6,) or saccharin (3 mg/kg/day, n=6) or sucralose (1.5 mg/kg/day, n=6) in the drinking water. Following 6 weeks, passive avoidance learning (PAL) test was performed to evaluate the neurobehavioral effects of sweeteners. Then, brains were removed and assessed for hippo-

campal neuronal (CA1-CA3) density and GFAP immunohistochemistry.
RESULTS: Our results demonstrated that chronic consumption of sweeteners significantly impaired PAL performance in all groups compared to control ($p<0.0001$). Furthermore, histological evaluation of hippocampal CA1-CA3 areas revealed significantly lower neuronal cell numbers and increased GFAP expression in aspartame ($p<0.0001$) and sucralose-treated ($p<0.05$) groups compared to control.
CONCLUSIONS: It can be concluded from these data that long-term consumption of artificial sweeteners may have harmful effects on learning and memory performance and hippocampal neuronal density in rats.

OC34

Lignosus Rhinocerotis* Protects Axotomized Sensory Neurones *in vitro

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AIM: To test whether hot water extract (HWE) and cold water extract (CWE) of *Lignosus rhinocerotis sclerotim*affect the axon length and the survival of axotomized sensory neurons in an *in vitro* model.
METHODS: Sensory neurons were cultured by dissociation of mouse dorsal root ganglia. The neurons were treated with CWE (25µg/ml) and HWE (25µg/ml) one hour prior to axotomy. The nerve growth factor(NGF), (50ng/ml) as a positive control and phosphate buffered saline (PBS), a negative control were used in our experiments. Axon transections were performed with a laser microdissections system equipped with UV laser unit. Exact points of transection was 150 µm distance from soma. Totally 327 neurons were axotomized in the all groups(64 in CWE, 55 in HWE, 51 in NGF, 71 in control). After the microdissection procedure, the preparations were transferred to time-lapse microscopy system. To visualize the death and survival of the neurons, propidium iodide(7.5µM) and calcein AM(1µM) was added to the culture medium. Phase contrast and fluorescence images of cells were captured digitally with a 40X objective with 5 min intervals over the course of 24 h.
RESULTS: Our experiments demonstrated a statistically significant ($p<0.01$) difference in the axon length following the treatment with CWE (59.68µm) or NGF (68.65µm) compared to the control treatment (27.10µm). However the difference between CWE (59.68µm), HWE (45.78µm) or NGF (68.65µm) were not statistically significant. In addition, we determined the neuron viability following axotomy. A highest number of viable neurons were found in CWE (81.25%) treatment groups that was followed by the NGF (70.59%) and HWE (56.36%) as compared to the control group (29.58%). The differences among the groups were statistically significant and also all treatment groups compared to the control showed a statistically significant higher rate of neuron viability.
CONCLUSIONS: Our study for the first time demonstrated that the cold water extract of Lignosus rhinocerotis sclerotim prevents neuron death after axotomy damage.

OC35

The Effect of Melatonin on the Exosome Release and Content in *in vitro* Amyloid-beta Toxicity Model

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AIM: Alzheimer's Disease (AD) is the most common and progressive neurodegenerative disorder. The main pathology of AD is the presence of extracellular senile plaques and intracytoplasmic neurofibrillary tangles (NFTs). Senile plaques are comprised of amyloid beta peptide (Aβ), whereas NFTs contain primarily hyperphosphorylated tau. Knowing the increasing involvement of exosomes in the spread of molecular pathology of AD, our aim was to investigate the possible role of melatonin treatment in the releasing of exosomes and exosomal tau content in an in vitro AD model.
METHODS: In this study, SH-SY5Y cell line was used and the optimum concentration of Aβ has been determined colorimetrically by cell viability (Lactate Dehydrogenase Kit) and cell proliferation tests (WST-1 Kit). Melatonin (100µM) was applied before and after Aβ application. After 48 h of Aβ application, cell culture medium was obtained and exosome isolation wasperformed by Total Exosome Isolation Kit. Isolated exosomes were immunoprecipitated with marker antibodies. The amount of released exosomes and their tau content were analyzed by Western blot technique. Data werestatistically evaulated by using ANOVA.
RESULTS: Our results showed that the application of Aβ led to a decrease in exosome release (56.68%, $p<0.001$), whereas both pre- and post-treatment of melatonin caused an increase (60.2%; $p<0.001$ and 139%; $p<0.001$). Pre-treatment of melatonin led to an increase in exosomal total tau (15.22%; $p<0.01$), but its post-treatment caused a decrease of total tau carried by exosomes (83.66%; $p<0.05$).
CONCLUSIONS: Melatonin treatment clearly affects the release of exosomes in our in vitro SH-SY5Y cell line model, and the amount of total tau carried by exosomes seems to depend on whether melatonin is applied before or after the Aβ application. The effect of melatonin on exosomes would shed light on the spreading mechanism(s) of neurodegeneration.

OC36

The Effect of Melatonin on the Alzheimer's Disease: Relationship with FEZ1 Gene Expression

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AIM: Alzheimer's Disease (AD) the most common neurodegenerative disorder, which affects more than 35 million people worldwide. Melatonin may play a role in the neuro-protective mechanism in the AD. The present study was designed to determine the relation

between the Fasciculation and elongation protein zeta-1 (FEZ1) and AD in melatonin deficiency.
METHODS: 30 Male rats weighing 220-280 g were used in the study. The rats were divided into 3 groups: sham pinealectomy (PnX), PnX+streptozotocin (STZ) and melatonin+STZ+PnX groups (n=10). The PnX process was performed to the rats before the STZ applications and the intracerebroventricularly STZ injections were applied to the rats on the 1st and 3rd days as 3 mg/kg. Melatonin applications (intraperitoneally 10 mg/kg/day) were started 1 h before the first dose of STZ administration and continued for 14 days. 14 days after the first STZ application, the behavioral tests were performed for 5 days. In the end of behavioral tests, the rats were sacrificed and their hippocampus tissues were collected. Protein levels of FEZ1 were measured by Western Blot method.RESULTS:While the levels of FEZ1 in STZ+PnX group were similar to sham groups, the levels of FEZ1 in the STZ+PnX+melatonin group were found to be lower than both STZ+PnX and sham groups ($p<0.05$).
CONCLUSIONS:Exogenous melatonin administration reduced levels of FEZ1 and contributed to the prevention of the development of AD. However, results of the study showed that absence of melatonin did not have any effect on the development of AD.This study was supported by TUBITAK (Project no:214S410).

OC37

The Effect of Alpha Lipoic Acid on the Hypothalamic-pituitary-adrenal Axis and Cholinergic System in an Experimental Alzheimer's Model

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AIM: The aim of this was to investigate the effect of alpha-lipoic acid (ALA) on the learning and memory performance, cholinergic function, and hypothalamic-pituitary-adrenal (HPA) axis in an experimental sporadic Alzheimer's-type dementia model in rats.
METHODS: The study was conducted with 24 male Wistar rats in 3 groups. The control group received only tap water (p.o.) and physiologic saline (i.p.). In Al group, aluminum chloride (1600 mg/L) was prepared and added to drinking water daily to generate dementia model. In treatment group, ALA (100 mg/kg, i.p.) was administered daily alongside in-drinking-water aluminum. Learning and memory performances were evaluated by Morris' water maze test 8 weeks later. Rats were sacrificed following the behavioral test. ACTH and CORT were measured from serum for evaluating HPA axis activity whereas hippocampal acetylcholine and acetylcholinesterase were estimated for evaluating cholinergic activity by ELISA method. Non-parametric data (platform-latency) were assessed with Kruskal-Wallis post hoc Dunn's tests whereas parametric data (all other) were analyzed with one-way-ANOVA post hoc Tukey's tests.
RESULTS: No significant difference for body weight was observed between groups (CON: 409.9±23.86;AL:392.6±24.14; AL+ALA: 398.9±27.12; $p=0.3954$). The escape latency was prolonged in the Al group compared to the other groups in the last two days of the training trials ($p<0.05$). In the probe trial, the time elapsed in target quadrant (CON:25.43±6.6;AL:13.43±5.4;AL+ALA:23.1±5.2;$p<0.05$) and the platform crossings (CON:7.12±1.9; AL:2.87±1.6;AL+ALA: 6.9±3.5;$p<0.05$) were found to be lower in the Al group. The hippocampal acetylcholine level was decreased; acetylcholinesterase activity was increased in the Al group (CON:1.089±0.38; AL:1.713±0.32;AL+ALA:1.015±0.52;$p<0.05$). Serum ACTH (CON: 186.8±40.8; AL:138,7±13.2;AL+ALA:191.6±40.5;$p<0.05$) and CORT levels (CON:163.5±4.6; AL:130.8±30.1;AL+ALA: 181.1±16.3; $p<0.05$) were found to be lower than others in Al treated ones.
CONCLUSIONS: In-drinking-water aluminum treatment diminishes the learning and memory performance in rats while ALA attenuates this disruption. The beneficial effect of ALA on the learning and memory activity is associated with both the HPA axis and cholinergic transmission.
This study was supported by Selçuk University Research Foundation (BAP project # 15401131).

OC38

Effect of RFRP-3 on Anxiety-like Behaviour and Hippocampal Neurogenesis in Rats

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AIM: RFamide related peptide-3 (RFRP-3) is homolog of gonadotropin inhibitory hormone and plays role in hypothalamic regulation of reproductive functions. RF9 is a RFRP-3 receptor (GPR147) antagonist. There is no evidence regarding the effect of RFRP-3 on hippocampal behavioural processes and neurogenesis. The aim of present study is to investigate possible effects of RFRP-3 and GPR147 signalling on neurogenesis in rat hippocampus and anxiety-like behaviours.
METHODS: 18Adult male rats were divided four groups as control, RFRP-3 (1nmol/day), RF9 (10nmol/day) and RFRP-3+RF9 in present study. Osmotic brain minipumps were implanted to rats and drug infusions into lateral ventricles were performed for 15 days. Behavioural tests associated with anxiety were applied to rats. Individual anxiety parameters were evaluated. mRNA levels of neurogenesis markers in hippocampus tissues were determined by RT-PCR analysis.
RESULTS: RFRP-3 administration reduced the percent time spent in open arms of elevated plus maze test ($p<0.01$). RFRP-3 decreased numbers of entries into open arms and increased numbers of entries into closed arms ($p<0.05$). Significant reduction in time spent in centre of open field test was solely found in RFRP-3 group compared to others ($p<0.05$). RFRP-3 enhanced time spent in the corner ($p<0,05$) and diminished rearing behaviour ($p<0.01$). As for RT-PCR analysis we determined an important reduction on nestin expression in RFRP-3 group compared to control ($p<0.05$). Expressions of nestin, doublecortin, calbindin and neuron specific nuclear antigen were decreased in RFRP-3 group compared to RF9 administered group ($p<0.05$). Nestin expression in RFRP-3+RF9 group was decreased compared to control ($p<0.05$). All of genes in the same group were also decreased compared to RF9 group ($p<0.01$).
CONCLUSIONS: RFRP-3 showed anxiety like effect and suppressed neuronal progenitor proliferation in adult rat hippocampus. These results suggested that adult hippocampal neurogenesis may play a mediator role for the mechanism of anxiogenic effect of RFRP-3.

OC39

Role of Calcium Sensing Receptors on GLP-1 and PYY Secretion After Acute Intraduodenal L-tryptophan Administration in Rats

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AIM: L-tryptophan, which is an essential amino acid, increases insulin level and decreases food intake. It is thought that L-tryptophan causes release of glucagon-like peptide-1 (GLP-1) and peptide YY (PYY) hormones from intestinal enteroendocrine L cells and calcium-sensing receptors (CaSR) play a role in this effect. In this study, we aimed to investigate the effect of acute intraduodenal L-tryptophan administration on GLP-1 and PYY levels and the role of CaSR in this effect in rats.
METHODS: Male Wistar rats (n=21) were divided into L-tryptophan, L-tryptophan+CaSR antagonist and L-tryptophan+vehicle groups. All solutions were directly given to the intestines with intraduodenal catheter. Before (min 0) and after (min 30, 60, and 90) intraduodenal infusions, blood samples were taken from tail vein for plasma glucose, L-tryptophan, insulin, GLP-1 and PYY measurements. Blood glucose was measured by test stripes. L-tryptophan level was measured by HPLC and GLP-1, PYY and insulin levels were measured by ELISA kits. Area under the curves (AUCs) were calculated for glucose, insulin, GLP-1 and PYY levels obtained throughout 90 min.
RESULTS: In all groups, plasma L-tryptophan levels were maximum on the 30th min ($P<0.05$). Plasma insulin and GLP-1 secretions were lower in the antagonist group compared to other groups ($P<0.05$). PYY levels were not different between groups and time points. Although plasma glucose levels were higher in the antagonist group, there was no significant difference between groups.
CONCLUSIONS: This study demonstrates that L-tryptophan causes intestinal GLP-1 release and CaSRs play a role in this effect. As a result, targeting these pathways in L-cells can be used to increase GLP-1 secretion, so it could be possible to develop new treatments to prevent or treat diseases like diabetes and obesity.

OC40

Sinapic Acid Ameliorates Gut Inflammation Induced by Trinitrobenzene Sulfonic Acid in Rats

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AIM: Inflammatory bowel disease is the inflammation of gastrointestinal system concomitant intense immune response associated with mucosal barrier dysfunction. Recruitment of inflammatory cells and subsequent release of inflammatory mediators all cause tissue damage and contribute many of the clinical features of colonic inflammation. Sinapic acid (SA), a cinnamic acid derivative, is obtained from various fruits and vegetables. Recently, anti-inflammatory effects of SA have been shown in several *in vitro* and *in vivo* experimental models; however, there is no report for the effects in the gastrointestinal system. The present study was undertaken to examine the anti-inflammatory effects of SA on trinitrobenzene sulfonic acid (TNBS)- induced colitis in rats.
METHODS: The colonic inflammation was induced in Wistar-Albino rats (250-300 g; n=9-10/group) by intrarectal administration of 1ml of 30 mg/ml TNBS in 40% ethanol under light isoflurane anesthesia. Control rats received the same volume of saline by the same route. In the treatment group, rats were treated with SA (20 mg/kg in olive oil/per oral) 10 min after induction of colitis and continued for 3 consecutive days. On the 4th day, rats were decapitated and distal colon were removed for the macroscopic damage scoring, determination of tissue wet weight index (WI), malondialdehyde (MDA), glutathione (GSH) levels and myeloperoxidase (MPO) activity. Values were compared by ANOVA.RESULTS: The macroscopic score and WI of colitis group was significantly higher compared with control group ($p<0.001$) and SA treatment ($p<0.01$) reduced these parameters. Increase in colonic MDA levels and MPO activity in rats with colitis were attenuated by SA treatment ($p<0.05$ and $p<0.01$, respectively). In addition, the GSH depletion in colitis group was prevented by SA treatment ($p<0.05$).
CONCLUSIONS: Results demonstrate that SA exerts anti-inflammatory effects by inhibiting tissue neutrophil infiltration, suppressing the activation of release of oxygen free radicals and preventing lipid peroxidation.

OC41

The Role of Central Oxytocin in Chronic Homotypic Stress-induced Gastric Motor Adaptation

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AIM: In modern societies, individuals experience various types of stressors in daily life. Chronic exposure to a repeated stressor can lead gastric motor dysfunction due to the permanent changes in central stress circuitry and brain-gut axis, while some individuals can adapt without developing gastric symptoms. The mechanism of the relevant adaptation is not fully investigated, however the role of hypothalamic oxytocin (OXT)-induced inhibition on corticotropin releasing factor (CRF) has been reported. Besides its well-known endocrine-fashion effects such as uterine contraction and milk ejection, OXT plays a pivotal role as a neurotransmitter and a neuromodulator in regulation of stress response and stress-related behaviours. Furthermore, OXT-ergic neurons in hypothalamic paraventricular nucleus (PVN) projecting on dorsal vagal complex in brain stem are known to regulate gastric motor functions. The aim of the present study is to elucidate the role of the central OXT in gastric motor adaptation following chronic homotypic stress (CHS).
METHODS: For the adaptive stress model CHS, adult male rats were exposed restraint stress (RS) 90 min/day for 5 consecutive days. Microdialysis samples were collected every 30 min from parvocellular region of hypothalamic PVN during pre-RS, RS and post-RS periods on 1st and 5th days of CHS. OXT levels in samples were assayed by EIA method. Solid gastric emptying (GE) was measured following acute and CHS. To evaluate the role of endogenous OXT in CHS-induced gastric motor adaptation, selective OXT receptor antagonist L-371257 was daily administered throughout the CHS. One-way (GE) or two-way (microdialysis) ANOVA with repeated measures followed by an appropriate post-hoc analysis were used to determine the significance among the groups (n=8).

RESULTS: CHS-loading for 5 days significantly ($p<0.05$) increased the OXT levels in RS and post-RS samples. Following CHS, acute RS-induced delayed gastric emptying was restored which was abolished by chronic central administration of L-371257.
CONCLUSIONS: Hypothalamic endogenous OXT plays a role in gastric motor adaptation occurred following CHS. OXT receptor antagonists seem to be a candidate for treatment of stress-related gastric motility disorders.

OC42

Central Apelin Inhibits Gastric Motility via APJ Receptor-mediated Vagal Efferent Pathway

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AIM: Apelin is the endogenous ligand of G-protein coupled receptor APJ. In brain, expression of APJ mRNA in autonomic centers including hypothalamus, amygdala, nucleus tractus solitarius (NTS) and rostral ventrolateral medulla (RVLM) suggests that apelin may be a central regulator of gastrointestinal (GI) motor functions. Gastro-inhibitory effect of central exogenous apelin was reported in rodents indicating that apelin may alter gastric motility through APJ receptor in brain. The aim of the present study is to investigate whether (1) centrally administered apelin alters gastric motility and (2) apelin exerts its relevant effects through APJ receptor expressed on stomach-projecting neurons of dorsal motor nucleus of N.vagus (DMV).
METHODS: Seven days prior to the experiments, a 26G guide cannula was stereotaxically implanted into the lateral ventricle of male adult Wistar rats. A neuronal florescent retrograde tracer, fast blue solution was injected into antrum. For recording of gastric postprandial contractions, a strain gage transducer was implanted onto the antral surface in vagatomized or sham animals. After a 7-day recovery, gastric contractions were monitored in conscious state using a Wheatstone bridge bioamplifier and a digital data acquisition system for 3-4 hours. The changes in motility index were evaluated before and after apelin administrations. After euthanization, brainstems were removed and fixed in 10% formalin solution. APJ and c-Fos co-expressions on gastro-projecting vagal efferent cells in DMV were monitored using immunofluorescence method on 50 µm coronal brainstem sections.
RESULTS: Antral contractions were inhibited following central administration of apelin which was abolished by truncal vagotomy. The gastro-projecting neurons of DMV were marked by florescent fast blue. In apelin-treated rats, c-Fos expression on APJ-positive DMV cells was more remarkable compared with vehicle-injected rats.
CONCLUSIONS: Apelinergic system is widely produced in brain. Apelin may be a central regulator of GI motor functions through APJ receptor-mediated vagal efferent pathways.

OC43

A Novel Effective Myokine in the Control of Reproduction Behaviour; Irisin

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AIM: Irisin was defined as a myokine with a peptide structure in 2012. The demonstration of the existence of irisin in cerebrospinal fluid and testis shows that this peptide may have roles in the hypothalamus-hypophysis-testicular axes. This study aims to examine the influences of the irisin on reproduction function in molecular and biochemical levels.
METHODS: 40 Wistar-Albino male rats were used in the study, and the rats were evenly distributed into 4 groups (n=10): Control group did not receive any applications. Osmotic mini pump was implanted to the sham group, and infusion of artificial cerebrospinal fluid (solvent) was applied for 7 days at 10µl/h. The study groups received infusion of irisin as physiological (10nM) and pharmacological (100nM) doses for 7 days at 10 µl/h. At the end of the infusion, the animals were decapitated, and the brain (hypothalamus), testis and blood tissues were collected. The serum LH, FSH and testosterone levels were determined by ELISA method. The GnRH mRNA levels in the hypothalamus were determined with RT-PCR method. The examinations were performed from the testis tissues with sperm analyze.
RESULTS: Both concentrations of the irisin decreased the GnRH mRNA and protein levels in the hypothalamus ($p<0.05$). In addition, it was also determined that the serum LH, FSH and testosterone levels decreased depending on the irisin infusion ($p<0.05$). It was also observed upon the sperm analyses that the sperm density and activity decreased depending on the irisin application ($p<0.05$).
CONCLUSIONS: Our results have shown that the irisin may play active roles in regulating the reproduction funtions in a central manner; and meanwhile, may also suppress the LH and FSH release, and decrease the testosterone level. These results show that the irisin receptor antagonists may be beneficial in the treatment of infertility.
This work is supported by TUBITAK (Project#214S567).

OC44

Effect of Metformin on the Myometrium

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AIM: Myometrium; smooth muscle of uterus, ready to labor during pregnancy and it is very active during labor, also it is functional in non-pregnant women. Therefore, it is important to understand contraction and relaxation mechanisms of myometrium. Metformin is a biguanide derivative oral antidiabetic drug, which is the first choice in the treatment of type II Diabetes Mellitus patients especially if they are obese. In recent years, metformin extensively studied due to its smooth muscle relaxant, antioxidative and antineoplastic activities. Also, metformin acts as an adenosine monophosphate activated protein kinase (AMPK) and nitric oxide synthase (NOS) activator. It has been shown that by using NO metformin causes vasodilation. Its effect on the genital system is also widely investigated but still there is only very little information compiled on the effect of metformin on myometrium. Since, it is clinically important to understand these effects on myometrium contractility we conducted present study. Firstly; we aim to investigate effect of metformin both on spontaneous and evoked myometrial contractions. Secondly; we aim to investigate role of AMPK and NO pathway on presumed response to metformin.
METHODS-RESULTS: Myometrial strips are obtained from adult female rats and our results has shown that metformin decreases frequency of spontaneous contractions and amplitude of KCl and KCl+oxytocin induced contractions ($P<0.05$). Dorsomorfin (AMPK inhibitor) attenuates effect of metformin on the spontaneous contractions but could not alter any other parameter. L-NAME (NOS inhibitor) decreases frequency of spontaneous contractions, amplitude; area under the curve of KCl and oxytocin induced contractions, amplitude of KCl+oxytocin induced contractions ($P<0.05$).
CONCLUSIONS: In conclusion; our findings suggest that metformin may have a relaxant effect on the myometrium and this effect could be mediated via AMPK pathway.

OC45

Nesfatin-1 may Interfere with Kisspeptin/kiss1 System in Gonadal Activity of Female Rats

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AIM: Nesfatin-1, a hypothalamic anorexigenic neuropeptide, is suggested to have a role for central reproductive functions. Although specific receptor(s) of nesfatin-1 are still not to be identified, it is known that its putative receptor autoradiography areas are located in the brain and peripheral organs. The aim of this study was to determine the role of nesfatin-1 on gonadotropin levels, ovarian follicle counts and its interaction with peptide 234 (p234, an antagonist of kiss1 receptors) in rats.
METHODS: Female Sprague-Dawley rats were weaned on post-natal day (pnd) 21. The animals were intracerebroventricularly cannulated under general anesthesia on pnd 23. Groups of female rats were daily administrated with nesfatin-1 (25 pmol/rat), p234 (1 nmol/rat), and nesfatin-1 plus p234. Blood samples and ovarian tissues were obtained from all animals after pnd 60th day in diestrus, which was determined by vaginal smears.vations of LH levels compared to controls ($P<0.001$, 7.23±0.33ng/ml and 4.31±0.34ng/ml, respectively). Administrations of nesfatin-1 plus P234 (4.82±0.31ng/ml) significantly decreased LH levels compared to nesfatin-1 group ($P\leq0.001$). FSH levels did not differ among groups. Although the counts of small, medium, antral follicles and corpus luteum did not differ between nesfatin-1 and control groups, their counts significantly decreased in nesfatin-1 plus P234 group compared to the nesfatin-1 administered group.tin/kiss1r system in the female rats.

OC46

The Effects of Urotensin II Agonist and Antagonist on the Testicular Damage of Streptozotocin-induced Diabetic Rats

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AIM: Diabetes mellitus (DM) is one of the most common chronic diseases. Besides, DM causes testicular damage, decrease in sperm count and abnormal spermatogenesis as well as many systems damages. Urotesin-II and Urotesin-II receptors are widely available in testis tissue. The aim of this study is to investigate the therapeutic effects of UTR agonist and antagonist treatment on streptozotocin (STZ) induced diabetes in testicular tissue.
METHODS: In our study, 50 Sprague Dawley male rats weredivided into 5groups (control, DM, DM+Ago, DM+Anta, DM+Ago+Anta). All rats except for the control group were induced diabetes by administration of 60mg/kg STZ intraperitoneally (IP) and the control and DM groups after proof of diabetes 0.09% NaCl solution ip daily for 6 weeks. Human Urotensin II (10 nmol/kg: ip) was given to DM+Ago group for 6 weeks. Urantide (0.6 mg/kg; ip) was given to DM+Anta group for 6 weeks. Human Urotensin II (10 nmol/kg; ip) and Urantide (0.6-mg/kg; ip) were given to DM+Ago+Anta group for 6 weeks. At the 6-weeks later, all rats were euthanized under anesthesia (tiyopental-sodyum, 50mg/kg). The collected testis tissues from rats were used for analysis of gene expressions and histopathology. The gene expression analysis results were evaluated by ANOVA, Tukey test. $P<0.05$ was considered significant.
RESULTS: mRNA expression level of Cox-2, Tnf-α and Urotensin II receptor (UTR), the antagonist administration significantly decreased ($P<0.05$) and significantly increased DM groups ($P<0.05$), while agonist administration did not ($P>0.05$). In addition, expression level of these gene decreased with the treatment of agonist and antagonist doses in DM+Ago+Anta groups ($P<0.05$). The testicular parenchyma was observed as normal structure with in control group animals, but severe intertubular edemas were observed in DM group. However, the edema and disorganization of seminiferous tubules were decreased in DM+Anta and DM+Ago+Anta groups.
CONCLUSIONS: This study revealed that administration of the Urotensin-II antagonist decreased the DM-mediated testicular damages.

ACTA PHYSIOLOGICA

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Poster Communications

PC001

Bradycardia in Hypothyroidism is Caused by Intrinsic Remodelling of the Sinus Node

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AIM: To investigate characterise the hypothyroid (HT) sinus node and identified the important mechanisms responsible for the bradycardia.
METHODS: Rats (n=18) were made HT with 6-n-propyl-2-thiouracil (10 mg/kg/day for 15 days). Control cohort (n=20) received vehicle. ECGs were recorded in anesthetised animals and after complete autonomic block with propranolol (2 mg/kg) and atropine (1 mg/kg). Hearts extracted and Langendorff perfused and intrinsic heart rate measured. In sinus node, atrial and ventricular voltage channel components mRNA abundance was measured using qPCR. Data are presented as mean±SEM and one-way ANOVA was used for statistical comparison.
RESULTS: After complete autonomic block the intrinsic heart rate recorded *in vivo* was 223±9 bpm in HT and 404±19 bpm in control animals. In vitro, the intrinsic rate measured in HT and control hearts was 186±9 and 238±7 bpm (P<0.01), respectively. In the HT sinus node, transcripts proprortion for key voltage-clock components were significantly downregulated: funny channel (HCN4 down by 79%, P<0.05), L-type Ca2+ channel (Cav1.2 down by 66%, P<0.05) and T-type Ca2+ channel (Cav3.1 down by 77%, P<0.05). Similar downregulation was observed in Ca2+-clock components: sarcoplasmic reticulum Ca2+ ATPase (SERCA2a, down by 90%, P<0.01) and ryanodine receptor (RyR2, down by 77%, P<0.05). The plasma membrane Ca2+ ATPase (PMCA1) responsible for Ca2+ extrusion out of the cell was downregulated by 85% (P<0.05) in the HT sinus node. Consistent with these findings, we identified potential thyroid hormone response elements in the 10 kb promoter region of HCN4 using in-silico analysis.
CONCLUSIONS: In the HT sinus node, downregulation of HCN4, Cav1.2 and Cav3.1 coupled with significant loss of SERCA2a and RyR2 is likely to compromise the voltage- and Ca2+-clock pacemaker mechanisms. Thus, ion channel remodelling intrinsic to the sinus node is the likely cause of bradycardia in hypothyroidism.

PC002

The Effect of Apelin on the Expression of Atrial Natriuretic Peptide in Cardiac Tissue

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AIM: Stress is an important etiologic factor in cardiovascular diseases. It has been shown that stressors lead to the increased expressions of apelin and atrial natriuretic peptide (ANP) in cardiac tissue. The aim of the present study was to investigate whether stress-induced apelin has an effect on the expression of ANP in cardiac tissue.
METHODS: A total of 24 adult male Wistar albino rats were used in this study. The rats were divided into control (n=8), stress (n=8) and F13A+stress (n=8) groups. In the stress group, the conscious rats were restrained individually in rectangular polypropylene cages (28x8x8 cm) and immersed up to the depth of the xyphoid process in a 23oC water to induce stress for 6 hours. In the F13A+stress group, apelin receptor antagonist F13A was injected intravenously immediately before application of water immersion and restraint stress. The plasma corticosterone levels using enzyme immunoassay kit and the plasma ANP levels using enzyme-linked immunosorbent assay kit were measured. The samples obtained from atria were used for immunohistochemistry and western blot analysis. Kruskal-Wallis and Mann-Whitney U tests were used for statistical analysis.
RESULTS: Stress application increased the expression of apelin, HIF-1α and ANP in atrial cardiomyocytes. F13A prevented the stress-induced increase of HIF-1α and ANP expression in cardiac tissue.
CONCLUSION: The increased expression of apelin under stress conditions to be effective in ANP production, which is demonstrated by the use of apelin receptor antagonist F13A and apelin may play a role in cardiovascular homeostasis by increasing ANP expression.

PC003

Growth Hormone Affects PI3K/AKT/mTOR Signaling Pathways in the Rat Heart Subjected to Exercise

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AIM: Recombinant hGH(r-hGH) is self-administered by athletes in the belief that it increases performance. Although it has been known that r-hGH administration increases in cardiac hypertrophy the molecular mechanisms have not been indicated completely. The study aimedto examine (1) the role of r-hGH and exercise on cardiac PI3K/AKT/mTOR and ERK signalling pathways and (2) the role of miR21 and miR133 expression on the heart tissue.
METHODS: Adult male Sprague-Dawley rats were divided into sedantary control (SC, n=9), swimming exercise (SE, n=8), r-hGH (GH, n=10), swimming exercise-r-hGH (SE-GH, n=9) groups. r-hGH wasadministered at a dose of 0.3 mg/kg/day during 8-weeks subcutaneously. Exercise groups wore caudal dumbells weighing 5% and completed 1-h swimming exercise 5 times a week during 8-weeks. PI3K, AKT, ERK, miR21 and miR133 gene expressions were performed by real-time PCR in the left ventricle muscle. Protein expression of PI3K, AKT, ERK and mTOR determined with immunohistochemistry technique. Immunoreactivities were scored as

mild, moderate, strong and very strong. Statistical differences between mean values were analyzed using two-way or one-way ANOVA followed by Tukey's post hoc test.
RESULTS: PI3K and AKT gene expressions were increased when SE-GH group compared with SC group (4.45 and 3.6 fold, p=0.006, p=0.008,respectively). mTOR protein expression was higher for GH and SE-GH groups compared with the SC group (p=0.003, p=0.001respectively,). ERK gene/protein expression were similar in all groups. miR21 was up-regulated 2.10 fold in GH group when compared with SC group (P=0.010). miR133 expression was showed increase in GH, SE and SE-GH (2.61,2.30, 1.44 fold change,respectively,) groups when compared with SC group.
CONCLUSIONS: Growth hormone and swimming exercise appear to affect PI3K/AKT/mTOR signalling pathway in the left ventricular tissue in rats. Furthermore, r-hGH administration resulted in increased miR21 gene expression.This study was supported by Trakya University Scientific Research Projects Unit (TUBAP-2015-36).

PC004

Lithium's Effect on Streptozotocin-induced Experimental Diabetes Rats of Vascular Smooth Muscle Cell Proliferation

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AIM: Lithium which is used to treat bipolar disorders, is also reported to have detractive effect on abnormal vascular smooth muscle cell proliferation in addition to its neuroprotective effects. It is known that, vascular smooth muscle cell proliferation is increased in diabetes mellitus. Therefore, in this study on experimental diabetes model (STZ-DM) induced by streptozotocin, we aim to investigate that lithium's effect on vascular smooth muscle cell proliferation.
METHODS: In our study, Wistar male rats weighing 180-200 g were used for animal experiments. Streptozotocin (45 mg/kg) was intravenously administered into the tail vein to generate the STZ-DM group. Streptozotocin-treated rats were followed up for blood glucose levels for 8 weeks. Primary culture cells were obtained from aortic smooth muscle tissue of normal healthy and STZ-DM rats. The number of cells per milliliter was determined manually counting the cells obtained on thoma counting chamber. The cultivation was homogeneously made into ninety-six culture vessels in equal numbers. After 24 hof incubation, the cells in both groups were treated with 15 mM lithium chloride. At the end of 24 h of incubation period, cell proliferation and viability were assessed spectrophotometrically by MTT (tetrazolium salt 3-[4,5-dimethythiazol-2-yl]- 2,5-diphenyltetrazolium bromide). SPSS was used to analyze all the data which was analyzed by Student's t-test.
RESULTS: Streptozotocin treated rats blood glucose measurement during 8 weeks was significantly increased compared to normal healthy rats (12.5 ±2.8 mg/dL; 398.0±2.5 mg/dL,respectively; p<0.001). Lithium application, while increasing cell proliferation in normal healthy rats (p<0.01) reduced in STZ –DM (p < 0.05).
CONCLUSIONS: Lithium can be an agent to prevent STZ -DM comprising vascular smooth muscle cell proliferation.

PC005

Effect of Nicotine on The Smooth Muscle Cell Proliferation and Intracellular Calcium Levels

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AIM: Studies reported that nicotine both increase and reduce the proliferation of vascular smooth muscle cells (VSMC) through the nicotinic acetylcholine receptors. It is suggested that intracellular calcium concentrations increase the effect of stimulants for proliferation. Therefore, in our study, we aimed to investigate the effects of nicotine on vascular smooth muscle cell proliferation and free cytoplasmic calcium level.
METHODS: Wistar male rats weighing 180-200g were used for animal experiments. Primary culture cells were obtained from aortic smooth muscle tissue of rats. The number of cells per milliliter was determined by manually counting the cells obtained on thoma counting chamber. The cultivation was homogeneously made into ninety-six culture vessels in equal numbers. After twenty four hours incubation, the cells were treated with 10 µM, 100 µM ve 1000 µM nicotine. At the end of 24 h of incubation period, cell proliferation and viability were assessed spectrophotometrically by 3-[4,5-dimethythiazolyl-2]-2,5-diphenyltetrazolium bromide. Intracellular calcium levels were measured by micro spectrofluorimetric method. The cells were plated on 24 mm diameter coverslips before measurement and treated for 1 h with the calcium indicator Fura-2 AM. The 10 µM, 100 µM nicotine and solution of high concentration KCl was acutely applied to the cells during measurement. All data were analyzed with SPSS using paired t-test and ANOVA methods.
RESULTS: The 10 µM nicotine concentration did not change cell proliferation. The 100 µM and 1000 µM concentration of nicotine raised cell proliferation significantly (p<0.05). In addition, 10 µM and 100 µM nicotine administration significantly increased intracellular calcium when compared to the controls (p<0.001).
CONCLUSIONS: It may be suggested that administration of nicotine results in increased healthy VSMC proliferation and is associated with increased intracellular calcium.

PC006

Effects of L-NAME, DEXA and L-NAME+DEXA on Systemic Blood Pressure of Spontaneous Hypertensive Pregnant and Non-Pregnant Wistar Albino Rats

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AIM: Chronic L-NAME does not always cause a sustainable NO-inhibition, but addition of dexamethasone (DEXA) strengthens its effect, and in hypertensive subjects, endothelium-derived relaxant substances-NO-releasing response to stimuli is decreased. This study aimed to determine effects of L-NAME, DEXA and L-NAME+DEXA on systemic blood pressure of spontaneous hypertensive Wistar albino rats.

METHODS: Approximately 3-moths old 62 rats were used in two simultaneous experiments. Sperm positive (n=33) and negative (n=29) animals were each divided randomly into 4 groups. Blood pressures were recorded at 15-day of pregnancy/experiment by non-invasive method, then animals were given physiologic saline (Control), L-NAME (150mg/kg/day), DEXA (100µg/kgBW/day) or L-NAME+DEXA (150mg and 100µg per kg BW/day) for consequent 5 days. At 19 day of pregnancy, blood pressures were measured again before applications. 24-h urines were collected in individual metabolic cages. Body weights, 24-h urine, urinary proteins, blood glucose and weights of some organs and fetuses were determined. Data were analyzed by ANOVA and ANOVA for repeated measures.
RESULTS: Compared to L-NAME, DEXA and L-NAME+DEXA caused remarkable decreases in body weights of animals (P=0.021 and P=0.012, respectively). In non-pregnant animals, only the weights of DEXA-given animals was significantly reduced when compared with controls (P=0.042). Systolic and diastolic blood pressures of the population varied between 145-170mmHg vs 118-135mmHg, respectively. Interventions influenced only the diastolic blood pressure of pregnant animals (P<0.043). The difference between DEXA and L-NAME+DEXA was significant (P=0.044). Other variables were not affected by interventions in both experiments.
CONCLUSIONS: Animals used in this study showed resistance against both L-NAME and DEXA in regarding hypertension.

PC007

Effects of Phenoxybenzamine after Hypothermic and Normothermic Ischemia Injury in Rat Aorta

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AIM: Paraplegia can develop due to spinal cord ischemia during thoracoabdominal aortic surgery. In this study, effects of phenoxybenzamine on spinal cord blood flow wereinvestigated by dilatation of aorta after *in vitro* rat aorta ischemia.
METHODS: In this study we used 48 Wistar albino rats in 4 groups (n=12): Control- phenoxybenzamine group, ischemic normothermia-hypothermia group, ischemic normothermia-hypothermic phenoxybenzamine (treatment) group, after phenoxybenzamine ischemic normothermia-hypothermia (prophylaxis) group. Organ bath temperature was reduced to 32°C, H2O2 10^{-8}-10^{-4}M was cumulatively administered in 20 min and ischemia was made in Group 2-3-4. After 10 min following last dose, temperature was raised to 37°C again and phenylephrine (PE 10-6M) was applied. Phenoxybenzamine (10mg/ml) 10^{-10}-10^{-4}M was given cumulatively in Group 1-3. 10 minafter phenoxybenzamine's last dose PE (10^{-6}M) was administered. Phenoxybenzamine (10^{-6}M) was given after spontaneous contractions in Group 4. PE was administered 10 min later and contractions were recorded. When contractions were stable, temperature was reduced to 32°C within 20 min, H2O2 was added cumulatively and ischemia was made. Then temperature was raised to 37°C, second dose PE (10^{-6}M) was given.
RESULTS: After phenoxybenzamine, first PE contractions were inhibited increasingly in Group 1. After ischemic hypotermia, H2O2 (10^{-4},10^{-5},10^{-6}M) revealed significant inhibition of spontaneous contraction in Group 2 ($p<0.05$). Inhibition of first PE contractions continued after ischemia hypotermia with phenoxybenzamine. There was no significant contractions according to last PE dose in Group 3. After phenoxybenzamine application, we found significant contractions both in the first PE and second PE doses following ischemic hypothermia in Group 4 ($p<0.05$).
CONCLUSIONS: Increasing blood flow mediated hypothermia and phenoxybenzamine vasodilation may prevent ischemia injury in rat aorta. Therefore, this method can be considered as an alternative treatment for the prevention of spinal cord ischemia during thoracoabdominal aortic surgery.

PC008

The Effects of Increasing Load During Exercise on Heart Rate Recovery and the Position Change Maneuver During Rest on QT Dispersion

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AIM: Heart Rate Recovery (HRR) is procured by deducting the heart rates at 1st, 2nd, and 3rd min of recovery from the heart rate at maximal exercise. Subnormal values of HRR is found correlated to diseases like myocardial infarction and diabetes mellitus. The difference between the longest QT interval and the shortest QT interval on ECG is called QT dispersion. QT dispersion is the indicator of ventricular arrhythmia of heart. It is shown that the QT dispersion is correlated to increased cardiovascular morbidity and mortality in ischemic heart disease, dilated and hypertrophic cardiomyopathy, and hypertension. Our study aims to research into the effects of gradually increased load on HRR time and how movements depending on position affect the QT dispersion in healthy individuals.
METHODS: In our study, healthy male individuals (n=20, 19.9±2.1 years old, 75.1±9 kg) were practiced on treadmill a)free effort, b)10 and c)20kg loaded effort tests at different times, and by deducting the 1st, 2nd, 3rd minutes from maximum reached heart rates of each; indexes of HRR were found. How movements depending on position affects ((a)lying right, b)lying left, c)lying back, d)sitting, e)upright positions) the QT dispersion of healthy individuals was calculated based on Bazett's formula by measuring the QT intervals of ECG recordings. Tukey test was used as the statically method.
RESULTS: Practicing effort tests by gradually increasing loads in healthy adult individuals showed that the raise of load did not change the HRR (1st min. HRR; i=25.59±7.60, ii=25.27±6.15, iii=26.09±10.19 beats/min.). Since the research findings of movements depending on position of healthy adult individuals did not cause any significant difference on QT dispersion (a=39,91±4,60, b=41,70±5,19, c=41,17±4,92, d=40,35±4,44, e=42,70±4,20). At the same time, there is no difference seen at the P dispersions that are the indicator of atrial arrhythmia.

CONCLUSIONS: Results of effort tests practiced by gradually increased loads to healthy individuals showedthat there is no correlation between increasing load and HRR. It is detected in our study that any of these movements depending on position did not cause any significant difference on QT dispersion; therefore it does not cause ventricular arrhythmias.

PC009

Probing the Mediation of Central Cyclooxygenase and Lipoxygenase Pathways in Cardiovascular Responses Following Central Injection of Orexin A

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AIM: Central administration of Orexin A (OA), a neuropeptide in hypothalamus, is known to induce pressor response not only through its self-receptors, but also through central histaminergic and cholinergic systems. Experiment performed in our laboratory demonstrated that arachidonic acid and its metabolites induced cardiovascular responses which were identical to those generated by OA. Based on this comparability, the fundamental purpose of the experiment was to demonstrate the mediation of central cyclooxygenase (COX) reaction products like prostaglandin (PG) E,D and F2a lipoxygenase (LOX) pathways in OA-induced cardiovascular responses.
METHODS: 85 Male Sprague-Dawley rats were used in the experiment. Initially, the cardiovascular responses were investigated by administrating different doses of OA given intracerebroventricularly. Then, to demonstrate the mediation of COX, PGE, PGD, PGF2a and LOX pathways in OA-induced cardiovascular reponses, pretreatments with non-selective COX inhibitor ibuprofen, PGE and PGD receptorantagonist AH6809, PGF2a receptor antagonist PGF2a dimethylamine (PGF2aDMA) and non-selective LOX inhibitor NDGA were performed on separate groups and cardiovascular parametres were recorded upto 60 min following OA administration.The data obtained from 5 animals were provided as average ±standard error. To perform statistical evaluation, posthoc Benforoni test of RM-ANOVA was employed. $p<0.05$ was considered to be statistically significant. Groups were as follows (n=5/group): 0.9% Saline; Orexin (0.75, 1.5, 3nmol); 30% DMSO; Saline+ Saline; Saline+ Orexin; DMSO+ Saline; DMSO+ Orexin; Ibuprofen+ Saline; Ibuprofen+ Orexin; NDGA+ Saline; NDGA+ Orexin; AH6809+ Saline; AH6809+ Orexin; PGF2aDMA+ Saline; PGF2aDMA+ Orexin.
RESULTS: Centrally injected OA elicited a rise in blood pressure and heart rate. Pretreatment with ibuprofen blocked OA-induced cardiovascular responses while, AH6809, PGF2aDMA and NDGA pretreatments inhibited OA-inducedcardiovascular responses partially.
CONCLUSIONS: The present findings show pressor and tachycardiac cardiovascular responses of OA and complete mediation of COX pathway and partial mediation of PGE, PGD, PGF2a and LOX pathways in these responses. This study was supported by TÜBİTAK (214O728) grant.

PC010

Atherogenic Indices and Lipid Profile in Acute Ischemic Stroke Patients

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AIM: Stroke is one of the important cerebrovascular diseases lead to morbidity and mortality. Free radicals produced in ischemic stroke may affect lipid and lipoproteins via oxidative damage, and lead to deterioration of cerebral blood flow. Increasing of plasma low-density lipoprotein cholesterol is an important risk for cardiovascular system. Recent studies suggest that atherogenic indices are also associated with vascular damages. The study was carried out to investigate the values of atherogenic indices and lipidprofile in patients with acute ischemic stroke.
METHODS: This study were performed on 51 acute ischemic stroke patients and 49 healthy controls. Mean age of the patients was 68.37±12.72 andof controls was 65.04±10.79 years. The values of systolic and diastolic blood pressure, and lipid profile such as triglyserid (TG), total cholesterol (CHOL), high density lipoprotein-cholesterol (HDL-C), low density lipoprotein-cholesterol (LDL-C), and rates of the TG/HDL-C and TCHOL/HDL-C were determined in all samples. Data were analysed by SPSSsoftware program.
RESULTS: The values TG ($p=0.049$), CHOL ($p=0.023$), LDL ($p=0.050$), atherogenic indices such as TG/HDL-C ($p=0.004$) ve TCHOL/HDL-C ($p=0.004$) were in creased in patient with acute ischemic stroke, but HDL ($p=0.042$) levels was significantly decreased in these patients. On the other hand, there were not differences ($p>0.05$) between the values of the blood pressure in patients and control groups.
CONCLUSIONS: The levels of HDL were significantly decreased while the values of CHOL, LDL, TG, TG/HDL-C and TCHOL/HDL-C were increased in the patients with acute ischemic stroke. Based upon these results, the decreasing of HDL and the increasing of CHOL, LDL, TG, and atherogenic indices (TG/HDL-C and TCHOL/HDL-C) may be important risk factors for atherothrombotic cerebrovascular diseases such as ischemic stroke. However, further studies are necessary in order to evaluate the atherogenic index in ischemic stroke patients.

PC011

Investigation of the Effect of Nifedipine on Heart Glutathione Reductase Enzyme of Ischemia/Reperfusion Injured Rat

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AIM: The purpose of this study was to investigate the effect of nifedipine drug on rat heart tissue glutathione reductase (GR) enzyme in ischemia/reperfusion (I/R) and I/R injured rats.

METHODS: Control, sham, I/R and nifedipine + I/R are as follows: A total of 30 male Wistar albino rats weighing 250-300 g were equally and randomly divided into four groups. In the last group, nifedipine was administered at the 4 mg/kg dose before intraperitoneal ischemia period. Heart tissues were removed after bilateral I/R process. Tissue levels of enzyme activity of glutathione reductase (GR) were measured. Enzymatic activity was measured by using Beutler's method by using a spectrophotometer. The assay system contained 100 mM Tris-HCl buffer pH 8.0, including 0.5 mM EDTA, 3.3 mM GSSG and 0.1 mM NADPH.
RESULTS: Specific activity values were determined for GR enzyme at four different experimental groups. Groups were determined as follows: Control group 0.187 ± 0.006 EU/mg protein, sham group 0.162 ± 0.004 EU/mg protein, I/R group 0.220 ± 0.008 EU/mg protein, and nifedipine + I/R group 0.160 ± 0.005 EU/mg protein. ($p \leq 0.05$).
CONCLUSION: As a result, the activity of the GR enzyme was determined to be mostly inhibited in nifedipine + I/R group among all applications.

PC012

The Effect of Exenatide Treatment on Myocardial Alterations in a Rat Polycystic Ovary Syndrome Model

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AIM: Metabolic characteristics of polycystic ovarium syndrome (PCOS) are composed of insulin resistance, obesity, type II diabetes and lipid anomalies. Especially insulin resistance is an important risk in tendency to cardiovascular diseases. Exenatide (Exe-4) is a natural GLP-1 agonist and it contributes to decrease insulin resistance. The current study was designed to evaluate the effect of PCOS on myocardial tissue and therapeutic effect of Exe-4 on PCOS-related myocardial damage.
METHODS: Rats were assigned into four groups as control, solution, PCOS and PCOS+Exe-4. For PCOS model, DHEA (6mg/100g) in 0.2 ml sesame oil was applied subcutaneously to 21-day Spraque-Dawley rats while 0.2ml sesameoil was applied subcutaneously to the rats in solution group. In PCOS group increase in weight and HOMA-IR, deficiency in eustrus cycles and cystic structures were observed. During the following four weeks, Exe-4 was applied intraperitoneally (10µg/kg/day) to the rats representing insulin resistance. Assessment of cardiac injury was performed using the following criteria; cardiomyocytes with eosinophilic cytoplasm and pyknotic nuclei, cytoplasmic vacuolization, and disorganization of cardiomyocytes.The histological changes and caspase-3 immunoreactivity were graded according to the extent of the lesion from 0 to 3.
RESULTS: In the histological examination, disorganization of cardiomyocyte and intracytoplasmic vacuolization were observed in PCOS group. Moreover eosinophilic cells with pyknotic and heterochromatic nucleus among normal myocardial fibers were also observed. Although administration of Exe-4 restored the myocardial structures, the lesions did not completely alleviated. There was no statistically significant difference between PCOS group and PCOS+Exe-4 in terms of histological alterations($p>0.05$). Immunohistochemical analysis showed that PCOS significantly($p<0.005$) increased the expression of caspase-3 protein expression in the myocardium when compared to control group. By the treatment of Exe-4, the expression of caspase-3 protein didn't change statistically when Exe-4 group was compared with PCOS group ($p>0.05$). treatment partially ameliorated PCOS induced myocardial damage.

PC013

Effect of Salusin-α and Salusin-β on Heart Damage Following the Renal Ischemia/Reperfusion

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AIM: The ischemia-reperfusion (I/R) damage is known as the damage as a result of the re-oxygenation of the hypoxic organ. Together with the local tissue damage, it may cause the damage of the organ at distant. Acute kidney injury (AKI) is associated with high mortality resulting from extra-renal organ damage, particularly the heart. In this study, we investigated whether salusin-α and salusin-β which have been found in the kidney, heart tissues and demonstrated to have protective against cardiac I/R damage features have protective effect of salusin-α and salusin-β against remote cardiac and damage induced by renal I/R.
METHODS: Sprague-Dawley rats were divided into six groups (control group and 5 I/R groups (1 h ischemia followed by 23 h reperfusion). The treatment groups were subcutaneously administered 1 and 10 µg/kg salusin-α and, 1 and 10 µg/kg salusin-β at the beginning of ischemia. At the end of the study, heart tissue samples were taken from rats. The heart samples were processed by routine tissue techniques and embedded in paraffin. 5µm thick sections of tissues were cut, mounted on slides, stained with Hematoxylin-Eosin (H-E) and examined under a Leica DFC280 lıght microscope by Leica Qwin and Image Analysis System.
RESULTS: In control group, heart tissue showed normal histological appearance. In I/R group, we detected some histological changes. These histopathological changes are eosinophilic cytoplasm and pyknotic nuclei cells, mononuclear cell infiltration, intracytoplasmic vacuolisation, vascular congestion, necrosis and hemorrhage. These histological changes significantly decreased in I/R+salusin-α 1 µg/kg, I/R+salusin-α 10 µg/kg, I/R+salusin-β 1 µg/kg, I/R+salusin-β 10 µg/kg groups, especially salusin-β groups.
CONCLUSION: It is concluded that salusin-α and salusin-β exerted protective effects on renal IR-induced heart injury as a remote organ.

PC014

Protective Effect of Alpha-Lipoic Acid on Methotrexate-induced Cardiac Injury

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AIM: Methotrexate (MTX) is used as a cytotoxic agent in the treatment of a variety malignancies and autoimmune diseases.Unfortunately, the curative potential of MTX is accompanied by multi-organ toxicity.However, the mechanisms of MTX-induced toxicity have not been completely determined. Alpha-lipoic acid (ALA) is a powerful antioxidant that protects tissues against oxidative damage and inflammation.This study was designed to investigate protective effect of ALA on cardiac damage induced by MTX.
METHODS: In this study, Wistar albino female rats, aged 10-12 weeks and weighing 200-300 gwere divided into 4 groups; control ALA, MTX, MTX+ALA. ALA (50mg/kg) was performed intraperitoneally daily during the experimental period (24 days). MTX (20mg/kg) was given intraperitoneally as a single dose on day 21. At the end of the experiment, myocardial tissue was evaluated for histological changes and in terms of caspase-3 immunoreactivity. MDA levels were also measured.
RESULTS: Control group showed a normal histological appearance.In MTX group, we observed intensive eosinophilic cytoplasm-pyknotic nuclei with cardiomyocytes and disorganization of cardiomyocytes.The damage score in the MTX group was statistically higher than control group (P<0.05).Although, the myocardial injury was markedly reduced in MTX+ALA group, histological alterations were still present in some areas.In the immunohistochemical evaluation, the control group showed slight expression of caspase-3.On the other hand, caspase-3 expression was significantly increased in MTX group in comparisonto control group (P<0.05).ALA administration significantly reduced the expression of caspase-3 (P<0.05).Malondialdehyde (MDA) was found to be increased in MTX group compared to the control group.However, this increase was not statistically significant.ALA administration did notaffect MDA level.
CONCLUSIONS: While giving ALA decreases the cardiac tissue damage histologically caused by MTX, it didn't change oxidative stress.Findings of the study give rise to the thought that protective effects of ALA on myocardial tissue take place over a different mechanism rather than antioxidant mechanism.

PC015

Novel *in vivo* Angiogenesis Model:"Pecten Oculi"

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AIM: Pecten oculi, located in bulbus oculi of birds, is a vascular sac formed by vessel folds. In this study, we aimed to investigate availability of pecten oculi as an *invivo* angiogenesis model.
METHODS: Development of pecten oculi in fertilized chicken eggs begins at 5th-day and completed in 17-18th-days. Therefore,agents which their effects on angiogenesis proven previously, were injected into albumen on 6th-day of development. Previously proven effects of agents were investigated in development of sac, its availability as *invivo* model was evaluated.Na-nitrit (0.5ml 80mM stocksolution), nitroglycerin (6mg/0.5ml), adenosine (2.5mg/0.5ml), ethanol (0.5ml-98%) were used as (+)angiogenic agents. Heparin (1500IU/0.5 ml), Heparin+corticosteroid combination (2500IU/0.5 ml+5 mg/0.5 ml) and vitamin-D3 (1666IU/0.5ml) as (-)angiogenic agents. No agent was injected into control group. 8 fertilized eggs were used in each group. Sacrification was done on 19th-day. Pecten was examined histologically. Angiogenesis was evaluated according to pecten development, vessel diameter, vascular index and basalmembrane thickness.
RESULTS: In terms of embryo development, pecten oculi presence, number of folds, vessel diameters, vascular index, basalmembrane thickness and pigmentation; well-developed embryos, similar number of folds were noticed in (+)angiogenic groups compared to control. Vascular index, basal membrane thickness, vessel diameters and pigmentation was higher (p<0.05). No embryo development was seen in heparin+corticosteroids group. Compared to control, underdeveloped embryos were observed in low-dose-heparin and vitamin-D3 groups. Number of folds, pigmentation, vessel size and number were low (p<0.05).
CONCLUSIONS: Although sample size is low, our data suggests pecten may be useful as an *invivo* angiogenesis model. Since pecten is only composed of vessels; development, maturation and diameters of vessels, thickness of basal membrane, vascular surface index are assessable factors. Compared to CAM-model, application is easier. Since given agents are metabolized by embryo, we believe that our findings are more significant and pecten is a useful anatomical structure for angiogenesis studies.

PC016

The Effect of Long Term and Acute Administration of Genistein on Ischemia-reperfusion-induced Arrhythmia

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AIM: Genistein is a phytoestrogen that has been used to decrease symptoms of menapose in estrogen replacement therapy in women. The resistance against the cardiovascular disease and the sudden death due to coronary artery occlusion increases in women after menapose. In this study, we investigated effects of genistein on the ischemia-reperfusion-induced arrhythmia in rats.
METHODS: 64 Female, 12 male rats (6-7 months old) were used in this study. In one group, genistein were intraperitoneally given in 100ug/kg dose daily for 4 weeks. In another group, 1mg/kg dose genistein were given intravenously just before reperfusion. Six minof myocardial ischemia was produced by ligation of left coronary artery (LAD) and reperfusion by releasing of this artery. The type and duration of arrhythmia and blood pressure were analysed by using one way ANOVA. All operations on the animals were approved by the Abant İzzet Baysal University Animal Research Ethical Committee (protocol number: 2012/49, 2014/30).
RESULTS: Reperfusion- induced arrhythmias decreased in overiectomised group that genistein was administered just before reperfusion in respect to sham and overiectomised groups (P<0,05). Long

term genistein administration was not effective on the ischemia or reperfusion induced arrhythmia. The blood pressure and heart rate did not significantly change when genistein administered in the long term or just before reperfusion.
CONCLUSIONS: Lesser ventricular arrhythmia observed during reperfusion in overiectomised rats that genistein administered just before reperfusion in respect to sham or only overiectomised animals shows that this effect might be depend on preconditioning of early surgical operation but not on genistein.
This study was supported by Abant İzzet Baysal University Research Fund.

PC017

Inhibition of AMPK by Doxorubicin Exacerbates Cardiomyocytes Death: Role of TLR4

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AIM: Doxorubicin (DOX) is an anticancer drug widely used for cancer treatment, but has toxic effects on many tissue including the heart. DOX may exacerbate the defect of energy production by decreasing mitochondrial energy production, blocking the AMP-activated kinase and trigger apoptosis known as programmed cell death pathway. AMPK hasbeen associatedbetween cell's survival and death pathways. DOX inhibits AMPK. However, the mechanism of AMPK by DOXis not completely understood. The aim of the study was to investigate whether inhibition of AMPK in heart failure-induced by DOX is through TLR4 and/or mTOR or not. METHODS: 5 groups were: control, DOX, DOX+TLR4 (Resatorvid, DT), DOX +mTOR (Rapamicin, DR), and DOX+mTOR+TLR4 (DRT) by using H9c2 cell line. At different time points, western blot and qRT-PCR were performed to identify the protein and gene expressions related to apoptosis. Using the same time points, apoptosis was determined by using TUNEL and FITC-IETD-FMK methods. One-way-ANOVA was used for evaluating statistical analysis.RESULTS: TLR4 protein expression was decreased in DOX group, but high at DR and DT groups. AMPK and PAMPK protein expressions were decreased, AMPK elevated at DR. PAMPK was high at DR, DT and DRT groups. The protein expression of cytochrom-c increased at DOX group, but decreased at DR, DT and DRT groups. The number of TUNEL positive and active caspase 8 cells at DOX group was higher than control. However, the number of TUNEL positive and active caspase-8 cells at DR, DT, DRT was lower vs DOX group.
CONCLUSIONS: AMPK inhibition through TLR4 receptor, resulting from energy deficiency via MAPK at heart failure-induced by DOX plays an important role for triggering apoptosis. HMGB1 plays an important role as amplifying DOX toxicity in the heart by TLR4 via MAPK signal transduction.This study was financially supported by TUBITAK (114S118).

PC018

Evaluation of Blood Flow Heterogeneity During Reperfusion by Using Laser Speckle Imaging technique

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AIM: Reperfusion process following ischemia leads to impairment of local microvascular control mechanisms. Impaired control mechanisms leads to perfusion heterogeneity. Previous studies related to perfusion heterogeneity using Laser Speckle Imaging (LSI) technique has only been experimentally performed on kidney. We investigated the link between prolonged period of ischemia and reperfusion heterogeneity by using LSI technique in human skin microcirculation.
METHODS: Healthy men and women volunteers were included (n=11). Ischemic processes were performed with pressure cuff connected to the right arm. Ischemia was confirmed with the pulse transducer simultaneously connected to finger. Thirty-45 and 60 seconds ischemic episodes were performed in groups. One-minute reperfusion period was provided following each ischemic period. All perfusion images from the outer-surface of the hand were recorded by using LSI device. Moreover, perfusion heterogeneity was determined with histogram analysis. All data were presented as mean±SD. All datawere analyzed using Student's t-test and ANOVA. $P<0.05$ was considered to be statistically significant.
RESULTS: Baseline perfusion value was found to be as 355.2±30.1 PU. While pulse is not received in the process of ischemia, perfusion values were measured as 28.7±1.7 PU ($p<0.001$). The maximum perfusion values after 30-45-60 seconds ischemic episodes were measured respectively as 408.3 ± 60.5 ($p>0.05$), 422.2±60.8 ($p<0.05$) and 479.2±86.0 PU ($p>0.05$). However, when compared to baseline, the percentage changes of maximum perfusion after ischemia were found to be as 61.8±17.3, 21.8±8.5 ($p<0.05$; compared to 30s ischemic group) and 20.8±7.4 ($p<0.05$; compared to 30s ischemic group). At the end of one min of reperfusion, percentages of changes were significantly difference found as 41.8±12.1, 8.9±6.4 in 30 and 45-second ischemic episodes ($p<0.05$). In addition, a normal distribution histogram at the baseline was found around 1,000 perfusion unit, while an asymmetric histogram distribution around 700 PU, shifted to left was measured in one minutes of reperfusion.
CONCLUSIONS: Prolonged ischemic period leads to decrease in reactive hyperemia response and results to perfusion heterogeneity.

PC019

The Effects of Ghrelin and Orexin Antagonists in LPS-induced Sepsis Model

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AIM: Sepsis is a generalized inflammatory response, which involves organ systems remote from the locus of the initial infectious insult,

involves the release of cytokines and the subsequent formation of reactive oxygen and nitrogen species. In recent years, there is increasing evidence implicating that appetite-regulating peptides have anti-inflammatory effects. We aimed to investigate the roles of ghrelin and orexin in LPS induced endotoxemia by using antagonists of these peptides. METHODS: Sprague Dawley rats (male=female) (250-300g; n=8/group) were randomly divided into 4 groups: (1) Control group was treated with saline for 4 days; (2) Endotoxemia (E) group was treated with saline for 3 days and on 4th day was injected with LPS (E. coli serotype 0111:B4; in saline; 10 mg/kg ip); (4) E + ghrelin antagonist group was treated with D-Lys3-GHRP-6 (6 mg/kg ip) for 3 days and on 4th day was injected with LPS; (5) E + orexin antagonist group was treated with almorexant (30 mg/kg ip) for 3 days and on the 4th day was injected with LPS. All rats were decapitated 6 h after LPS injection and their duodenum, stomach, liver and colon samples were collected. Tissue samples were analyzed for myeloperoxidase (MPO) activity as the indicator of neutrophil infiltration. Student's t test was used for statistical analysis. RESULTS: LPS injection increased MPO activity in all tissues ($p<0.05$-0.01). While MPO activitiesin duodenum, stomach and colon tissues were decreased with ghrelin antagonist, MPO levels increased in kidney and liver tissues compared with endotoxemia group. Besides, orexin antagonist caused decreases in MPO activity in duodenum and increases in colon and kidney tissues ($p<0.05$).
CONCLUSIONS: The results of our research give rise to the thought that ghrelin and orexin may have different effects on LPS-induced sepsis. Further experiments are needed about the effects of these peptides in different inflammatory conditions.

PC020

The Importance of Acetylcholine Esteraseand Nitric Oxide Changes in Monosodium Glutamate (MSG)-induced Oxidative Damage: The Role of Melatonin

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AIM: In this study, the effects of monosodium glutamate (MSCG)-induced oxidative damage on liver and erythrocytes and related changes in acetylcholine esterase and nitric oxide (NO) levels, and also in hematological parameters and possible role of melatonin as protective were investigated.
METHODS: Sixty Wistar albino rats were used (male, 4-5 months old) in the experiments. One ml saline to control group rats, 4 mg/kg ve 8 mg/kg monosodium glutamate to MSG group rats were administered by gavage for 21 days. The other three MLT group rats received 10 mg/kg melatonin by ip, one day before MSG feeding, during the same period. Hematological parameters in blood samples (erythrocyte count, % hematocrit, hemoglobin, MCV, MCH and MCHC values) by automated analyzer, liver and erythrocyte acetylcholine esterase (AChE)levels and plasma and liver malondialdehyde (MDA) and NO amounts were measured by ELISA method.Comparisons between groups were performed by using one-way ANOVA.
RESULTS: Erythrocyte count, hemoglobin amount and MCHC values were decreased, but MCV values were increased in MSG administrated rats. There was no significant difference in % hematocrit and MCH values.When compared with control group values, plasma and liver MDA and NO amounts were found to be significantly higher, whereas erythrocyte and liver AChE levels have decreased in MSG toxicity groups ($p<0.05$). However, in MSG+MLT groups, melatonin treatment partially suppressed all these changes.
CONCLUSIONS: Consequently, MSG causes oxidative damage in liver and erythrocytes and also leads to a decrease in the levels of acetylcholinesterase enzyme and increase in nitric oxide levels. These changes may negatively affect erythrocyte function and microcirculation This means that the oxygen demand of the tissues cannot be efficiently provided. However, melatonin, as an antioxidant, partly prevents these negative changes.This work was supported by Erciyes University Research Fund (Project # TYL-2013-4825).

PC021

Effect of Thymoquinone Administration on Erythrocyte Fragility in Diethylnitorsamine Administered Rats

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AIM: Diethylnitrosamine is used as preservative in foods but found to exert carcinogenic effects. *Nigella sativa* plant has anti-tumoral, anti-inflammatory and antidiabetic activity. Aim of this study wa to investigate the effect of thymoquinone which is one of the active ingredients of *Nigella sativa* on erythrocyte fragility in diethylnitrosamne administered rats.
METHODS: 28 male Wistar-albino rats were divided into four groups; Control group (Saline/5 days, i.p.), thymoquinone group (4 mg/kg/5 days/p.o.), diethylnitrosamine group (SF/5 days /i.p. and diethylnitrosamine 200 mg/kg/i.p. for two consecutive days) and diethylnitrosamine + thymoquinone group (4 mg/kg/5 days thymoquinone p.o. and diethylnitrosamine 200 mg/kg/i.p. for two consecutive days). Erythrocyte fragility, hemoglobin and hematocrit counts were performed. Kruskal-Wallis and Tukey tests were performed for statistical analysis.
RESULTS: Number of erythrocytes was increased in diethylnitrosamine administered groups significantly compared with other groups ($p<0.05$). Hematocrit value was found to be higher in dietilnitrosamine group compared to control and thymoquinone groups ($p<0.05$). Hemoglobin value was found to be higher in dietilnitrosamine administered groups than groups without diethylnitrosamine administration ($p<0.05$). No significant change in erythrocyte fragility was observed.
CONCLUSIONS: Augmentation in erythrocyte, hemoglobin and hematocrit count due to diethylnitrosamine administration and an opposite impact of thymoquinone administration were observed.

PC022

Evaluation of the Prevalence of Thyroid Autoantibodies in Patients with Alopecia Areata

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AIM: Alopecia Areata (AA) is a disease characterized by hair loss from the body. Although some factors such as genetic, atopy, otoimmunity, endocrine dysfunctions, stress, and infections play role in pathogenesis of AA, the etiology of AA is not fully understood. Prevelance of thyroid dysfunctions and autoantibody positivity are more common compared to general population. We aimed to investigate the prevelance of thyroid dysfunctions and autoantibody positivity among the AA patients.
METHODS: AA patients who presented our dermatology clinic between January 2009 and August 2015 were reviewed. The patients who had thyroid function tests (TSH, FT3, FT4) and thyroid autoantibodies (anti-TG, anti-TPO) were enrolled in the study. Pregnant patients and the patients who had not these tests results were excluded from the study.
RESULTS: 448 AA patients were detected during the period. Among these patients, 195 patients had TSH, 153 patients had FT4, 132 patients had FT3, 81 patients had anti-TG, and 130 patients had anti-TPO test results. The thyroid function and autoantibody test result revealed that the prevalence of FT4, FT3 deficiency and anti-TG, anti-TPO positivity were 8.5%, 1.5%, 14.8%, 18.5%, respectively.
CONCLUSIONS: Thyroid dysfunctions and autoantibody positivity may occur concurrently with AA. The thyroid function tests and autoantibody levels should be followed-up in AA patients.

PC023

The Levels of CD35, CD46 on Peripheral Leukocyte and Erytrocyte in Turkish Population: The Sample of Antalya Education and Research Hospital

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AIM: The complement system and complement regulatory proteins (CRP) play important roles in the physiopathology of many diseases. CD35 (complement receptor 1,CR1) and CD46 (membrane cofactor protein, MCP) are CRPs that are related to diseases. Many studies reported infections, thrombosis, and autoimmune diseases developing due to genetic variations of these proteins. In this study, we aimed to measure the expression levels of CD35 and CD46, on peripheral leucocytes and erythrocytes in healthy Turkish population.
METHODS: The study included in 20 healthy volunteers whose ages ranged from 20 to 40 years. Blood samples were analysed by flow cytometry by using CD35 (PE Mouse Anti-Human), CD46 (FITC Mouse Anti-Human) antibodies. The data were evaluated by IBM SPSS Statistics 20 (SPSS/IBM, Chicago,IL,USA).
RESULTS: CD35 level was found to be 92% on neutrophils, 84% on monocytes, 34% on erythrocytes and 17% on lymphocytes. CD35 levels were significantly lower on erythrocytes and lymphocytes, compared to monocytes and neutrophils ($p<0.05$). The CD46 level was detected approximately 99% on lymphocytes, monocytes and neutrophils whereas no expression was detected on erythrocytes. CD46 levels of erythrocytes were significantly lower compared to lymphocytes, monocytes, and neutrophils ($p<0.05$).
CONCLUSIONS: Reason of genetic variations, CRP levels of special to the population should be kept in mind in CRP-related diseases such as infection, cancer, autoimmune diseases and Alzheimer's Disease. We think large scale studies in Turkish population are essential to investigate CRP and diseases relationship.

PC024

Protective Effect of Polydatin on Spleen Ischemia-reperfusion Injury in Rats

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AIM: Polydatin (3,4',5-trihydroxystibene-3-β-mono-D-glucoside), isolated from the Polygonum cuspidatum, is widely used in traditional Chinese medicine (1). Polydatin is a compound with antioxidant and anti-inflammatory effects. The aim of this study was to investigate whether there is a protective effect of polydatin in spleen ischemia-reperfusion injury.
METHODS: Fifty adult male Sprague-Dawley rats (250-300gr) were randomly divided into 5 groups as: control, sham, ischemia (I), ischemia/reperfusion (I/R), and polydatin+I/R. Polydatin was administered intraperitoneally 1 h before I/R. Splenic artery and vein were ligated. 30 min of ischemia and 60 min of reperfusion was performed. The spleen was excised. MDA, SOD, CAT as biochemical parameters; caspase-3 for apotosis and proliferating cell nuclear antigen (PCNA) for cell proliferation as immunohistochemical parameters were determined. Descriptive statistics, normality test, Kruskal-Wallis, one-way ANOVA and post hoc Tukey tests wereused. $P<0.05$ was considered statistically significant.

RESULTS: Caspase-3 level showed a significant decrease in polydatin + I/R group compared to I/R group. PCNA levelshowed a significant inrease in polydatin + I/R group compared to I/R group. Tissue MDA level showed a significant increase in polydatin + I/R group compared to I/R group. CAT level showed a significant increase in polydatin + I/R group compared to I/R group. SOD level showed a significant increase in polydatin + I/R group compared to control group.
CONCLUSIONS: Our results indicate that 20 mg/kg dose of polydatin can prevent I/R-induced spleen injury.

PC025

Mean Platelet Volume and Platelet Distributed Width Levels in ABO Blood Groups

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AIM: Although there are many researches to indicate the relationship between ABO blood groups and atherosclerosis and thrombosis, there is no data explaining these relations precisely. Most of previous studies have shown the lower risk of O blood group than others in terms of the severity of atherosclerosis and acute thrombotic events. We aim to investigate if there are differences in platelet counts (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) among ABO blood groups.
METHODS: We prospectively recruited 301 healthy subjects (99 women and 202 men, mean age; 33±8 years) who were followed up in the Internal Medicine and Cardiology Outpatient Clinic, Harran University and Yüzüncü Yıl University Medical Faculty because of dyspeptic complaints and atypical chest pain. Previously, subjects with known blood groups were included in the study. The PLT, MPV, PDW and PCT values of all subjects were evaluated by complete blood counts. All statistical analyses were performed using IBM SPSS 20.0 (Chicago, USA).
RESULTS: There were no statistically significant differences between the ABO blood groups with regard to age, gender and Rh factor ($p>0.05$). MPV levels were found to be significantly lower in the O and A blood group subjects than B and AB blood group subjects ($p<0.05$). Similarly PDW levels were found to be significantly lower in the O and A blood group subjects than B blood group subjects ($p<0.05$). In terms of hematological parameters, there were no any significant difference between Rh+ and Rh- factors.
CONCLUSIONS: These findings speculate that the lower MPV levels in O and A groups and lower PDW levels in O group may be protective factors against acute thrombosis and atherosclerosis. However, further prospective studies with larger number of participants are needed to gain a better understanding of ABO blood groups' effect on platelet functions.

PC026

The Effect of Gonadectomy, Exercise and Borax Application on Serum Immunoglobulin Levels Among Male and Female Rats

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AIM: We investigated the effects of gonadectomy, exercise among rats and borax added to their normal diet on immunoglobulin levels.
METHODS: Eight-week-old Wistar albino rats (64 males, 60 females) were used in the experiments. Male and female rats were randomly divided into 16 groups. 62 of the rats were applied with gonadectomy, 62 of them were applied with sham- gonadectomy. Borax in the amount of 0.7gr/L was added into drinking waters of the groups to be applied with borax for a month. The exercise groups were exercised in forced swimming exercise for a month. Intracardiac blood samples were taken from all groups before sacrification. The serum was separated, and IgG, IGM, IGA levels were evaluated using the ELISA method.
RESULTS: IgG levels in the male gonadectomy-exercise group were higher than the levels in the gonadectomy, gonadectomy-borax and exercise groups. IgG levels in the gonadectomy-borax-exercise group were higher than the levels in the control group, similar to other groups. IgG levels in the female group fed with borax and applied with ovariectomy were higher than the levels in the group fed with borax and applied with ovariectomy. Similar IgM values were found in the male and female groups. IgA levels were higher in the gonadectomy-borax-exercise group than the control group among female groups.
CONCLUSIONS: Consequently gonadectomy, exercise, and borax, when applied alone, were not effective in immunoglobulin levels in both sexes among rats. It was seen that gonadectomy-exercise and gonadectomy-borax applications caused an increase in IgG levels. While IgA levels increased among female rats applied with all three applications, IgM levels did not change in both sexes. We suggest that borax preparations and exercise might make positive contributions to the immune system in case of gonadal hormone deficiency.

PC027

Comparison of Cytotoxic Activity of Some Flavonoids on K562 and HL60 Human Leukemia Cell Lines

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AIM: Flavonoids are natural plant compounds occuring widely in the human diet. It has been suggested that flavonoids have cytotoxic effects *in vitro* in the various types of cancer. Some epidemiolo-

gic studies have been reported the association between dietary flavonoid intake and reduced some cancer types. In our previous studies, we showed the cytotoxic effects of some flavonoid compounds on K562 leukemia cell line. The present study was designed to compare of cytotoxic effects of apigenin, luteolin and the recently synthesized 5-desmethyl sinensetin (6-hydroxyluteolin 6,7,3‘,4’-tetramethyl ether) on K562 and HL60 human myeloid leukemia cell lines.
METHODS: Cell proliferation was detected by MTT assay. K562 and HL60 cells were incubated with apigenin, luteolin, 5-desmethyl sinensetin (3-(4,5-dimethylthiazol-2-yl)-2,5-diphentyltetrazolium bromide) flavonoids, ranging from 50 to 200 μM concentrations for 72h.
RESULTS: IC50 values detected by MTT assay. The results indicated significant cytotoxic activities with apigenin IC50: 140 μM, luteolin IC50: 100 μM, 5- desmethyl sinensetin >200 μM concentration for the same incubation period, against K562 leukemia cells and IC50 values for HL60 apigenin IC50: 180 μM, luteolin IC50: 150 μM, 5-desmethyl sinensetin IC50>200 μM.
CONCLUSIONS: While apigenin and luteolin have significant cytotoxic effect on acute myeloid (HL60) and chronic myeloid (K562) leukemic cell lines, 5-desmethyl sinensetin does not. We concluded that apigenin and luteolin are more sensitive for cytotoxic activity on K562 cells than HL-60 cell lines, but 5-desmethyl sinensetin is not effective for these cancer types.

PC028

The Effects of Dental Bleaching Agent and *Crithmum Maritimum L.* on Dental Pulp Stem Cell (DPSC)

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AIM: Tooth bleaching agents contain peroxide are asserted to cause potential cellular damage. For that reason, our study aimed to find the effects of application of hydrogen peroxide on dental pulp stem cell (DPSC) cultures and whether CM has any protective effects against the potential damage to occur.
METHODS: Five study groups were performed, control (C) group, 2 Hydrogen Peroxide (2HP) (2 μg/ml), 6 Hydrogen Peroxide (6HP) (6 μg/ml), CM (2 μg/ml)+2HP, CM (2 μg/ml)+6HP groups. Reproduced DPSC in culture media and treated according to the assigned groups, the cells were removed from their media at 0, 24, 72 hours, and DNA damage was measured using comet assay method and TNF-alpha, IL-6, TOS, TAS levels were measured using ELISA method. Kruskal Wallis variance analysis was used for independent samples and Mann Whitney-U Test with Bonferroni correction was used for post hoc comparisons.
RESULTS: Tail intensity was observed significantly increase in groups treated with only HP compared to the control group (p=0.000). Measurements performed at 24 hours showed significant decrease in CM groups versus 2HP group. Tail intensity in CM groups at all time was found lower significantly than the 6HP group. Tail moment was observed significant increase in 2HP and 6HP groups at all time compared to the control group. At 24 hours, it was found significant decrease in CM groups compared to the 2HP group. Tail moment was observed significantly different between CM groups and the 6HP groups at all time points. We have not observed a significant difference between TNF-alpha, IL-6, TAS, TOS and OSI levels of the groups.
CONCLUSIONS: As a result, our findings demonstrate that HP leads to genotoxicity, and that CM decreases HP-induced DNA damage. Our results indicated that the HP dosages used have not effect on the oxidative and inflammatory processes.

PC029

Effect of Wireless Networks on the Lymphocyte DNA and the Role of Vitamin C

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AIM: In this study, we investigated the effect of 2450 GHz electromagnetic radiation (EMR) on the lymphocyte DNA and the role of vitamin C.
METHODS: A total of 18 female Sprague-Dawley rats (6-8 months old) were used in this study. These animals were separated into three groups; control, EMR, EMR+vitamin C. Control group: 1 hour/30 day, it was incubated at restrictive cage and was given-saline by gavage. EMR group: 1 hour/30 day, 2.45 GHz frequency (SAR: 2, 24 kW / kg) was applied electromagnetic radiation. EMR+vitamin C group: 1 hour/30 day EMR and vitamin C (100mg/kg) was administered by gavage. Blood samples were collected for biochemical analysis. DNA damage was investigated by the comet assay method (DNA damage in the cells were studied were numbered 0,1,2,3,4, and each pair of samples. Scoring was performed by counting 100 cells). Also, MDA and complete blood count were investigated.
RESULTS: MDA was not statistically significant between in groups ($p>0.05$). Comet score of EMR group was significantly higher than the control group ($p<0.005$). Comet score of EMR and vitamin C group was significantly decreased compared to the EMR group ($p<0.05$). Platelet large cell ratio (P-LCR) in the EMR group than the control group increased significantly ($p<0.05$).
CONCLUSIONS: As a result of this study, it was demonstrated that DNA damage was generated by 2.45 GHz electromagnetic radiation. Also, vitamin C was detected to protect the lymphocyte DNA against electromagnetic radiation.

PC030

Investigation of the Effect of CAPE on Urotensin II and TGF-β1 Levels on Experimental Osteonecrosis Rat Model

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AIM: Urotensin II (UII) which has a role with its profibrotic features on fibrosis diseases is known the most vasoconstrictor agent. It is thought that these profibrotic features can be formed through transforming growth factor (TGF-β1) and Rho-kinase. In our study, weaimedtoinvestigatetheeffect of CAPE on UII and TGF-β1 levels on steroid-induced osteonecrosis in rats.

METHODS: 30 male Wistar albino rats were classified into 4 groups as groupI: control (C) (n=7); group II: methylprednisolone acetate (MPA) (n=8); group III: CAPE (n=7) and grup IV: CAPE with methylprednisolone acetate (CAPE+MPA) (n=8). Group III andIVreceivedCAPE intraperitoneally at a concentration of 10 µmol/kg for two weeks. After treatment of CAPE, group IV and II received a single dose of 15 mg/kg MPA subcutaneously once a week for 2 weeks and so osteonecrosis model was induced. At the end of study, femur and blood samples were collected for biochemical and histopathological analysis by sacrificing rats. Hematoxylin-eosin and immunohistochemical stains (4 –HNE, 8-OHdG) were used for histopathological evaluation.

RESULTS: In histopathological evaluation, it was found that the fatty degeneration increased significantly in the MPA group as comparison with the other groups ($p < 0.05$). Although there were myeloid necrosis and osteocyte necrosis in the MPA group, myeloid necrosis and osteocyte necrosis were not observed in the CAPE and CAPE+MPA groups. At the same time plasma UII and TGF-β1 levels were statistically higher in MPA group than control group ($p < 0.05$). But plasma UII and TGF-β1 levels were significantly decreased in treatment group (CAPE+MPA) than the MPA group ($p < 0.01$). Moreover, it was found that there was a significant correlation between UII and TGF- β1 ($p=0.003$, r: 0.920).

CONCLUSIONS: The result of this study supported that CAPE may be an effective agent on steroid-induced osteonecrosis by decreasing UII and TGF-β1 levels.

PC031

Cytotoxic Effects of Ursolic Acid and its Derivative on Breast Cancer Cell Lines

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AIM: Terpenoids are one of the important secondary metabolites of the plants. Triterpenoids have skeleton with 30 carbons, consisting of different pharmacological features due to diversity of their chemical structures. They are antimicrobial, anti-inflammatory, antihyperlipidemic, anti-ulcer, hypoglycemic, antifertility, anticarcinogenic, cytotoxic and protect against toxicity activities. The present study was designed to investigate their cytotoxic effects on MDA-MB 231 cell line.

METHODS: Cytotoxic activity measurement wasdone with xCELLigence System. MDA-MB-231 breast cancer cells were reproduced in a suitable medium and incubator. Antiproliferative effect of ursolic acid and 3-hydroxyimino ursolic acid were measured using a real-time cell analysis system (xCELLingence System). Cell were cultured in 96-wellplates with 10000 cells in each well. We evaluated the cytotoxic effects of these terpenoids at 0 µM dimethyl sulfoxide (DMSO)50,100,500,1000 µM concentrations for 72 h of incubation with cells. Antiproliferative effect was evaluated for 72 h after determining the number of cells. IC50 values of compounds were measured with a special quantitative value software. Statistical analysis was performed using one-way ANOVA. $P \leq 0.05$ was considered to be statistically significant.

RESULTS: In this study, ursolic acid and 3-hydroxyimino ursolic acid were analysed at 0,50, 100, 500, 1000 µM concentrations against MDA-MB-231. 3-hydroxyimino ursolic acid showed cytotoxic effect at 25 µM and higher doses and did not show any significant cytotoxic effect at 6.25 and 12.5 µM. There was no cytotoxic effect on human umbilical vein endothelial cells (HUVECs).

CONCLUSIONS: These terpenoids can be possible candidates for anticancer activity in breast cancer treatment. Our studies are still going on other natural and synthetic triterpenoids.

PC032

Effect of Tetracycline Antibiotic Minocycline on Oxidant/antioxidant Parameters on Burn-induced Remote Organ Damage in the Rat

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AIM: Systemic inflammation due to thermal injury is an important cause of morbidity and mortality. Second generation, semi-synthetic tetracycline analogue minocycline has anti-inflammatory and anti-apoptotic effects in addition to its antibacterial action. This study aimed to evaluate the effect of minocycline on burn-induced remote organ damage.

METHODS: Thirty-two female Sprague-Dawley rats (250-300 g) were used. Burn and sham burn groups were immersed in 90°C and 25°C waterbaths for 10 s under ether anesthesia, respectively. Treatment groups received minocycline (20 mg/kg; twice daily; orally) or inducible nitric oxide synthase (iNOS) inhibitor aminoguanidine (100 mg/kg/day; intraperitoneally) following burn. Trunk blood, liver, lung and kidney samples were collected 24 h after burn or

sham burn. Liver and renal function tests, total oxidative status (TOS) and total antioxidant capacity (TAC) were measured in the blood. Tissue samples were used for the measurement of malondialdehyde (MDA), glutathione, myeloperoxidase (MPO) levels and oxidant production via chemiluminescence. Student's t test or Mann-Whitney U test were used for statistical analysis.
RESULTS: Burn caused deterioration of liver (ALT and AST: $p<0.001$) and renal function tests (BUN and urea: $p<0.01$; creatinine: $p<0.05$) and increased TOS ($p<0.001$) compared to sham burn. Minocycline reversed the increase in TOS ($p<0.01$). Burn increased liver and kidney MDA ($p<0.001$), glutathione ($p<0.05$ and $p<0.001$, respectively) and luminol chemiluminescence ($p<0.01$) compared to sham burn. Minocycline reversed luminol chemiluminescence levels back to control in liver ($p<0.001$) and kidney ($p<0.01$). Burn-induced severe microscopic tissue damage was slightly decreased by minocycline in the liver ($p<0.01$). Aminoguanidine decreased luminol chemiluminescence in both liver and kidney ($p<0.01$), and liver damage microscopically ($p<0.05$) due to burn; but was not effective when other tissue injury parameters were considered.
CONCLUSIONS: Treatment with minocycline caused partial improvement in liver and kidney injury due to oxidant stress in a rat model of burn injury.

PC033

The Healing Effect of Resveratrol on Excisional Wound

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AIM: We aimed to investigate the healing effect of a cream containing 1% and 5% of resveratrol in excisional wound model in rats.
METHODS: Wistar albino male rats (250-300 g) were divided into four groups.Each group contained 8 rats. Rats were anaesthesized by using ketamine/xylazine and with 5-mm punch biopsy apparatus excisional wounds were made on their dorsal regions. Madecassol-base cream, as a vehicle in madecassol, was applied to the animals in the control group. Madecassol was applied to the second group (group M), madecassol base containing 1% resveratrol and madecassol base containing 5% resveratrol were applied third and fourth groups, respectively. Applications were done topically each day for 5 days. Wounds were photographed and calculated by ImageJ software. In the twelfth day all rats were sacrificied and tissue samples were histologically analyzed.
RESULTS: Wound surface areas at 2nd and 8th days did not show any significant difference with respect to control group. On the 4th day a significant difference was observed between the group M and controls ($P=0.048$), and on the 6th day significant differences were determined in third ($P=0.005$) and fourth groups ($P=0.004$) with respect to control group. Statistically significant differences were also observed between control group and group M ($P=0.01$), third group ($P=0.026$) and fourth group ($P=0.000$) on the 10th day of the study; at the end of the study (twelfth day) the only significant differences were in the group M ($P=0.037$) and the fourth group ($P=0.003$) with respect to controls. In the histological examination, there were no significant differences in the third and fourth groups with respect to control group in terms of epidermal, dermal regeneration, granulation and angiogenesis,
CONCLUSIONS: Creams containing 1% and 5% resveratrol may have positive effects on excisional wound healing.

PC034

Effect of Hyperbaric Oxygen and Ozone Therapy on Wound Healing in Diabetic Rats

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AIM: Although Hyperbaric Oxygen (HBO) therapy is commonly used to increase the oxygenation of the wound area in clinical practise, the use of ozone therapy is limited. In this study, our aim is comparing of HBO therapy and the effects of the ozone therapy on would healing processes.
METHODS: One week after 50mg/kg intraperitoneal streptozotocin was administered to the experimental animals, a full-thickness skin wound (3x3cm) was created on the experimental animals' back under anesthesia. After this step, the experimental animals were split into 3 groups at random. HBO was administered for 90 min once a day under 2.5 ATA pressure in treatment group, while ozone treatment was administered intraperitoneally once a day for 6 days at the dose of 1mg/kg. On the 7th day, surface areas of the wounds of the experimental animals were measured and wound tissues were removed under anesthesia. VEGF, TGFβ1 and MMP-1 measurements were made on the wound tissues with commercial ELISA kits. SPSS.15.0 program was used for statistical evaluation and significance was set at $p<0.05$.
RESULTS: Wound surface areas of the treatment groups were smaller ($p<0.05$) than control group. It was found that there was no significant difference between HBO and ozone groups. In terms of VEGF levels, both of the treatment groups were significantly higher ($p<0.05$) than control group, but it was seen that the VEGF levels of the HBO group were higher ($p<0.05$) than the ozone group. In addition, it was detected that HBO group TGFβ1 levels were significantly ($p<0.05$) higher than the other groups.
CONCLUSIONS: Our study shows that both ozone therapy and HBO therapy accelerate wound healing. According to the present results, main effect of HBO therapy is dependent on VEGF, TGFβ1 and oxygenation increase. On the other hand, it is thought that positive contribution of ozone therapy to the wound healing processes may be explained by immunomodulation like different mechanisms.

PC035

Revealing the Epigenetic Mechanisms on the Pathogenesis of Lung Damage Caused by Mustard Analogue Mechlorethamine

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AIM: Besides the lack of antidote, the popularity of mustard gas results from its easy produce, low cost and long storage time. Mustard gas causes DNA alkylation, nitrooxidative stress and inflammatory reactions by binding to macromolecular structures on DNA. “Mustard lung” can occur years after mustard exposure, suggesting that epigenetic changes may cause damage in the chronic phase.
METHODS: In this study, 300-330g weight, 138 Sprague-Dawley male rats were used. Mustard toxicity was established as a transdermal application of 25mg/kg dose of mechlorethamine to the shaved back of the rats. The rats were divided into 5 groups, including the Sham, Control (Mechlorethamine), Mechlorethamine+ Valproic acid (VA), Mechlorethamine+Azacitidine (AZ) and Mechlorethamine+Valproic acid+Azacitidine (VA+AZ) by a simple random sampling method.
RESULTS: At the end of the study, the average weights of rats were decreased significantly in all groups compared to the sham group but only average weights in the VA group increased significantly compared to the control group. Also highest survival rate was obtained for VA group (%65). Urine NOx levels, tissue apoptosis, oxidant-antioxidant, cytokine, Nrf2 and COX2 levels were analyzed. Analysis showed that VA group is superior to the other treatment groups.
CONCLUSIONS: The study compared Histone Deacetylase (HDAC) inhibitor VA and DNA Methyltransferase inhibitor AZ. VA showed an obvious superiority in many parameters. Inhibition of histone deacetylation, probably paved the way for a group of repair enzymes or pathway. When all the results are evaluated, inhibition of HDAC enzyme with VA, runs an important epigenetic mechanism in mustard damage. Anti-inflammatory agent combination with VA at the next stage is thought to be the ideal treatment option. This study also “112S628” coded TUBITAK project.

PC036

Comparison of the Effectiveness of Various Antioxidants on Lung Damage Caused by Sulfur Mustard And Presenting Their Effects on Serum Parameters

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AIM: Mustard as an important chemical warfare agent causes damage in body through DNA alkylation, nitrooxidative stress and inflammatory reactions. After mustard gas exposure some symptoms appear in the body, especially in lung, eyes and skin, in a dose dependent manner. Lots of antioxidants were tried in the treatment of mustard damage, which is still incurable. We targeted at this study presenting the effectiveness of the various antioxidants against lung damage caused by sulfur mustard.
METHODS: 60 male rats were used in our study. By setting the model “2 chloroethyl sulfide”(CEES), which is known as a sulfur mustard agent and is half-mustard, is applied as 1 mg/kg single dose via intracheal route. The animals were separated into 6 groups as Sham, Control (CEES), CEES+N-Acetyl Cysteine (NAC), CEES+Lipoic acid (LA), CEES+Mesna, CEES+ Amifostine (AMF). Within 15 min after setting of toxicity model,the curative therapeutic agents were started to be applied. Treatments were applied for 3 days. Then, the rats were sacrificed; blood and lung tissue samples were taken for histopathological examination and biochemical analysis.
RESULTS: When we look into results of death rates, we observed that 60%of death rate in CEES group was decreased only in AMF and LA applied groups ($p<0.05$). At histopathological examination, increased edema, hemorrhage and inflammation were decreased in AMF and LA applied groups ($p<0.05$). There were no significant results in biochemical analysis.
CONCLUSIONS: In the light of these data, it is understood that it should be tested with an more appropriate model if the measured parameters in serum were used or not in assessment of situation and follow up of acute lung toxicity and besides we concluded that antioxidants like Amifostine and α-lipoic acid promises hope in acute lung toxicity caused by sulfur mustard.

PC037

Assessment of Respiratory Function Test Parameters for Workers and Officers Who Work in Various Business Lines

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AIM: It is thought that the microparticles adversely affect the human lung mechanics in many studies on asbestosis, silicosis and coal worker pneumoconiosis. We aimed to compare Pulmonary Function Tests (PFT) that the clay, wood and poultry (chicken) dust in exposed workers with office staff on living at the same altitude.
METHODS: In order to separete factors which can affect lung mechanics, face-to-face interviews and questionnaires were applied before pulmonary function test. After Ethics Commissions permission and approval of related work place, the pulmonary function tests were repeated 3 times and the results are obtained for working at least for 5years of 25 workers of clay package, 18 workers of poultry farm, 27 workers exposed to wood dust and 40 office workers as a control group. PEF(l/min), FEV1(l), FVC(l), Ratio(%),FEF25 75 (l/sec) results were examined by expert counselor and appropriate results were used for evaluation.For the statistical analysis of obtained data SPSS 16.0 program was used. The data were evaluated

independent samples t, Mann-Whitney U test and chi-square test.
RESULTS: There were statistically significant no differences age, gender, income, residential areas, smoking and alcohol use patterns. PEF(I/min), FEV1(I), FVC(I), Ratio(%),FEF25 75 (I/sec) values were different between working groups compared with control group ($p<0.005$).
CONCLUSIONS: It was found to be effective on pulmonary mechanics of encountered at any time of the powder in the atmospheric air, except of irritants also. On occupational health and safety, it should be aimed to increase training on wearing mask and glasses and increase safety measures for employees' health at workplace.

PC038

Influence of Exercise Intensity on Ventilation During Constant Load Exercise Test in Sedentary Male Subjects

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AIM: During exercise, increased metabolic demand must be accompanied with an increased ventilation (VE). Anaerobic threshold (AT) and critical power output (CPO) describe two important exercise intensity associated with specific metabolic set points. In the present study, influence of exercise intensity corresponded to AT and (CPO) on VE were evaluated.
METHODS: Sedentary (n=11, 20.8±0.6 yr, 74.9±1.7 kg) male subjects, initially performed an incremental exercise test using a cycle ergometer to determine AT, CPO. Then, each subjects performed three constant load exercise tests: work load 25% below AT (97.8±4.7 W), at the AT (130.4±6.4 W) and at the CPO (156.7±7.2 W) for 15 min. The study protocol was approved by Local Ethics Committee. Ventilatory and pulmonary gas exchange parameters were evaluated breath-by-breath using metabolic gas analyser. Values are expressed as means±S.E.M., compared by ANOVA test and $p < 0.05$ was accepted as statistically significant.
RESULTS: VE were found to be 43.68±1.7 L/min (25% below AT), 59.65±2.9 L/min (AT) and 74.12±4.7 L/min (CPO). Tidal volume (VT) were 1.628±0.1 L (25% below AT), 1.875±0.1 L (AT) 2.192±0.1 L (CPO). Despite significant differences between VE values among the tests ($p<0.05$), there were no statistically significant ($p>0.05$) differences between VE values normalised to body weight (BW) and applied work load (W): 5.96±0.30 ml/min/BW/W, 6.10±0.35 ml/min/BW/W 6.31±0.39 ml/min/BW/W.
CONCLUSIONS: VE response to the work load 25% below AT (low intensity), AT (highest work load without increased metabolic acidosis, moderate intensity) and CPO (highest sustainable work load without fatigue, high intensity) were coincided approximately with the value of 6.00 ml/min/BW/W. Increased VT is an important factor on VE despite altered metabolic intensity. Importantly, further studies with higher number of subjects with different fitness status need to be performed to support 6.00 ml/min/BW/W values could be use as an criteria to evaluate ventilatory efficiency to applied exercise work load.

PC039

FEF25–75/FVC Measurements in COPD, Asthma and Sarcoidosis Patients

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AIM: It was suggested in 1970s for the first time that the variables of maximal flow caused by unequal growth between lung parenchyma and airway. It was indicated that FEF25-75/FVC rate (DYSANAPSIS) is the best parameter, which shows the relationship between airway and parenchyma (1). Also, it was stated that FEF 25-75/FVC rate is associated to the hypersensitivity of the airway as well (2). It was indicated that FEF25-75 and FEF25-75/FVC values of the non-smoker, immediate relatives of the early-onset KOAH patients are lower than the control subjects (3). Presence of the negative correlation between HCRT consolidations and FEV1, FEV1%, FEF25-75, FEF25-75 % of sarcoidosis patients, despite the lack of significant changes in the respiratory functions, the importance of individual changes were argued. In another study that is conducted with juveniles, no such correlation was observed.
METHODS: Our study was especially conducted for the investigation of the link between FEF 25-75/FVC ratio and respiratory functions in different disease groups that includes airway disease or parenchymal involvement. In our study, the relationship between FEF 25-75/FVC rate and pulmonary functions on 623 patients in total, who are treated at Istanbul University, Cerrahpasa Medical Faculty for KOAH (GOLD, 22 Women/196 Men), asthma (GINA, 129 Women/57 Men) and sarcoidosis (162 Women/57 Men) was analyzed. The pulmonary function tests of patients were performed via SensorMedics Vmax22 spirometer. Data was analysed by SPSS20.
RESULTS: Although a correlation was found in the FVC and FEF 25-75/FVC in KOAH and asthma cases, it was not observed in the cases of sarcoidosis. FEV1, FEV1%, FEV1/FVC, FEV1/FVC%, FEF25, FEF25%, FEF50, FEF50%, FEF25-75, FEF25-75%, FEV25-75/FVC parameters was found different as istatistically in all groups($P<0.001$). Further, although a correlation was found in the FVC and FEF25-75/FVC in KOAH and asthma cases, it was not observed in the cases of sarcoidosis.
CONCLUSIONS: Our findings indicate that patients' obstruction parameters (FEV1, FEV1%, FEF25-75, FEF25-75%) worsen, as long as FEF25-75/FVC rate decreases and it supports Green and his friends' hypothesis (1) that 'the changes on airway's radius affect pulmonary functions independentlyon lung parenchyma'.

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PC040

Comparison of Peak Expiratory Flow (PEF), Vital Capacity (VC) and FEV1/FVC values of Healthy People Considering Their Exercise Status

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AIM: Respiratory capacities of exercising people had been shown to be higher than those who do not. PEF, VC and FEV1/FVC are fundamental parameters to interpret pulmonary functions. The rising muscles' O2 requirement during exercise forces cardiac, circulatory and respiratory systems to adapt to the changing metabolism. To look into respiratory adaptation, therefore, this study aimed to compare the expected PEF%, VC% and FEV1/FVC% of pulmonary function tests (PFT) of sedentary individuals and exercising ones.
METHODS: Thirty-four non-smoking healthy men and women volunteers (22-65 years of age) with similar social characteristics volunteered after signing informed consent forms. PFT was performed with spirometer (Spirolab III; USA) according to ATS/ERS criteria. Data collection forms used to determine the participants exercise (walking, running, swimming, ball games and similar physical activities) frequency (never,1-2 times a week,or every day). Expected PEF%, VC% and FEV1/FVC% values of participants who grouped according to their physical exercise frequency, were compared. SPSS 20.0 software was used for statistical analysis. $p<0.05$ was considered significant.
RESULTS: VCs of who exercise are higher than who do not; VCs of who exercise every day are higher than VCs of who exercise 1-2 times a week. Between the VCs of who exercise every day and who do not exercise, there was a significant difference statistically ($p=0.018$). Additionally, PEF values of who exercise are higher than who do not. However, based on the exercise frequency the difference for PEF values between groups was not significant. Similarly, any significant difference was not detected for FEV1/FVC parameter between groups.
CONCLUSIONS: Increasing muscle strength and physiological adaptations with physical activity can positively affect respiratory functions such as VC, FVC, FEV1 and PEF. Sedentary people having significantly lower PEF and VC values than those who exercise may benefit from exercising regularly. Starting physical training, therefore, may strengthen respiratory muscles and lead to improved dynamic and static pulmonary functions.This work was supported by Erciyes University Scientific Reserarch Projects with TDK-2015-6077 registration number.

PC041

The Protective Role of Erdosteine Pre-treatment on Oleic Acid-induced Acute Lung Injury

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AIM: Acute lung injury is a condition characterized by acute respiratory failure with high mortality rate. Erdosteine is a mucolytic agent with antioxidant and anti-inflammatory effects. It reduces the severity of injury by preventing neutrophil accumulation. It is particularly used in chronic lung diseases. However, there are few studies on its acute effects. Therefore, we aimed to investigate the protective effect of erdosteine pre-treatment on oleic acid (OA)-induced acute lung injury.
METHODS: 24 male Wistar albino rats were assigned into four groups: Control group received oral saline and one hour later 50 microliters of i.v. saline. OA group was administered oral saline and one hour later 50 microliters of i.v. OA. Erdosteine group received a single dose of erdosteine (150 mg/kg) orally and one hour later 50 microliters of i.v. saline. OA + Erdosteine group received oral erdosteine (150 mg/kg) and one hour later 50 microliters of i.v. OA. Tail vein was used for all i.v. injections. Four hours later following OA injection, rats were anesthetized. Lung tissues were excised to evaluate the tissue malondialdehyde and protein carbonyl levels, catalase activity, and histopathological changes. Data were analyzed by ANOVA followed by Tukey's test.
RESULTS: OA administration increased lung weight ($P<0.05$), tissue malondialdehyde and protein carbonyl levels ($P<0.05$) and decreased catalase activity ($P<0.01$). Erdosteine pre-treatment ameliorated all these changes and OA-induced alveolar fluid, capillary congestion, interstitial edema, macrophage and neutrophil accumulation.
CONCLUSIONS: Erdosteine pre-treatment reduces OA-induced inflammation and oxidant stress and protects the lung tissue against acute lung injury.This work was supported by Hacettepe University Scientific Research Coordination Unit. Project Number:THD-2015-7586.

PC042

Investigation of the Relationship Between Pulmonary Function Test and Different Somatotypes

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AIM: Pulmonary function tests (PFT) are useful tests used for diagnosis and monitoring of diseases that affect the lungs. Somatotype is convenient shorthand description of all physician terms that is independent of body size in terms of body shape and composition. This study, putting out aerobic capacity variables between somatotype, aimed to identify how PFT changes in which body type in healthy individuals.
METHODS: 120 people ranging from 20-26 years old, using no alcohol, cigarette and tobacco materials, without having any pulmonary disease and surgical operation were included in this study. Carter and Heath somatotype determination technique was used for determining somatotype. Except those, anthropometric measurements that impact on lung capacity, such as biachromial diameter, chest depth, chest width, neck circumference, chest circumference and waist circumference were measured. In PFT application, application form was explained to the patient within the framework of rules and was made at sitting position as rested, in compliance with all commands by Minispir device. Evaluation of the data was performed using the Kruskal-Wallis H test and correlation analysis.
RESULTS: No statistically significant difference was determined between different somatotypes and PFT values (FVC,FEV1, FEV1/FVC, PEF, FEF25-75) ($p>0.05$). Statistically significant differences were found between anthropometric measurements that effect on lung capacity and different somatotypes ($p<0.05$). A positive significant

relationship between PFT and anthropometric measurements was determined by using correlation analysis ($p<0.05$).
CONCLUSIONS: This study conducted on healthy individuals showed that PFT was not associated with body type, but it waslikely be determined by measurements taken from the body. The significant difference was determined between expected and observed values and as a result, that was considered to the participants were not use their lung capacity sufficiently.

PC043

The Effects of Medical Ozone on Oxidative Stress in Lung Tissue of Diabetic Rats

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AIM: Ozone is a trivalent form of oxygen. Medical ozone is a mixture of ozone and oxygen. Relationship between oxidant stress and diabetic complications has been shown previously. In this study, it was aimed to investigate the effects of medical ozone on oxidative stress/antioxidant balance in the lung tissue of diabetic rats.
METHODS: 42 adult male Sprague-Dawley rats were randomly divided into 6 groups (n=7): Control (C), ozone (O), diabetic (D), ozone-treated diabetic (DO), insulin-treated diabetic (DI), and ozone- and insulin-treated diabetic (DOI). Diabetes was induced by a single injection of streptozotocin (60 mg/kg, i.p.), after which insulin was administered (3 IU, i.p., once a day) to the DI and DOI groups for 6 weeks, and 1.1 mg/kg (50 µg/ml, i.p., once a day) ozone was given to the O, DO, and DOI groups for 6 weeks. 6 weeks after the induction of diabetes, the oxidative stress tests (Total Oxidant Status, Total Antioxidant Status, Oxidative Stress Index) were made in lung tissue samples. Data were analysed using One-way ANOVA and post hoc Tukey tests. $p<0.05$ was considered statistically significant.
RESULTS: Oxidative stress index values of D group were higher than the C, DO and DOI groups ($p<0.01$). There were no significant differences among the other groups in terms of oxidative stress index.
CONCLUSIONS: In conclusion, medical ozone therapy alone or in combination with insulin can reduce the development of complications induced by oxidative stress in diabetic rats.

PC044

Comparing the Levels of IL-6, Oxidant and Antioxidants on Kidney of Trained and Untrained Rats After an Exhausting Exercise

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AIM: We tried to find out whether an exercise training has a protective effect on kidney damage, which can be caused by exhausting exercise. We examined the cytokine IL-6 and the free oxygen radicals (TOS) which are thought to be responsible to this damage, and the antioxidants (TAS) in exercise trained and untrained rats.
METHOD: Forty Wistar albino rats were divided into groups as; sedentary controls (Con), acutely forced to exhausting exercise (Acute) group, and exercise trained group (Chronic) which had run for 3 months, 30 min/day, 15 m/min speed and15° slope in the treadmill. Exhaustion was determined by lying down of the rats, on the electrically-shocked-given grid for a few minutes. Acute and chronic groups; immediately after exhaustion (Acute-Immediate, Chronic-Immediate), and a day after exhaustion (Acute 1 day and Chronic 1 day) were sacrificed. The TOS and TAS in the kidney tissue are examined with Rel Assay Diagnostic kits, and IL-6 was assesed with Eliza kits. As statistical analysis, SPSS program was used and the $p<0.05$ value was accepted as significant.
RESULTS: TOS levels increased both in the Acute immediate and Chronic immediate groups, comparing the controls ($p<0.05$). IL-6 increased in the Acute 1 day group, without increasing in the Acute immediate group ($p<0.05$), and it is found enhanced in the Chronic immdiate group, comparing to Acute group and Controls ($p<0.05$). TAS, was found in higher levels in the Acute 1 day group, comparing the Acute immediate group ($p<0.05$), but it was higher in the Chronic immediate group ($p<0.05$).
CONCLUSIONS: Although there was an increase of oxidant stress in all Acute and Chronic groups after exhaustion, the antioxidant mechanism, and the IL-6, which has an antiinflammatory effect on exercise, were higher in the Chronic immediate group, probably to start the regenerative processes.
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PC045

Non-invasive Determination of Physiological and Psychological Stress Level of Cortisol Hormone which Comes out of Football Match

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AIM: A high level of physiological and psychological endurance is required in sports branches performed under high pressure like footboll. The aim of this survey was to determine the stress level of athletes, via measuring the possible changes in spit as non-invasive, at match day's waking up level and pre match, through match and post match levels of football playerws.
METHODS: Male football players, from 18 to 27 age range (n=14), attended this survey. Spit samples were taken at regular season period in 3 different days (the day before match, match day and the day after match as waking up, 0, 30, 45 and 60th minutes) so as to determine waking up responses. Besides, the spit samples were taken for cortisol analyses in match day 30th and 15th minutes before competition, half time and after the game. The spit cortisol levels of athletes were analysed with ELISA method. The findings were analysed with Mann Whitney-U test and $P<0.05$ values were considered as significant.

RESULTS: It was appeared as a result of analyses that waking up responses of spit cortisol level increase in game day and decrease the day after. It is seen in the samples taken in match day, cortisol levels of athletes increase 30 minutes before competition and decrease in the samples taken in half time. It is determined that the samples taken the day before match and the day after match are similar to each other. No significant difference is appeared statistically considering the different days (P>0.05).
CONCLUSIONS: According to the findings, no significant difference was observed in the cortisol levels of waking up responses considering different days. Moreover, it was observed that athletes are able to control their stress levels particularly according to the samples taken match day.

PC046

The Relationship Between Some Respiratory Functions and Maximal Oxygen Consumption in Prepubescent Girl Football Players

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AIM: The purpose of this study was to examine the relationship between various respiratory parameters and maximal oxygen consumption determined by YO-YO test in football trained girls.
METHODS: Twenty two girls who were engaged in football training (mean age: 12.95 ± 1.96 years; mean height: 151.20 ± 9.35 cm; mean weight: 42.99 ± 10.32 kg) volunteered to participate in the study. All subjects had trained at least 90 minutes per day, 4-5 days a week and were members of the same team that gained success at the national level. Forced vital capacity (FVC), forced expiratory volume in one second (FEV1), maximum expiratory flow (PEF), forced expiratory flow rate medium (FEF25-75) and maximum voluntary ventilation (MVV) measurements were taken to determine the respiratory function using the Spirolab III spirometry (Medical International Research). Maximal oxygen consumption (VO2max) were calculated using the "(Distance x 0.0084) +36.4" formula where the distance was determined by YO-YO test. The study was approved by the Anadolu University Ethical Committee.
RESULTS: The mean values of distance and the VO2max determined by YO-YO test were 420.00 ± 127.24 (m) and 39.98 ± 1.10 (ml.kg.min-1), respectively. Additionally, the mean values of FVC, FEV1, FEV1/FVC, PEF, FEF25-75 and MVV were 2.97 ± 0.60 (L), 2.42 ± 0.66 (L), 82.46 ± 14.19 (%), 3.68 ± 1.31 (L/sec), 2.77 ± 0.90 (L/sec) and 90.88 ± 25.08 (L), respectively. A statistically significant relationship was determined between the FVC values and YO-YO test distance and VO2max (r = 0.662 and r = 0.583; p<0.01). Furthermore, a statistically significant relationship was determined between the MVV values and YO-YO test distance and VO2max (r = 0.520 and r = 0.500; p<0.05).
CONCLUSIONS: The results of the present study are in concordance with studies that put forth the positive effects of exercise programs on the respiratory functions of individuals who have not yet completed their developments. On the other hand, because of the FCV, FEV1 and PEF variables have been shown to be associated with age, height and weight, this effect may be a natural consequence of the growth.

PC047

Investigation of NRF-1 Genotypes and ACE Gene Polymorphism in Elite Athletes

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AIM: The present study aimed to investigate the genetic polymorphisms in Nuclear Respiratory Factor-1 (NRF-1) and angiotensin converting enzyme (ACE) in elite athletes who have diverse professions.
METHODS: 240 male athletes from diverse disciplines and 250 male controls were included in this study. Athletes were assigned into 4 groups (n=60 in each) as "football", "basketball", and "volleyball" which are endurance sports, and "wrestling" which is a strength sport. Blood samples were obtained and stored at -20 °C until the PCR analyses. Following the DNA extraction, NRF-1 and ACE gene regions were amplified by using the primers in the PCR. The acquired products were cleaved by the restriction enzymes MFE-1 and RSAand the polymorphisms for the mentioned genes were investigated by using the RFLP-PCR assay.
RESULTS: Of the athletes, ACE DD genotype was detected in 27.5% (66/240), ACE ID genotype in 32.9% (79/240), and ACE II genotype in 36.5% (88/240), whereas those three genotypes were found to significantly lower than the athletes in the control group (p<0.05). In regard to the professions, a significant difference between footballers and wrestlers was determined for ACE DD and ACE ID genotypes (p<0.01) while no statistical significance was found between volleyball and basketball players for ACE gene polymorphism (p>0.05). We assume that this result may depend on that those two sports require higher physical performance than volleyball and basketball. Considering the NFR-1 gene polymorphism, a statistical significance was found in wrestlers, football and basketball players as compared to the controls (p<0.01).
CONCLUSIONS: Our results suggest that the distributions of the ACE and NRF-1 genotypes may be used as a genetic factor for electing athletes in early ages.

PC048

Effect of Mesenchymal Stem Cell Applications on the Rat Muscle Damage

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AIM: The aim of the present study was to investigate the apoptotic effects of mesenchymal stem cell (MSCs) transplantation on the rat musle tissue after exhaust swimming exercise. METHODS: A total of 30 Spraque-Dawley male rats (250-280g/12 weeks) were used..They were divided randomly into five groups: Control (C), Mesenchymal Stem Cell (SC), Exercise (E), Mesenchymal Stem Cell and Exercise (ESC1) and Exercise and Mesenchymal Stem Cell (ESC2). The rats swam every day during one month until exhaust, resting two days a week. The exhaust point will be accepted when the rats still remain 8-10 sec. Isotonic saline was givenas placebo to C and E groups and $1X10^6$MSC/1.5ml/dose of MSCs was applicated by intramuscular injection in equal doses tofive parts of rats' bodies (upper and lower extremities (right-left) and tail muscle) at 4th week two times per 24 hours. Muscle sampleswere taken for apoptotic assay after sacrifiation of rats. The level of apoptosis was detected by using TUNEL method. The study was approved by Erciyes University Animal Experimentation Ethics Committee. Data were evaluated with ANOVA and Student T test in computer environment and the significance level was taken as $p<0.05$.
RESULTS: MSC and swimming exercise applications were found to be substantially effective both morphologically and physiologically. The apoptotic cells number decreased significantly by MSC applications to tissue damage derived after exercise ($p<0.05$). Swimming time of rats were increased significantly between two groups ($p<0.05$).
CONCLUSIONS: The MSC and swimming exersice applications increased the rats' swimming performance and cell damage induced by exhausted swimming exercisewas significantly decreased. The common use of MSC in many clinical disciplines for treatment can contribute significantly to increase the athletic performance, to preventsport's injuries and tissue damage induced by exercise.This study was supported by Erciyes University SRP (Project Number: TYL-2014-5270)

PC049

The Effects of Probiotic VSL#3, on Zonulin and Some Inflammatory and Oxidative Parameters in Rats Subjected to Moderate and Intensive Swimming Exercises

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AIM: The disruption of intestinal barrier and concomitant inflammatory and oxidative processes may cause some gastrointestinal and upper respiratory tract complaints after intensive exercise periods, but moderate exercises improve immunity and oxidative balance. We tested that the effects of moderate and intensive swimming exercise on zonulin, an intestinal barrier marker, and some cytokines and oxidative parameters and also tested the effects of probiotic administration in both exercise regimens. METHODS: Twenty-eight rats were randomly divided into 4 equal groups: Control-C, Probiotic-P, Exercise-E, Probiotic+Exercise-PE. The rats in group E and PE underwent moderate swimming exercise 1 h/day, 5 days per week for 5 weeks. Following moderate swimming period, the same rats were subjected to intensive swimming exercise (1 h) with 150 min interval, 3 times/day for 5 days. Group C and group P were sedentary which were not subjected to swimming exercise. Probiotic VSL≠3 was given to group P and group PE in tap water. At the end of the experiments, serum zonulin, TNF-α, IL-6, IL-10, TGF-β, MDA, and protein carbonyl levels were determined. Data were analysed with oneway ANOVA and post-hoc Duncan tests.
RESULTS: It was determined that serum zonulin and MDA levels decreased after moderate exercise in group E ($P=0.01$). TNF-α ($P=0.003$), IL-6 ($P=0.022$), TGF-β ($P=0.04$), and MDA ($P=0.01$) levels decreased, but the reduction in zonulin levels was not statistically significant in group PE.
CONCLUSIONS: Moderate swimming exercise improves intestinal barrier integrity and reduces oxidative stress. During this period, probiotic VSL≠3 supplementation also improves inflammatory response. On the other hand, intensive exercise does not stimulate any inflammatory response and/or oxidative stress, but beneficial responses induced by moderate exercise disappeared possibly due to intense exercise-induced mild stress.

PC050

The Effect of Full Body Massage on the Excretion of Creatinine, Uric Acid and Microprotein Levels in Urine

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AIM: The purpose of this study was to determine the effect of massage on some biochemical parameters excreted by urine. METHODS: The study was carried out on with 42 attendees (21 study-21 control group). Both groups performed submaximal exercise, whereas the study group was given massage following the submaximal exercise. During the study group's massage, the control group was allowed for passive resting and was not given any massage. Urine samples were collected twice from the study groupboth before and after the massage (following the 35 minutes of massaging and the waiting period)-and analyzed. Massage manipulations were done by eflorage, friction, petrisoge, pression, deep friction and vibrations. Creatinine, uric acid and microproteins in urine were analysed using Olympos AU 5200 kit with strict adherence to the company's recommendations. In the statistical analysis within groups, we used paired t test, in between groups and independent samples t test was for comparison. There were no significant differences in the comparison of the experimental and control groups. Uric acid, creatinin and microproteins datas were respectively analysed before and after massage. Data are presented as mg/dl, mean +/- SD.
RESULTS: The analysis results suggest that massage the treated experimental group received urine creatinine and uric acid value were detected increased significantly ($P<0.01$). There were no significant

differences in the comparison of the experimental and control groups.
CONCLUSIONS: In the light of results obtained, massage has some effects on the parameters measured by this study. However, the actual mechanism by which such effects occur is not clear. We suggest that massage may cause some alterations by affecting anti-oxitan protection system. It has been suggested that creatinine, uric acid and microprotein levels in urine after massage might be taken into consideration to increase performance and to regulate and balance the relaxation time of athlete.

PC051

Negative Effects of the Stimulant of Light on Performance and Elimination of this Effect Through Hypnotic Suggestion

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AIM: A great number of hallucinations can be generated to affect sportive performance in humans by means of hypnotic suggestion. The light that comes to the eyes in critical moments may distract the sportsmen and affect their performance negatively. This study was carried out in order to investigate the physiological response caused by light stimulants of all the stimulants that negatively affect the sportsmen's performance on strength performance and to determine the effects of these hypnotic suggestions on those responses.
METHODS: This study was carried out on 28 volunteer national male athletes in the international standards. The subjects were made to use strength twice: In the first, the responses to direct light stimulants were determined during strength application. In the second, the same subjects were hypnotised and given the same stimulants, but before giving the stimulants, they were inculcated that "A light will come to your eyes. When you see it, you will feel quite stronger, be able to squeeze what you hold in your hand, and see that it will nearly be crushed and disappear." Then the physical changes in the strength re-entered. The changes in the strength were determined as paw strength in TMR EST 1000 isometric muscle exercise measurement device. During strength application; 100, 150, and 200 W lights was sent as stimulant to the eyes from 50 cm distance with 450 angle. As a result, the changes caused by extra light stimulants affecting the strength during the suggestion with and without hypnosis were statistically evaluated. The findings were analysed with paired t test, and the values at the level of $P<0.05$ were considered significant.
RESULTS: It was determined that there was statistically significant difference between the strength values (100 W: $p<0.001$, 150 W: $p<0.001$, 200 W: $p<0.001$).
CONCLUSIONS: It was found that the light that came to the eyes during strength application affected the performance negatively, but it could be eliminated with hypnotic suggestion; and even it affected the strength positively. Therefore, it is suggested that the hypnosis will be effective in performance loss caused by distraction in exercise forms related with competition and struggle.

PC052

Investigation of the Relationship Between the Reaction Time and Hand Grip Strength in Boxing

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AIM: Mostly, the motor ability of hands is often evaluated by measurements of hand grip strength. Reaction time is defined as the time between stimulus and response and the time is also the most important component taken as a criterion for sports performance because its one of the indicators of the neuromuscular performance. Thus, the purpose of the present study is to examine the relationship between reaction time with hand grip strength of the professional boxers.
METHODS: An elite-level struggling twenty-eight male boxers, between the ages of 16 and 20 years, participated in this study. The MOART (Lafayette USA) measurements equipment was used in reaction time measurements of the boxers. The measurements were carried out in two ways as simple and multiple visual reaction measurements. The hand grip strength mesaurements were performed by hand dynamometer grip-D (Takei, Japan) measuring force within the range of 0 to 100 kg. The findings from this study were analyzed by Pearson's correlation test and $P<0.05$ values were considered statistically significant.
RESULT: It was determined that there were statistically positive correlations among the basic auditory reaction time with simple visual reaction time, multiple visual and auditory reaction times with simple visual reaction, left hand grip strength with right hand grip strength ($P<0.05$). There were no found significant relationships among reaction time parameters with the left and right hand grip strength ($P> 0.05$).
CONCLUSIONS: According to these findings, it has been observed that the visual and auditory reaction times have a coordinated structure with each other in boxers. In this respect, it has been determined that hand grip strength an indicator of the multiple body function is not related with reaction time. Results obtained from these parameters suggest the forms of training are effective in boxing which came into prominence of the time dependent struggle.

PC053

The Reliability of Ultrasonographic Measurement of Biceps Brachii Muscle Thickness and Stiffness

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AIM: Estimation of muscle thickness from anthropometric measurements are not precise so further utilization of advanced methods

are recommended to measure muscle thickness. Muscle stiffness, an important measure in exercise science can be objectively measured using a recent ultrasound technology, shear-wave elastography(SWE). Aim of our study is to measure the precise thickness and stiffness of biceps brachii muscle non-invasively with a cost-effective method, ultrasonographic imaging and calculate its reliability.
METHODS: The sample size is calculated as 11 participants, at ANOVA axis with 3 repeated measurements, 0.5 effect size, 95% confidence and 90% power. Thickness measurements were done on 17(11 male, 6 female) volunteers with brightness mode(B-mode) ultrasound by an experienced Sports Physician in 3 consecutive days triple times from 60% distal point of the upper arm of their non-dominant side. Participants were sitting, relaxed and elbow flexed at 90 degrees. Also stiffness of biceps brachii was measured from 3 different randomly chosen points at a shear-wave cycle using a diagnostic ultrasound device. Friedman test was used in order to evaluate differences. Intraclass Corelation Coefficient(r) and 95% Confidence Interval(CI) were calculated for reliability measures between sessions.
RESULTS: There was no statistically significant difference between thickness measurements inside sessions, and in between sessions ($p>0.05$). Inter-sessions thickness measurements reliability was found very high r=0.993 (CI: 0.985–0.997). No statistically significant difference was found among stiffness measurements of intra-session ($p=0.307$, $p=0.529$ and $p=0.234$ for day 1, 2 and 3 respectively) and of inter-sessions ($p=0.529$). However day-to-day stiffness measurements reliability was moderate, r=0.678 (0.13–0.91).
CONCLUSIONS: B-mode ultrasonographic imaging can reliably be used in order to measure biceps brachii muscle thickness and SWE can reliably be used to quantify human biceps brachii muscle stiffness. Repeating measurements 3 times inside a session yields better reliability.

PC054

The Relationship Between Incidence of Deformity in the Lower Limbs of Cases with Cerebral Palsy with Ambulation and without Ambulation

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AIM: Contractures, bone or articular deformities which accompany to cerebral palsy (CP) greatly restrict the movement of the child. Besides dynamic deformities and movement disorders are becoming more pronounced with ambulation and activities. Therefore, we aimed to compare the incidence of lower extremities deformity between CP patients with ambulation and CP patients without ambulation.
METHODS: This study was doneon CP patients who have outpatient physiotherapy in Hatay Drops of Hope Special Education and Rehabilitation Center. 23 patients (12Females-11Males) whose avarage of ages are 18.91±6.24 were assigned to 2 groups as groupI: CP with ambulation (n=13); groupII: CP without ambulation(n=10). Information of patients as demographic information, clinical type of disease, disease involvement and level, lower limb deformities and presence of epilepsy were written down. Gross Motor Functional Classification System (GMFCS) and Functional Mobility Scale (FMS) were used for evaluation and posture analysis was done. The analyses were performed using SPSS-V19. The data were analyzed by chi-square test for correlation between categorical variables. Statistical significance was considered to be $p<0.05$.
RESULTS: In the study, knee flexion deformity was frequently observed (30.43% of CP with ambulatin, 34.78% of CP without ambulation). But there was no significance between the incidence of knee flexion deformity and ambulation($p>0.05$). There was no significant difference between ambulation and pes planus, pes cavus, equinovarus, equinovalgus, flexion in the knee, hallux valgus, hammer finger, tibial torsion, calcaneovarus, calcaneovalgus and genu varum($p>0.05$). However it was observed that genu valgum deformity was higher in CP with ambulatin than CP without ambulation($p<0.05$).
CONCLUSIONS: In patients which were evaluated in our study, the most common observed lower extremities deformity was the knee flexion deformity. The statistically insignificant results are associated with the limited number of cases. We think that this study may be concluded with definitive results when studies included more patients will perform.

PC055

Examination of PTX-3, IL-6 and CRP Levels in a Rat Model of Short and Long-Term Exercise

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AIM: Different types of exercise may occurs damage in the muscles with different rate ratio in the cellular level. Muscle damage caused by exercise is determined by increasing rate of creatine kinase, myoglobin, and acute phase protein and interleukin levels in blood. The purpose of this study was to investigate the levels of PTX-3 (Pentraxin-3), IL-6 (interleukin-6) and CRP (C-Reactive Protein) in rats that underwent acute or chronic exercise.
METHODS: Thirty Wistar Albino male rats were grouped in to three equal groups as control, long-term and short-term. The short-term exercise group was performed 3 days/week, 10 min/day, 20 m/dk for a week. In long-term exercise groups was performed 7 days/week, 60 min/day for 4 weeks. At the end of the experiment, plasma PTX-3, IL-6 and CRP levels were measured by ELISA method. The results were evaluated with SPSS 17.0 software program by using Mann-Whitney U, Kruskal-Wallis, Wilcoxon and pearson correlation tests.
RESULTS: No significant difference between the levels of PTX-3, IL-6 and CRP was observed among the control, short and long-term exercise groups. The levels of IL-6 and CRP were not significantly different in short and long-term exercise groups. However, the level of PTX-3 was found higher in the long-term exercise group (3.04± 0.37) compared to the short-term exercise group (2.27± 0.58).
CONCLUSIONS: The level of PTX-3 increases in the muscle damage caused by long-term exercise compared to short-term exercise muscle damage. This increase shows that PTX-3 may have a protective role on muscle damage.

PC056

Comparing Accelerometer and International Physical Activity Questionnaire for Assessing Physical Activity Levels

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AIM: Physical activity (PA) may contribute to the development of healthy lifestyle. The importance of increasing PA for preventing obesity and diseases is known in literature. Many methods are used for assessing PA levels. Two of them are triaxial accelerometer and questionnaire. In our study it was aimed to assess the PA levels of groups according to body mass index (BMI) and to investigate the consistency between accelerometer and International Physical Activity Questionnaire (IPAQ).
METHODS: 64 participants between 18-30 years of age were included in our study in terms of their BMI values as underweight, normal, overweight and obese. Before accelerometer was used by participants, device was programmed with the participant's data and set to capture movements continuously in 1-minute intervals. Accelerometer was worn by the participant on the right or left hip which is used actively and then asked them to use consecutive 7 days through their daily life. After following 7 days, participants completed IPAQ. ANOVA, Tukey, LSD, Intraclass Correlation Coefficient and confidence interval were used for statistical analysis.
RESULTS: According to questionnaire's data, mean value of light intensity time in obese group was significantly higher than normal group (p=0.031). In normal (p=0.034), overweight (p=0.006) and obese (p=0.023) groups, mean value of light intensity time obtained from accelerometer was significantly higher than underweight group. There was no consistency between light (ICC=0.04; [-0.2092]-[0.2784]), moderate (ICC=-0.04; [-0.3198]-[0.2425]) and vigorous (ICC=-0.01; [-0.5407]-[0.5240]) intensity time obtained from questionnaire and accelerometer.
CONCLUSIONS: According to accelerometer data, normal, overweight and obese individuals spent more time in light intensity activity than underweight ones. According to questionnaire, obese individuals spent more time in light intensity activity than normal individuals. Because of being objective method, accelerometer may be preferred for assessing PA levels rather than questionnaire.

PC057

Effects of Physical Activity on Metabolic and Cardiac Hemodynamic Alterations Related with Fructose-rich Diet

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AIM: Fructose-rich diet induces obesity and metabolic changes. This study was to investigate the effect of voluntary physical activity on metabolic, cardiac hemodynamic and inflammatory alterations result from the fructose-rich diet.
METODS: Male rats were divided as control (C; n=7), fructose group which was fed 10% fructose to drinking water (F; n=7) and fructose-active group (FA; n=7) housed with a running wheel during 10 weeks. Daily fluid intake and body weight of rats were measured weekly. Serum glucose, triglycerides, total cholesterol, HDL, LDL were assessed using enzymatic method. Insulin, TNFα and IL6 levels were determined by ELISA method. Heart and liver weight was determined following the blood samples collection. Left ventricular developed pressure, maximum and minimum rate of change and heart rate were recorded by Langendorff apparatus. Kruskal-Wallis and Mann-Whitney U test were used for statistical analysis.
RESULTS: Weight gain between the first and 10th weeks were significantly lower for FA group (95.1±14.3 g), in comparison to F (109.0±6.6 g) and C (113.4±10.9 g) groups (p=0.04 and p=0.03). Liver weight was significantly higher for F group (11,8±1,0 g), in comparison to C (9,7±1,3 g) and FA (10,2±0,7g) groups (p=0.01 and p=0.01). Serum levels did not significantly differ between the groups. The maximum rate of change was found higher in FA group (2351.6±442.2) than F (1320±542.2) and C groups (1756±468.7) (p=0.01 and p=0.05).
CONCLUSIONS: The present study indicated that voluntary physical activity decreased weight gain and increased cardiac contractility without affecting metabolic and inflammatory parameters in rats which were fed with fructose-rich diet.
This study was supported by TÜBAP (2015/27).

PC058

Effects of Central FGF21 Infusion on TRH and TSH Levels

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AIM: Fibroblast growth factor 21 (FGF21) is an important endocrine hormone regulating multiple metabolic pathways. For all of these effects, FGF21 requires FGFR1c receptor and β-klotho co-receptor and they are expressed in the brain and especially pituitary gland and suprachiasmatic and paraventricular nucleus in the hypothalamus. Thyrotropin releasing hormone (TRH) is synthesized in the paraventricular nucleus of the hypothalamus and regulates the synthesis and bioactivity of thyroid stimulating hormone (TSH) in the pituitary gland. The aim of the study was to evaluate the effect of intracerebroventricular chronic FGF21 infusion on hypothalamic-TRH gene expression and serum TSH hormone levels.
METHODS: A total of 30 male rats were used in this study. They were divided randomly into three groups: FGF21, sham and control. FGF21 (0.72 µg/day) and vehicle (artificial cerebrospinal fluid) were infused intracerebroventricularly,in lateral ventricle of rats for 7 days, except control group. The all animals were sacrificed at the end of 7days, and blood and hypothalamus were collected from animals. Serum TSH levels were measured with ELISA and TRH gene expressions in hypothalamus were determined by Real-Time PCR.
RESULTS: FGF21 treatment group was compared to the control and sham group in terms of hypothalamic TRH gene expression and serum TSH hormone levels. TRH gene expression and serum TSH hormone levels of FGF21 group were significantly higher compared to control and sham groups ($p<0.05$).

CONCLUSIONS: These results indicate that intracerebroventricular FGF21 administration may play important roles in centrally regulation of thyroid hormones.
This study was supported by the Inonu University-BAP (Project no: 2014/16).

PC059

The Effect of Visceral Fat Amount on Anxiety Scores in Different Age Groups: The Role of Gender

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AIM: It is known that increased body weight and obesity especially visceral fat amount becomes a public health problem and is associated with various diseases. The incidence of anxiety and related diseases are increasing and modulated by body weight. Based on these data, we aimed to investigate the relationship of body weight and anxiety in men and women between 18-60 years of age.
METHODS: 220 women, 160 men volunteers were participated in this study (n=380). The ages, heights, weights and waist circumferences of these individuals were recorded and anxiety scores were calculated out of the "Beck Anxiety Inventory" applied. The data was grouped on the basis of gender, age-group, waist circumference and analyzed with SPSS 22.0 software. $p<0.05$ considered statistically significant.
RESULTS: The comparison according to age groups (18-29, 30-49, 50-60) and waist circumference (102 cm in men, 80 cm in women) revealed higher anxiety scores in women (10.8±5.8) with more visceral fat than corresponding men (7.6±5.0). All the other comparisons did not show any significant differences between groups for age, gender or waist circumference.
CONCLUSIONS: The results obtained in this study, pointing out the difference between women and men in 30-49 age-group may help to explain the higher incidence of some gender dependent diseases e.g autoinflammatory conditions. The observation of higher anxiety especially in wider waist circumference group also supports the role of body weight in this difference. But the insignificant difference in other groups makes us to consider to repeat the study with other scales. It will be helpful to use state and trait inventories in further studies.

PC060

Protective Effect of 1,25 dihydroxyvitamin D3 on HCl/Ethanol-induced Gastric Injury in Rats

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AIM: Beyond its role in calcium and phosphate homeostasis, calcitriol - active form of 1,25 dihydroxyvitamin D3 (vitD) - is known as an important modulator of cellular proliferation, differentiation, inflammation, and immune systems. The aim of study was to determine if vitamin D3 has protective effect against tissue injury in rat model of HCl/ethanol-induced gastric ulcer.
METHODS: Sprague-Dawley rats of both sexes (250-300 g; n=8) were fasted for 24 hours. Gastric injury was induced by acidified ethanol solution (0.3 M HCl/60% ethanol) per os (0.2 ml). Control group received saline (0.2 ml, per os). Ulcer groups were treated with VitD (0.25 µg/kg; intraperitoneally) for 14 days alone or along with nitric oxide synthase inhibitor L-NAME, the inhibitor of sulfhydryl groups N-ethylmaleimide (NEM), ATP-sensitive K+ channel blocker glibenclamide or cyclooxygenase inhibitor indomethacin (Indo). The rats underwent ulcer induction and decapitated 60 min later. The stomachs were examined macroscopically. Stomachs and trunk blood were sampled for biochemical assays. Values are means±SEM, compared using ANOVA and Student's t-tests.
RESULTS: Gastric macroscopic lesion score of untreated ulcer group (33.13±5.09) was decreased by pretreatment with VitD (19.00±4.34; $p<0.05$) and this effect was augmented by L-NAME (0.11±0.05; $p<0.01$) and attenuated by Indo (45.33±6.04; $p<0.01$) given along with VitD. Ulcer group revealed increased gastric malondialdehyde (MDA) (15.20±1.64 nmol/g; $p<0.001$), reduced endogenous antioxidant glutathione (GSH) levels (0.69±0.09 µmol/g; $p<0.05$) and increased myeloperoxidase (MPO) activity (20.96± 0.86 U/g; $p<0.001$) in comparison to control. Changes in these parameters were effectively suppressed by VitD (7.63±0.31 nmol/g; $p<0.01$, 1.33±0.16 µmol/g; $p<0.01$ and 8.82±0.41; $p<0.001$ U/g, respectively). Indo reversed effect of VitD on MDA, GSH and MPO levels ($p<0.05$-$p<0.001$) whilst NEM had slighter effect on gastric MDA and MPO levels achieved by VitD ($p<0.05$-$p<0.001$); but no difference in catalase and SOD.
CONCLUSIONS: VitD protected gastric tissue against oxidant injury via mechanisms possibly involving cyclooxygenase system.

PC061

Effect of Intravenous Glucose Administration on Catecholamine Concentrations in Hypothalamic Ventromedial Nucleus in Rats: A Microdialysis Study

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AIM: Hypothalamic ventromedial nucleus (VMN) have role for satiety signal and termination of feeding. Catecholaminergic projections to VMN involve in regulation of feeding. It is not known whether catecholamine levels in VMN change according as blood glucose concentration. Purpose of present study is to determine effect of intravenous glucose administration on catecholamine concentrations in VMN in adult male rats after hungry period for 24 hours and during normal feeding.
METHODS: Adult male Wistar rats feeding normally (two groups) and exposed to hunger (two groups) were used for this study. Microdialysis probes were implanted into VMN according to stereotaxic coordinates after anaesthesia and artificial cerebrospinal fluid was infused via microdialysis pump. Physiologic saline and 50% glucose solution were intravenously administered to groups (1.4 ml/kg). Microdialysis supernatants were collected before (control)

and after (for three times) application for 20min periods. Catecholamine concentrations in microdialysis samples were detected with liquid chromatography as pg/ml. Wilcoxon test was used for statistical evaluation.
RESULTS: Concentrations of norepinephrine and its' metabolite, dihydroxyphenylglycol were not different compared to control in saline and glucose treatment groups. Dopamine concentrations did not change in physiologic saline groups and glucose treatment hunger group, while there was a slight increase in normal feeding group after glucose administration (Values as mean±SEM in control: 0.16±0.02 and after application 0.30±0.11, 0,26±0.07 and 0.27±0.08, respectively). DOPAC (dopamine metabolite) concentration was not differ in glucose administered hunger group, whereas its' levels after glucose treatment in normal group were statistically higher than control ($p<0.05$, control values as mean±SEM: 0.69±0.07 and after glucose treatment: 1.76±0.48, 1.54±0.48 and 1.73±0.67, respectively).
CONCLUSION: These results demonstrate that dopaminergic neurotransmission in VMN may change due to blood glucose concentration. Hyperglycaemia after feeding may contribute to satiety sense by increasing dopamine concentration in VMN. Noradrenergic innervation in VMN does not seem to be affected by blood glucose level.

PC062

***In vitro* Effects of Linuron on Luteal Progesterone Synthesis**

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AIM: Linuron is a widely used herbicide in agriculture which humans and animals have a risk of exposure to. The aim of this study was to assess the *invitro* effects of linuron on luteal progesterone synthesis.
METHODS: Midluteal bovine ovaries were used as luteal cell sources. The cells were dissociated in oxygenated culture medium containing collagenase, DNase, bovine serum albumin and antibiotic solution by shaking at 37°C. The cells were incubated without treatment for the first 24 h. Subsequently, the cells were cultured with serum free media containing Linuron (0 µM, 50 µM, 100 µM and 200 µM) for the remaining 96 h. After starting the treatment, spent medium was replaced with fresh medium every 48 h. Progesterone concentrations in the culture media were measured via radioimmunoassay (RIA) method. Statistical analysis was assessed with ANOVA followed by Duncan test for multiple comparison.
RESULTS: Incubation of the cells with 100 µM and 200 µM linuron resulted in significant reduction ($P<0.01$) on progesterone production both on days 3 and 5. On the contrary, treatment of cells with 50 µM Linuron did not effected luteal progesterone synthesis throughout 96 h incubation. Treatment of cells with 200 µM Linuron resulted in 41% and 45% inhibition in progesterone production on day 3 and 5 respectively.
CONCLUSIONS: Conclusively, certain doses of Linuron have adverse effects on the invitro synthesis of luteal progesterone. Reproductive health is important for animal breeding and livestock economy. Present results indicate that maximum precaution must be taken to avoid exposure of Linuron to living organism.
This research was supported by Scientific and Technological Research Council of Turkey (TUBITAK) (Project No: TOVAG-213O174).

PC063

Does Irisin Affect Uncoupling Protein Levels in Fat and Muscle Tissues?

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AIM: Irisin is a hormone which mediates the beneficial effects of exercise and releases from muscle tissue during exercise. Uncoupling proteins are considered as an indicator of energy metabolism in peripheral tissues and the increased levels of these proteins in the fat and muscle tissue use the energy. In this study, the effects of the irisin application were determined on UCP1 in white and brown adipose tissue and UCP3 gene expression in muscle tissue in rats.
METHODS: 40 Wistar albino rats were used in this study and the rats were divided into 4 groups (n=10 per group). No application was administrated to the rats in the control group. For 7 days, 10 and 100 nm of irisin in experimental group and the solvent (artificial cerebrospinal fluid) infusion in sham group were performed intracerebroventricularly by means of osmotic mini-pumps (10 ml/h). End of the experiment the animals were killed and the interscapular brown, white adipose tissue and the biceps muscle tissue samples were collected. UCP1 from the white and brown adipose tissue and UCP3 mRNA expression from muscle tissue were determined by RT-PCR.
RESULTS: Both concentrations of irisin increased the levels of UCP1 in white and brown adipose tissue and UCP3 gene expression in muscle tissue when compared to the control and sham groups ($p<0.01$). No significant changes between the concentrations were identified.
CONCLUSIONS: Irisin regulates UCP1 and UCP3 mRNA expressions which are the indicator of peripheral energy consumption and mediates the beneficial effects of exercise on the energy metabolism.
This study was supported by TUBITAK Project No. 214S640.

PC064

Effects of Endocrine Disrupting Compounds on Fetal Development During Pregnancy

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AIM: Chemicals that inhibit normal function of the endocrine system are generally known as endocrine disrupting compounds. Most recent studies have shown that endocrine disrupting compounds affect mammals during fetal and post-natal life periods more than in adulthood. The aim of the present study was to investigate the effects of exposure of rats during maternity to various doses of diethylhexyl phthalate (DEHP) and di-n-butyl phthalate (DBP) on fetal skeletal development.
METHODS: İstanbul University animal experiments ethics committee approval was obtained. Pregnant Sprague-Dawley rats (n=4) used in the study of lipid application in control-prenatal, low dose prenatal, high dose prenatal groups (3 groups). Between the 6th and 19th days of pregnancy, 61 µg/kg/day and 61 mg/kg/day DEHP and DBP were administered to the rats by gavage feeding each day at the same time. The rats were anesthetized using ether on the 20th day of pregnancy and cervical dislocation was performed. The X-ray images of the fetuses were taken on 20th day of pregnancy. X-rays were performed at 42 kVp, 160 mA, and 0.01 s rotation
RESULTS: The X-ray images revealed that bone density levels were low in the group exposed to DEHP and DBP in high and low dose groups compared with in-lipid application control-prenatal group. The bone and embryonic development was not complete. Results of the statistical analysis demonstrated that there was an advanced level of difference between the control and the groups ($p<0.001$).
CONCLUSIONS: We investigated the skeletal development of fetuses removed from pregnant rats. We found that the frequently used phtalates DEHP and DBP delayed the bone development. In addition, the present study showed that a low dose of 61 µg/kg/day DEHP and DBP was effective on the skeletal system of fetuses.

PC065

The Effects of Tumor Necrosis Factor Alpha Inhibition on Apoptotic Cell Death In B-Cell with Type-I Diabetes-Induced by Streptozotocin

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AIM: Patients with rheumatoid arthritis (RA) suffer from co-morbidities because inflammation is important for the development of some disease, for example, diabetes mellitus. Type 1 diabetes is one of the most common chronic autoimmune diseases characterized by loss of insulin-producing beta cells. Tumor necrosis factor alpha (TNF-α) promotes the inflammation response and apoptotic cell death. The approach of targeting TNF-α has considerably improved the success in the treatment of RA. TNF inhibitors may improve the glycemic control in patients with concomitant RA and diabetes mellitus. The aim of the study was to investigate whether TNF-α inhibition by adalimumab, etanercept or golimumab can be achieved to modulate beta cell loss by apoptosis or not.
METHODS: The current study was used to human β-cell line. Total of 5 groups were created as control (C) Diabetes (D), Diabetes+Adalimumab (10 µg/ml; DA), Diabetes+Etanercept (5 µg/ml; DE), Diabetes+Golimumab (10 µg/ml; DG). After diabetes was created by using streptozotocin (20 mM), TNF-α inhibitors were incubated for 24 h. Protein was isolated to measure some apoptotic proteins for Western blot analysis.
RESULTS: Diabetes gave rise to increasing energetic stress by diminishing AMP-kinase (AMPK) protein level and initiate to apoptosis by alteration of p53 protein level, resulting in Smac/DIABLO efflux from mitochondria to cytosol that occurs downstream of cytochrome c release. Pharmacological inhibition of TNF-α could modulate the energetic stress in a beta cell by increasing AMPK protein level in DA, DE, DG groups. Hence, all TNF-α inhibition groups restored to cell loss through apoptosis by rising of p53 protein level compared to the diabetic group.
CONCLUSIONS: Although type-1 diabetes leads to losing β-cell by apoptosis, resulting from inflammation response, TNF-α inhibitions might prevent to β-cell by decreasing apoptotic proteins.

PC066

Thymoquinone Reduces the Inflammatory Response in Adipocytes

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AIM: In response to inflammatory signals, adipocytes have been shown to induce the expression of several acute phase proteins and mediators of inflammation. Thymoquinone, the main bioactive component of the black seed oil has been reported to have anti-inflammatory effects. The aim of this study was to investigate the modulation of inflammation by thymoquinone *in vitro* using 3T3-L1 mouse adipocytes.
METHODS: 3T3-L1 adipocytes were pretreated with thymoquinone one hour before lipopolysaccharide (LPS) treatment. The gene expression of tumour necrosis factor-alpha (TNF-α), plasminogen activator inhibitor-1 (PAI-1), monocyte chemoattractant protein 1 (MCP-1), leptin, interleukin-1β (IL-1β), IL-6 and IL-10 were measured by qRT-PCR. All data are expressed as means ± SD from three independent experiments. SPSS v.10 was used for statistical analyses. Differences between the mean values of multiple groups were analyzed by one-way analysis of variance followed by Tukey's post hoc test. Statistical significance was considered to be $p<0.05$.

RESULTS: Our data demonstrated that thymoquinone significantly reduced the expression of TNF-α, IL-1β, IL-6, MCP-1 and leptin ($p<0.05$), as well as suppressed the overexpression of PAI-1 induced by LPS ($p<0.05$) but thymoquinone treatment didn't show any effect on IL-10 expression in 3T3-L1 cell line ($p>0.05$).
CONCLUSIONS: Our findings suggested that thymoquinone counteracted the stimulatory effect of LPS on expression of pro-inflammatory adipokines, implying a potential anti-inflammatory effect during the inflammatory process in adipocytes.

PC067

Investigation of Anti-cancer Properties of 2,2,4,4-Tetra (4′-oxy-substituted-chalcone)-6,6-diphenylcyclotriphosphazene Derivatives Against Human Ovarian (A2780) and Prostate (PC-3) Cancer Cell Lines

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AIM: Phosphazenes, which consist of repeating units of –P=N– in their structure, are compounds having linear or cyclic structure connected to the two organic or inorganic side groups (R) in each phosphorus atom. Due to the reactivity of -Cl atom in their structure, the type of organic or inorganic group bonded as side groups to the phosphazene compounds changes physical, biological and chemical properties of these compounds. Recently, phosphazenes derivatives were found to be effective on various cancer cells. In this study, the chalcone-phosphazene compounds bearing –CH3/OCH3/Cl/F side groups at ortho position were conducted to investigate the effects on human ovarian (A2780) and prostate (PC-3) cancer cell lines.
METHODS: In the present study, 2,2,4,4-tetra(4′-oxy-substituted-kalkon)-6,6-diphenylcyclotriphosphazene compounds (chemical formula: compound 1;2,2,4,4-tetra(4′-oxy-2-methylchalcone)-6, 6-diphenylcyclotriphosphazene ($C_{76}H_{62}O_8N_3P_3$), compound 2; 2,2,4,4-tetra(4′-oxy-2-methoxychalcone)-6,6-diphenylcyclotriphosphazene ($C_{76}H_{62}O_{12}N_3P_3$), compound 3; 2,2,4,4-tetra(4′-oxy-2-chlorochalcone)-6,6-diphenylcyclo-triphosphazene ($C_{72}H_{50}O_8Cl_4N_3P_3$) and compound 4; 2,2,4,4-tetra (4′-oxy-2-fluorochalcone)-6,6-diphenylcyclotriphosphazene ($C_{72}H_{50}O_8F_4N_3P_3$)) were synthesized. Anti-tumor properties of these chalcone-phosphazene compounds in the different concentrations (1, 5, 25, 50 and 100 μM) were determined on human ovarian and prostate cancer cell lines by using [3-(4,5- dimethylthiazol)-2-yl]-2,5-diphenyl-2H-tetrazolium bromide] (MTT) assay method. The LogIC50 values of chalcone-phosphazene compounds on PC-3 and A2780 cell lines were calculated by using inhibition % values by the GraphPad Prism 6 program on a computer.
RESULTS: As a result, the chalcone-phosphazene compounds containing the methyl (1), methoxy (2), chloro (3), fluoro (4) side groups at ortho position were found to be effective against A2780 and PC-3 cancer cell lines ($p<0.05$). At 1, 5, 25, 50 and 100 μM concentrations of all the compounds significantly reduced the percentage of viability of A2780 cells ($p<0.05$).
CONCLUSIONS: These results displayed that cyclophosphazene bearing chalcone and phenyl groups may be useful for anticancer drug development in the future.
This work is supported by TUBITAK (Project Number: 115Z101).

PC068

The Effects on the Thyroid Hormones of the Application of Peripheral-Adropin in Rats

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AIM: Adropin has been defined as a metabolic hormone responsible for the regulation of the lipid metabolism having a molecular weight of 4499.9 Da and having 76 aminoacids isolated from the liver and brain tissues. It is regulated with the nutrition amounts and ensures the sustainment of energy homeostasis. In our study, we have examined the effects of adropin hormone in different dosages on the thyroid hormones.
METHODS: A total of 40 Wistar albino rats were used in this study. Four groups were formed each included 10 animals. First group control, second group sham, adropin was administered intraperitoneally to third and fourth groups 4μg/kg and 40μg/kg, respectively, for seven days. At the end of the experiment, the animals were euthanized. The blood samples were kept at -80°C until serum levels of hormones were analyzed. The levels of the thyroid stimulating hormone (TSH), triiodothyronine (T3) and thyroxin (T4) were measured by using ELISA method. The statistical analysis was performed using Bonferroni posthoc analysis following one-way ANOVA test. All the results arepresented as mean ±SD.
RESULTS: When compared to control group, the increased TSH and T4 levels in the groups which adropin was applied havenot been found significant; but, T3 level has been increased significantly in the group which high dose of adropin was applied when compared to control group ($P<0.05$).
CONCLUSIONS: It has been shown that adropin hormone that is related to the energy homeostasis could have an effect on the thyroid hormones by increasing T3 level.This study was supported by Ataturk University BAP (Project No:2015/281).

PC069

Is there Any Relationship Between Obesity and FGF21?

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AIM: Fibroblast growth factor 21 (FGF21), a 208 amino acid protein, is predominantly expressed in liver and also expressed in multiple metabolic tissues such as skeletal muscle, adipose tissue and pancreas and plays very important roles in glucose uptake and oxida-

tion, lipid metabolism and energy balance. The present study was designed to determine the effects of chronic intracerebroventricular (icv) FGF21 infusion on food consumption and body weight changes.
METHODS: In the study, 30 Wistar albino male rats were divided three groups: control, sham and FGF21 (n=10, for all groups). Brain infusion kits were implanted into lateral ventricle and osmotic mini pumps were subcutaneously implanted to sham and FGF21 groups. The animals in the experiment group were infused with FGF21 (0.72 µg/day) for 7 days, while rats in the sham group were infused with artificial cerebrospinal fluid (vehicle; 0.72 µg/day) for 7 days. Food consumption and body weights of animals were daily recorded. All statistical analyses were carried out using SPSS version 22.0 and Wilcoxon test followed by Bonferroni correction were performed.
RESULTS: Food consumptions of FGF21 infused animals were not found different from control and sham groups. Infusion of FGF21 caused significantly decreases in the body weights of rats compared to sham and control groups ($p<0.05$).t affect to food consumption. This study was supported by the Scientific Research Funds of Inonu University (Project no: 2014/16).

PC070

Determination of Anticancer and Antimicrobial Properties of *Alcea calvertii*

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AIM: For long years, the plant derived drugs are used for anticancer and antimicrobial purposes due to have low cost and less side effects by the majority of the World's instead of synthetic drugs. *Alcea calvertii L.* is belonging to *Malvaceae* family, and it is an endemic perennial plant. Previous studies have been shown that Alcea species have anti-viral, anti-inflammatory, diuretic and antimicrobial properties. In this study, it was investigated that the antimicrobial and anticancer properties of endemic A. calvertii flowers aqueous, ethanol, methanol and acetone extracts.
METHODS: The anticancer activities of extracts in different concentrations were determined on the prostate (LNCaP), colon (HCT-116) and breast (MCF-7) cell lines by using MTT assay. The antimicrobial properties of extracts were determined against different microorganisms may caused infection, such as Bacillus megaterium, Bacillus subtilis, Escherichia coli, Pseudomonas aeroginosa, Listeria monocytogenes, Klebsiella pneumonia, Proteus vulgaris, Staphylococcus aureus bacteria and Candidia albicans yeast by using inhibition zone method.
RESULTS: It was observed that A. calvertii aqueous, ethanol, methanol and acetone extracts were caused a significantly reduction on the cell viability of prostate (LNCaP), colon (HCT-116) and breast (MCF-7) cancer cell lines when compared to control values ($p<0.001$). A. calvertii methanol extracts have been shown higher antimicrobial activity than standard antibiotic on E. coli, B. subtilis, L. monocytogenes and C. albicans microorganisms.
CONCLUSIONS: Consequently, A. calvertii aqueous, ethanol, methanol and acetone extracts were significantly reduced the cell viability of prostate (LNCaP), colon (HCT-116) and breast (MCF-7) cancer cells, and A. calvertii methanol extract has potent antimicrobial activity.
This study was supported by TUBITAK (Project number: 114Z124)

PC071

The Effect of *Hypericum scabrum* on the Human Prostate, Colon and Breast Cancer

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AIM: It is considered that plants are the ancient drugs used for treatment of cancer. Especially after 60s and 70s, it was determined that the compounds obtained from plants have a significant effect in the treatment of some cancers. *Hypericum scabrum L.* is belonging to Hypericaceae family, and it is a perennial herbaceous plant. Previous studies have been shown that H. scabrum have liver and kidney protective, wound healing, anti-inflammatory, anticonvulsant, antioxidant, antiradical, antimicrobial, antibacterial, insecticidal and DNA damage inhibitory effects. In this study, we aimed to determine the effects of H. scabrum flowers aqueous and ethanol extracts on the cell viability of human prostate (LNCaP), human colon (HCT-116) and human breast (MCF-7) cancer.
METHODS: In this study, three cancer cell lines [prostate (LNCaP), colon (HCT-116) and breast (MCF-7)] were used. Changes occurring in the viability of cancer cells were determined by 3-(4,5-dimethylthiazol)-2-yl]-2,5-diphenyl-2H-tetrazolium bromide (MTT) assay. Statistical analyses were performed by SPSS 17.0 software package. $p<0.05$ value was considered statistically significant. According to MTT results, logarithmic inhibitory concentration value (LogIC50) was calculated by Graphpad prism 6 software.
RESULTS: It was found that H. scabrum flower extracts administration was caused a very significant reduction on the cell viability in the prostate (LNCaP), colon (HCT-116) and breast (MCF-7) cell lines when compared to the control values ($p<0.001$), and it was observed that this reduction was dose dependent.
CONCLUSIONS: Consequently, it was determined that H. scabrum aqueous and ethanol extracts have potent anticancer activity on the prostate (LNCaP), colon (HCT-116) and breast (MCF-7) cancer cells.

PC072

Salivary Cortisol Levels in Hungry Fasting Individuals at the First Week of Ramadan

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AIM: Fasting from sunrise to sunset in the month of Ramadan is a Muslim prayer. A breakfast is eaten before the sunrise and nothing is drunk or eaten until the dinner at the sunset. Effect of fasting on circadian rhythm of the stress axis, namely hypothalamo-pitiutary-adrenal axis, is not known. Therefore the aim of the current study was to assess the changes in salivary cortisol levels in the fasting individuals in the first week of the Ramadan.
METHODS: Women (n=51) and men (n=39) (age= 18-50) fasting in the first week of Ramadan participated to this study. Saliva samples were collected before morning breakfast (about 02.00 am, respectively), and at before and after dinner (about 19.00 pm and 21.00 pm, respectively). Additionally, another saliva sample was taken at 60 min following awakening (approx. 09.00 am). Some participants did not sleep before breakfasts while all slept after the breakfast. Mood scales were filled and dietary preferences were recorded. Cortisol were analyzed by ELISA method. Non-parametric tests were used to statistical analyze the non-normally distributed cortisol data.
RESULTS: Gender did not affect cortisol concentrations ($p>0.05$). Cortisol levels at morning following awakening (136.0±64.1) was highest than all other times ($p<0.005$). Moreover, cortisol levels was higher at breakfast (116.4±59.2) than before (17.0±2.2) and after dinner (79.3±44.9) time ($p<0.005$). Cortisol levels at breakfast were higher in participants (n= 52) who slept before breakfast ($p<0.05$). However, cortisol concentration in the following morning was not different between the participants who slept or did not sleep in the preceding night ($p>0.05$). Cortisol levels at all times were higher in the participants (n= 18) preferring high sugar food ($p<0.005$).
CONCLUSIONS: Fasting for approximately 16 hours did not disrupt normally profile of circadian cortisol secretion during the 1st week of Ramadan. Sleeping in the preceding night does not appear to affect morning cortisol levels. Preferring high sugar foods might be due to homeostatic effects of cortisol on blood glucose levels.

PC073

Examining the Effect of Stress-induced Increases in Cortisol Levels on the Dynamic Balance Scores of Medical Students

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AIM: Test anxiety is the main factor that hampers the achievement of students. Stress affects the hypothalamic-pituitary-adrenal (HPA) axis, leading to an increase in the cortisol level. This study aims to examine the effect of stress-induced increases in cortisol levels on the dynamic balance scores of medical students.
METHODS: This study was conducted with the participation of 107 students from Faculty of Medicine. To examine the dynamic balance of the students, the Star Excursion Balance Test (SEBT) was performed to test both right and left feet of the students during the period of relax a month before the committee exams. Saliva samples were taken and the State-Trait Anxiety Inventory (STAI-1) was performed to analyze the stress levels. The same tests were repeated on the day of the committee exam. Saliva samples were obtained and STAI-1 was performed again. Cortisol concentrations in the saliva samples were analyzed.
RESULTS: The statistical analysis shows that there is a statistically significant relationship between the results obtained from the analysis of cortisol as a stress indicator and the dynamic balance test conducted during the period of relax and the results of the dynamic balance test performed during the period of stress ($p<0.05$). The correlation analysis shows that balance scores decrease with increased level of stress.
CONCLUSIONS: The present study has shown that stress-induced increases in cortisol levels have a negative effect on the dynamic balance scores of the medical students.

PC074

The Effect of Stress and Exercise on Behaviour

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AIM: While stress is known to have a negative effect on the brain and exercise has positive effects. The aim of this study was to observe the effect of stress and exercise on animal behaviour.
METHODS: A total of 40 adult male Sprague-Dawley rats were used and the study lasted 45 days. Rats underwent sexual behaviour test and the ones who showed 2-4 ejaculations a day were included in the study. Animals were separated in 4 groups according their weight: control, exercise, stress+exercise, stress. Animals in the stress group were exposed to stress in a cabin where their movement was restricted. Stress exposure was increased periodically (starting at 1 hour to a maximum of 3 hours). On the other hand, animals in the exercise group underwent exercise on a treadmill. The speed of the exercise starting from 15 m/min up to 25 m/min. The duration of the exercise was increased from 15 min to 50 min. In the stress+exercise group animals were exposed to both stress and exercise. 3 days interval from the twentieth day with applied behavioral tests for animals of all groups.
RESULTS: According to forced-swimming depression test, floating (immobility) time increased significantly in animals under stress. Tail-suspension tests revealed that exercise significantly decreases stress-related depression. Light/dark transition test was used to determine anxiety in animals and showed that in animals under stress, the time spent under the dark was significantly different to their preference to stay under light. In the open-area test, that indirectly measures locomotor activity, all parameters except for defecation, disclosed significantly important differences between the groups.
CONCLUSIONS: It can be concluded that stress, created as a result of chronic physical restriction, leads to depression. Exercise has a very important role in decreasing stress-related depressive effect in animals exposed to stress.

PC075

Role of Centrally Injected Leptin on Prostaglandin Release from Posterior Hypothalamus and Nucleus Tractus Solitarius

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AIM: Leptinergic and prostaglandinergic systems, located within central nervous system, possess neuromodulatory activity. Both these systems play their role in the regulation of cardiovascular system within the CNS. Recently, the experiment performed in our laboratory on leptin depicted that leptin is implicated in the regulation of cardiovascular system through the mediation of central histaminergic system. In the recent past, another experiment performed on arachidonic acid which is a component of prostaglandinergic system demonstrated that there is an interaction between central arachidonic acid and central cholinergic nervous system in the brain. The fundamental purpose of this study was to show the association between centrally injected leptin and extracellular total prostaglandin (T-PG) concentration in posterior hypothalamus (PH) and nucleus of tractus solitarius (NTS) and its involment in the regulation cardiovascular system,
METHODS: 20 male Spraque-Dawley rats were utilized in the experiment. Microdialysis analysis was employed for measuring extracellular concentration of T-PG in PH and NTS. A dose of 20 µg of leptin was administered intracerebroventricularly. ELISA method was utilized to measure T-PG in the microdialyzate samples. Data are given as mean ± SEM of five measurements. Statistical analysis was performed using RM-ANOVA with posthoc Bonferroni test. $p<0.05$ was considered significant.
RESULTS: Following intracerebroventricular administration and comparison of the test groups with salt water control groups, Leptin induced a decline in the concentration of T-PG by 26% / 10% at 20th minute, 19% / 15% at 40th minute and 29% / 3% at 60th minute in PH and NTS, respectively.
CONCLUSIONS: In conclusion, prostaglandinergic system found in the PH and NTS, important centres for cardiovascular regulation, could play a role as a mediator in the central leptinergic system based control of cardiovascular system.

PC076

Decreased Sleep Duration Reduces Hypothalamo-pituitary-adrenal Axis Activity Without Affecting Autonomic Nervous System

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AIM: Changes in sleep duration have been reported to affect hypothalamic-pituitary-adrenal axis (HPA) and the autonomic nervous system (ANS) activities. However, the number of studies on the effect of sleep duration on HPA activity is very scarce and also, there are no studies on the effects of sleep duration on ANS activity. Aim of the current study, was, therefore, to examine effects of changes in sleep duration on cortisol awakening response as indicator of HPA and heart rate variability (HRV) as indicator of ANS activity.
METHODS: In this study, two groups were formed consisting of second year medical students. Sleep duration the first group (n=27) was reduced (sleep at 02:00 p.m., waking up at 06:30 a.m.), the second group (n=25) was allowed to sleep in normal duration (sleep at 11:00 p.m., waking up at 06:30 a.m.). In each day, sleep dairies were filled; salivary samples were taken at 0, 15, 30 and 60 min post-awakening for measurement of CAR; and electrocardiogram was recorded for 5 min for determination of HRV. Cortisol concentrations were measured in the salivary samples by enzyme immunoassay. Mann-Whitney U test was used for the data distributed non-normally and $p<0.05$ denoted statistical significance.
RESULTS: Restricted sleep duration decreased cortisol concentrations 15 and 30 minutes following awakening ($p<0.05$). Changes in sleep duration did not affect time- and frequency-domain parameters of HRV ($p>0.05$). Daily awakening problems score were higher but daily disturbed sleep score was lower in the restricted sleep ($p<0.05$).
CONCLUSIONS: Sleep restriction decreases cortisol concentration and this, in turn, is associated with awakening problems. On the other hand, autonomic nervous activity as measured by heart rate variability was not affected by sleep restriction.
This study was supported by İnönü University BAP (Project #2015-96)

PC077

Investigation of Biphosphonate and Melatonin Combine Treatment on Bone Formation/Resorption Rate and Morphology in a Rat Model of Osteoporosis

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AIM: First line therapy for osteoporosis based on pharmaceuticals which maintains bone mass such as bisphosphonate alendronate (ALN). There are evidences that melatonin reduces inflammation and has a regulator role on bone physiology. The aim was to evaluate the possible anti-osteoporotic effect of melatonin.
METHODS: Under anaesthesia, Sprague-Dawley rats (n=56) underwent bilateral ovariectomy (OVX), while control group had sham-surgery (n=8). OVX rats were treated with saline, alendronate (70 µg/kg/week, subcutaneously), melatonin (25 mg/kg/day, orally), melatonin+alendronate, luzindole (10 µg/kg/day, intraperitoneally) or alendronate + melatonin + luzindole for 8 weeks. Rats were euthanized at the end of 4th week (n=8) and 12th week (n=56). Transcription factor associated with osteoblast differentiation was determined using real-time polymerase chain reaction of Runx2 expression. Tibiae were stained with TUNEL kit and Masson's trichrome. Statistical analysis was performed using Kruskal-Wallis and ANOVA tests.
RESULTS: Runx2 expression was depressed in all OVX groups. Serum oestrogen level in the saline-treated groups was decreased at both the 4th and 12th weeks ($p<0.05$), while melatonin abolished this reduction. In melatonin- or alendronatetreated groups, trabecular bones were mostly calcified, with new bone forma-

tion in some regions and less separated lamellae. In alendronate+melatonin-treated group, quite regular, mostly calcified trabecular bones were present, while trabecular thickness was similar to sham-operated group. Moderate decreases in calcified areas and in trabecular thickness, increased decalcified areas with severe separation of lamellae in trabecular bones were observed in melatonin + luzindole-treated group, while these were milder in melatonin+ luzindole+alendronate-treated group. TUNEL analysis revealed significant decreases in both alendronate-treated and melatonintreated groups.
CONCLUSIONS: Similar to alendronate, melatonin has direct antiapoptotic and bone-mass-preserving effects without any additive action. The stimulatory effect of melatonin on trabecular thickness appears to be receptor-mediated.
Supported by Marmara University Research Fund.

PC078

The Moleculer Mechanism of Squalen on Cisplatin-induced Nefrotoxicity

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AIM: Cisplatin, a platinum compound, is used as a first-line agent against various forms of solid cancers. The clinical use of Cisplatin is highly restricted, because of its nephrotoxicity. Nephrotoxicity is an important adverse effect of Cisplatin therapy, which involves increased oxidative stress, inflammation, apoptosis, and activation of the mitogen-activated protein kinase (MAPK) pathway. Squalene is a natural organic compound originally obtained from shark liver oil. In this study, the molecular effects of Squalen against Cisplatin-induced oxidative stress and nephrotoxicity was investigated in mice.
METHODS: Studies were performed on male BALB/c mice (n=7). Group1was administered a single dose of Cisplatin i.p (7 mg/kg, dissolved in %0.9 SF), Group2 was administered a single dose SF i.p (7 mg/kg), Group3 was administered corn oil by orogastric gavage, (10 days), Group4 was administered 100 mg/kg Squalen (by orogastric gavage, 10 days) and Group5 was administered both a single dose and 100 mg/kg Squalen by orogastric gavage (10 days). After 10 days, the experiments were terminated. Oxidative stress parameters were measured colorimetrically. Interferon-gamma, IL6, IL10, IL17 and TNF-alpha were evaluated by luminometric analysis. The differences in the levels of Akt, p-Akt, GSK-3B, p-GSK-3B, mTOR, p-mTOR and Nrf2 were investigated by Western blot. Kidney damage was evaluated using PAS staining. Alldata were evaluated by ANOVA.
RESULTS: Application of squalene combined with Cisplatin was decreased oxidative stress parameters. Interferone-gamma (47.73 %; $p<0.05$), phospho-Akt (34.45 %; $p<0.05$) and phospho-mTOR (51.63 %; $p<0.05$) levels increased. GSK-3B and Nrf2 levels did not change significantly. Histopathologically glomerular/tubular degeneration and mesengial matrix ratio were found to be increased in Cisplatin group, whereas these parameters decreased in Cisplatin with Squalen group significantly ($p<0.05$).
CONCLUSIONS: It is considered that Squalen might ameliorate the nephrotoxic effect of cisplatin via fosfo AKT and mTOR pathways.

PC079

The Effects of Nifedipine in Liver Injury Induced by Renal Ischemia-Reperfusion

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AIM: Acute renal injury developing due to ischemia-reperfusion (I/R) damage may lead to dysfunction in extra-renal organs including liver and brain. Reperfusion borne injury might occur due to the increase and activation of leucocytes, release of reactive oxygen types like hydrogen peroxide (H2O2), and intracellular calcium (Ca2+) increase. In our study, we examined the effects of nifedipine, which is a nonspecific calcium channel antagonist, in liver injury induced by renal I/R by determining some oxidative stress markers and the CD38 and cyclic adenosine diphosphate ribose (cADPR) levels that have roles in intracellular calcium regulation.
METHODS: 24 Wistar Albino male rats weighing 240-260g were used in our study. 4 groups were formed each of which had 6 animals. The 1st Group was the Control Group (C). In the 2nd Group, the Sham (S) Group; right kidney was dissected. In the 3rd Group (I/R), 1hour ischemia 24 hour reperfusion were applied to the left kidney after the right kidney was dissected. In the 4th Group (N), the same surgical procedures were applied as in the 3rd Group, and 4mg/kg nifedipine was administered intraperitoneally before the reperfusion started. The statistical analyses and the results are given as mean±SD. The differences were compared with the Tukey Post Hoc Analysis following the one-way ANOVA test.
RESULTS: It was observed that applying nifedipine in liver injury occurring due to renal I/R decreased the MDA, GSH, MPO and H2O2 levels in the group which received nifedipine, when compared with the I/R Group, and increased the SOD, Cat, CD38 and cADPR levels; however, these changes are not significant. In the histological examinations; the renal injury increasing with I/R, Caspase-3 expression have decreased with the application of calcium canal antagonists.
This study was supported by Atatürk University SRP (2014/146).

PC080

Effects of *Hypericum perforatum* on Renal Ischemia-Reperfusion Injury in the Rat

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AIM: Acute renal failure (ARF) is a common clinical problem with high rates of mortality and morbidity. Renal ischemia/reperfusion (I/R) is one of the most common causes of ARF. Renal I/R causes the occurrence of acute inflammatory response and formation of reactive oxygen species. *Hypericum perforatum* (HP) popularly called St. John's wort, is one of the most important pharmaceutical herbs and its extract contains flavonoids and phenolic acids, which have been demonstrated exerting very efficient anti-inflammatory effects and a free radical scavenging activity in animal model of acute inflammation. In this study, we investigated whether HP may have a protective effect against renal I/R damage.
METHODS: Male Sprague-Dawley rats (n=24) were divided into three groups, each including 8 animals: (1) Control group, in which the rats only underwent right nephrectomy; (2) I/R group, right nephrectomy and left kidney ischemia (45 min) and reperfusion (3 h); (3) I/R+HP group, right nephrectomy and left kidney ischemia (45 min) and reperfusion (3 h), HP administrated 50 mg/kg intraperitoneally at the beginning of ischemia. Changes in the rat kidney were observed by measuring the tissue levels of malondialdehyde (MDA), glutathione (GSH), and superoxide dismutase (SOD), glutathione peroxidase (GSH-PX), catalase (CAT) enzyme activity and serum levels of blood urea nitrogen (BUN), creatinine (Cre).
RESULTS: In the I/R group, serum levels of BUN and Cre, kidney tissue MDA level increased and kidney tissue GSH-PX, CAT, SOD enzyme activity levels decreased significantly compared to the control group ($P<0.05$). In the IR+HP groups' serum levels of BUN and Cre increased, and kidney tissue SOD enzyme activity levels decreased significantly compared to the control group ($P<0.05$). In the IR+HP groups' kidney tissue GSH-PX, CAT, SOD enzyme activity levels increased significantly compared to the I/R group ($P<0.05$).
CONCLUSIONS: This study showed that HP prevents increasing of MDA levels and decreasing of GSH-PX, CAT, SOD enzyme activity levels in renal induced by I/R but the other changes didn't the improvement.
This study was supported by İnönü University BAP (2016/40).

PC081

Effects of Maternal Nicotine Exposure on the Caspase-3 Expression in the Kidney Tubule Cells

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AIM: Maternal exposure to cigarette smoke has been shown to have detrimental effects on the development of fetuses and infants. Nicotine is an important component of cigarette smoke and offspring have been exposed to nicotine via the placenta and mother's milk. Nicotine has been reported to induced apoptosis in offspring tissue. Nicotine shows its effects through activating nicotinic acetylcholine receptors (nAChRs). For that reason, it has been thought that increased expression of apoptotic markers in the cells associated by activating of nAChRs. In the present study, we aimed to investigate the apoptotic effect of nicotine in renal tubule cells of offspring of rats exposed to nicotine during gestation and lactation period.
METHODS: Male and female Wistar albino rats weighing 200-250 gr were housed in cages throughout the study in a well ventilated room with a 12 h light/12 h dark cycle at 21 °C. Animals were fed standard rat chow ad libitum. After confirming pregnancy with the vaginal smear method, pregnant rats were randomly assigned into two groups; nicotine (3 mg/kg, intraperitoneally during pregnancy and lactation period) and control (0.5 cc, intraperitoneally nicotine solvent-normal saline). At the end of the experiment, renal tissue evaluated in terms of caspase 3 immunoreactivity. Mann-Whitney U test was used for comparison between groups. Values of $P<0.05$ were considered significant.
RESULTS: In histological evaluations, caspase 3 expression was observed locally and weak in the tubules of control rats. On the other hand, there was an increase in caspase 3 expression in the nicotine group. Moreover, intensity of caspase 3 staining has increased in this group. In the nicotine group, increase of caspase 3 staining in the tubules was determined as statistically significant when compared with control group ($p=0.001$).
CONCLUSIONS: This study showed that, maternal nicotine exposure increases the caspase 3 expression in renal tubule cells. As a result, this exposure induces the apoptotic cell death due to caspase 3 activation. Apoptosis of renal tubule cells has an important role in development of renal failure.

PC082

Importance of Urinary Platelet-derived Growth Factor in Early Diagnosis of Diabetic Nephropathy and the Relation Between Diabetic Neuropathy in Patients with Type 2 Diabetes Mellitus

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AIM: Diabetes mellitus (DM) is the most important reason of end stage renal failure in the most of the developed countries and Turkey. But, early diagnosis and treatment of this disease are delayed since nephropathy does not show any symptom or sign in early stage. Today, biomarkers are required for early diagnosis even before microalbuminuria. In this study, the relationship of PDGF-BB with the degree of albuminuria and neuropathy in diabetic nephropathy was investigated.
METHODS: 54 diabetic patients and 20 healthy volunteers were included in the study. Diabetic patients were divided into 3 groups such as normoalbuminuric, microalbuminuric and macroalbuminuric according to their levels of urinary microalbumin; and into 2 groups according to the existence of diabetic neuropathy and retinopathy. Urinary PDGF-BB, microalbumin, serum HDL, LDL,

triglyceride, total cholesterol, blood HbA1c levels were analyzed on each groups. Electromyography was done for the evaluation of diabetic neuropathy.
RESULTS: No significant difference was determined in the comparison of normo, micro, macroalbuminuric groups in terms of urinary PDGF-BB levels. The levels of cholesterol in macroalbuminuric group were significantly higher than the microalbuminuric (p=0.008), normoalbuminuric (p=0.001) and control group (p<0.001). The concentration of urinary PDGF-BB in neuropathic group was higher than in the non-neuropathic group (p<0.001). The levels of HbA1c in retinopathic group were higher than in the non-retinopathic group (p<0.001).
CONCLUSIONS: The results of this study revealed that urinary PDGF-BB cannot be used as a biomarker for the early diagnosis of diabetic nephropathy. In this study the association between the urinary PDGF-BB and diabetic neuropathy has been found to be significant for the first time. This work may inspire future studies on this subject.

PC083

Investigation of the Effects of Some Catecholamines on the Activity of Carbonic Anhydrase Enzyme Purified from Bovine Kidney Tissue

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AIM: Carbonic anhydrase (CA, EC 4.2.1.1) is known as a very important enzyme regulating CO2 levels in living organisms. CA which exists usually in mammalian tissues catalyzes interconversion hydration whereby carbon dioxide is transported to hydrogen ion. Since CA inhibitors decreases pressure in the eye they lead developing numerous medicines against glaucoma, antitumor, pain reliever, epilepsy, and neurological diseases.Therefore, the inhibition mechanism of CA enzymes must be explored clearly in order to synthesize new crucial compounds.It was aimed in this study to purify of CA enzyme from healthy bovine kidney tissue and investigate of inhibitory effects of catechol, tyrosine, noradrenaline, and adrenaline.
METHODS: Kidney tissue was fractionated by liquid nitrogen. 50 mM K- phosphate, (pH 7.5), buffer was used to prepare homogenate. It was centrifuged at 10,000 g for 30 min. Bovine kidney enzyme was isolated by means of cellulose-phenyl-sulphonamide affinity column. CA activity was determined by the esterase method which follows the formation of 4-nitrophenylacetate to 4-nitrophenol at 348 nm. Activit%-[Inhibitor] graphs were drawn and I50 values were calculated.
RESULTS: Bovine kidney CA enzyme was purified 43.35 fold with 813.33 EU/mg protein and 42.5% yield using affinity chromatography. Most of these compounds were observed to inhibit these enzymes at low concentrations. CA enzyme IC50 values of catechol, L-tyrosine, and adrenaline were 9.85 ± 0.07, 27.72 ± 0.11, and 30.13 ± 0.12 µM, respectively.
CONCLUSIONS: Bovine kidney CA enzyme was purified and inhibition effects of some catecholamines on the enzyme was investigated. The molecules were found to inhibit CA enzyme. Thus, use of these molecules in treating certain diseases can be beneficial due to the inhibition effects of these molecules on CA enzymes. This study was financed by Turkish Research Council-TÜBİTAK (KBAG 114Z731).

PC084

Investigation of Inhibitory Effects of Some Sulfonamides on Acethylcholinesterase Enzyme

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AIM: Acetylcholinesterase (AChE) hydrolyses the neurotransmitter acetylcholine to acetic acid and choline. It was aimed in this study to investigate inhibitory effects of benzenesulfonamide, p-toluenesulfonamide, sulfanilamide, mafenide, and 4-chloro benzenesulfonamide on AChE enzyme.
METHODS: The AChE inhibition assay was determined using the spectrophotometric Ellman's method. The absorbance was read at 412 nm and 5,5′-dithiobisbis nitrobenzoic acid (DTNB), and acetylthiocholine iodide (ATChI) were used as substrates. Activity%-[Inhibitor] graphs were drawn and IC50 values were calculated.
RESULTS: Benzenesulfonamide, p-toluenesulfonamide, sulfanilamide, mafenide, and 4-chloro benzenesulfonamide tested were observed to inhibit this enzyme at low concentrations.
CONCLUSIONS: Inhibitoryeffects of some sulfonamides on AChE enzyme was investigated. It was observed that IC50 values of benzenesulfonamide, p-toluenesulfonamide, sulfanilamide, mafenide, and 4-chloro benzenesulfonamide were 0.512, 0.543, 0.36, 0.457, and 0.243 µM, respectively. % Activity - [inhibitor] plots by plotting the calculated IC50 values were found to be significant when compared with literature. The error margin in the study was found to be in the range of 1-3%.

PC085

Purification of Carbonic Anhydrase Enzyme from Bovine Liver Tissue and Investigation of yhe Inhibitory Effects of Bischalcone Derivatives

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AIM: It was aimed in this study to purify carbonic anhydrase II (bCA II) enzyme from healthy bovine liver tissue by means of newly synthesized affinity gel and to investigate inhibitory effects of five different bischalcone, catechol, resorcinol, progallol, and acetazolamide (AZA).

METHODS: Bovine liver CA II isoenzyme was isolated by means of cellulose-phenyl-sulphonamide affinity column. Molecular weight and purity of the enzyme was determined by SDS-PAGE. CA activity was determined by the esterase method which follows the formation of 4-nitrophenylacetate to 4-nitrophenol at 348 nm. Activit%-[Inhibitor] graphs were drawn and IC50 values were calculated.
RESULTS: Bovine liver CA II enzyme was purified 59.4 fold with 1160 EU/mg protein and 40.14% yield. Most of these compounds were observed to inhibit this enzyme at low concentrations.
CONCLUSIONS: bCA II enzyme was purified and inhibitory effects of bischalcon derivative compounds, catechol, resorcinol, pyrogallol, and AZA on the enzyme were investigated. Inhibition effects on the enzyme wheras bischalcon derivatives, phenolic compounds moderate and AZA had strong inhibitory actions. The margin of error for the IC 50 values found in this study between 1-3%. This study was financed by Turkish Research Council-TÜBİTAK (KBAG 114Z731).

PC086

Bovine Liver Tissue on Glutathione Reductase Enzyme Determination of Effects of Thiamine, Tyrosine, Dopamine and Adrenaline

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AIM: It was aimed in this study to partially purify glutathione reductase (GR) enzyme from healthy bovine liver and to investigate inhibitory effects of thiamine pyrophosphate, L-tyrosine, dopamine, and adrenaline.
METHODS: Liver tissue used broken down into by liquid nitrogen. 50 mM K- phosphate, 1 mM EDTA (pH 6.0), buffer was prepared homogenates. It was centrifuged at 10,000 g for 30 min. (NH4)2SO4 precipitation and dialysis were performed purification. GR enzyme purified by 2', 5'-ADP Sepharose-4B affinity chromatography. GR activity was determined as substrates NADPH and GSSG at 340 nm. Activit %-[Inhibitor] graphs were drawn and IC50 values were calculated.
RESULTS: Used different purification method bovine liver GR enzyme was purified 41.89 fold with 12.944 EU/mg protein and 62.33% yield. Most of these compounds were observed to inhibit this enzyme at low concentrations.
CONCLUSIONS: Bovine liver GR enzyme was purified and inhibition effects of some natural amines on the enzyme was investigated. Liver GR enzyme IC50 values of thiamine pyrophosphate 6.79 µM, L-tyrosine 4.03 µM, dopamine 5.21 µM, and adrenaline 3.31 µM were determined. Values of inhibition obtained was determined to be statistically significant. The error margin in the study was found to be in the range of %1-3.

PC087

Investigation of Degeneration Process by Thiol-disulphide Homeostasis in Surgical and Natural Menopause

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AIM: Thiol-disulphide homeostasis indicates overall degeneration/regeneration status of the body and a shift towards thiol denotes the dominance of dejeneration. We aimed to investigate thiol-disulphide homeostasis in naturally or surgically induced postmenapausal women.
METHODS: After obtaining the informed consent, a total of 107 participants, who applied to the Ankara Training and Research Hospital, Department of Obstetrics and Gynecology, were divided into natural menopause (n=75) and surgical menopause (n=32) groups. The groups were compared for clinical findings determined by patient history and physical examination, and lipid profile, albumin, total protein, lipoprotein a, seruloplasmin, catalase, myeloperoxidase and thiol-disulfide balance measured in blood samples.
RESULTS: The study groups were similar for age, body mass index and the duration of the menopause. The serum thiol level was significantly higher in surgical menopause group (207.1±75.5; 282.6±86.5), (p <0.001) and the serum disulfide level was significantly higher in natural menopause group (24.8±7.7; 21.0±8.3), (p=0.03). Thiol-disulfide balance was shifted towards disulfide in surgical menopause group (Disulphide/thiol % ratio was 15.9±13.2 and 8.9±6.3 in natural and surgical menopause groups, respectively) (p=0.001). The serum thiol level was moderately correlated with lipoprotein a (r=-0.342, p=0.001), albumin (r=0.483, p<0.001) and total protein (r=0.468, p<0.001).The serum disulphide level was negatively correlated with albumin (r=-0.318, p=0.001) and total protein (r=-0.303, p=0.002).
CONCLUSIONS: The level of serum thiol-disulphide and their correlations with serum lipid and protein levels indicates a slower degeneration process in surgical menopause group. It can be suggested that compensation mechanisms in women experiencing surgical menopause, before completing the natural degeneration process, was stronger. The metabolic cost of the menopausal period is less.

PC088

Time- and Dose-dependent Effects of Lead on the Number of Cultured Granulosa Cells Showing Steroidogenic Activity

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AIM: It is well known that lead has adverse effects on biological systems. The aim of this study was to determine the time- and dose-dependent effects of lead acetate trihydrate on the number of cultured granulosa cells showing steroidogenic activity.
METHODS:Cattle ovaries were collected from the local abattoir. After dissecting the follicle from the ovaries, it (4-8 mm) was placed

in a petri dish. Granulosa cells were gently scraped from the inner surface of the follicular with an inoculation loop. The cells (25.000 cell / well) were incubated without treatment for the first 24 h. Subsequently, granulosa cells were incubated in media containing lead acetate trihydrate (500, 1000 and 2000 μM) for an additional 12, 24 or 48 h. After each incubation period, cells growing on the bottom surface of the plates were stained for 3beta-Hydroxysteroid dehydrogenase(3β-HSD)activity. Stained cells were counted on an inverted microscope.
RESULTS:Incubation of the cells with 3 different doses of lead for 12 hours did not induce any effect on the granulosa cells. In contrast, treatment of cells with increased lead doses for 24 hours resulted in significant decline ($p<0.001$) in the cell number only at the highest application. Additionally, incubation of the cells with 1000 and 2000 μM lead for 48 hours also induced significant ($p<0.01$) reduction. Rate of reduction changed between 28% and 57% depending on the doses of the lead used and duration of the incubation.
CONCLUSIONS: As a result, adverse effects of lead acetate trihydrate on the number of cultured granulosa cells were observed depending on the dose and incubation duration.

PC089

Cortisol Awakening Response, Ovarian Steroids and Premenstrual Symptoms in Healthy Premenopausal Women

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AIM: Premenopause, characterized by menstrual irregularities, endocrine changes and abnormal menses, coincides with psychological distress, instability, anxiety and mood disorders. Disruption in cortisol, estradiol and progesterone secretions may play crucial roles in manifestation of these symptoms. Thus, our aim was to assess progesterone and estradiol secretions and cortisol awakening response (CAR) at the menstrual and premenstrual stages in premenopausal women.
METHODS: CAR was assessed by measuring salivary cortisol at 0, 15, 30 and 60 min immediately following awakening (n=15, age= 41-50) at menstrual and premenstrual stages of the menstrual cycle. Saliva sample taken at 60 min was also used for determination of progesterone and estradiol. DRSP (Daily Records of Severity of Problems), STAI II (trait anxiety inventory) and VAS (visual analog scale) were used to assess presence of premenstrual syndrome, anxiety and pain, respectively.
RESULTS: CAR was lower during menstruation ($p<0.01$). Progesterone was significantly elevated during premenstrual period ($p<0.01$) but estradiol was unchanged ($p>0.05$). Positive significant correlations were found between cortisol and progesterone ($R2= 0.471$; $p<0.02$) at menstrual period; cortisol and estradiol ($R2= 0.418$; $p<0.05$) at premenstrual period. Negative significant correlations were found between menstrual cortisol and STAI II ($R2= -0.627$; $p<0.02$) or menstrual pain ($R2= -0.577$; $p<0.02$). Premenstrual syndrome scores were similar ($p>0.05$).
CONCLUSIONS: Decreased CAR during menstrual stage was associated with lower progesterone but higher anxiety and pain in premenopausal women. This suggests that CAR might be an important correlate of ovarian dynamics and behavior in menstrual cycle physiology.
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PC090

The Effects of Adropin Application on the Hormones Having a Role in the Reproduction Function

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AIM: Adropin, determined by Kumar et al in hypothalamus and many tissues in 2008, is a novel metabolic hormone. In our study, we examined the effects of different dosages of adropin hormone on hypothalamus hypophysis gonadal axis, modulating reproductive functions.
METHODS: A total of 40 Wistar albino rats were used in this study. 4 groups were formed each included 10 animals. First group control, second group sham. Adropin was administered intraperitoneally to third and fourth groups 4μg/kg and 40μg/kg, respectively, for 7 days. The hormone levels of follicle stimulating hormone (FSH), luteinizing hormone (LH), inhibin, activin and testosterone have been measured by using ELISA method. The statistical analysis was performed using Bonferroni posthoc analysis followed byone-way ANOVA test. All the results werepresented as mean±SD.
RESULTS: When compared to the control group; while FSH level does not change in the groups to which high dose adropin was applied, activin and LH levels were decreased ($P<0.05$), testosterone and inhibin levels were increased ($P<0.05$).
CONCLUSIONS: Administration of adropin may cause to the decrease of LH level due to the negative feedback by increasing the level of testosterone. In addition, we think that it may cause to the stability of FSH level due to the effects on inhibin and activin. This study was supported by Atatürk University BAP (Project no:2015/39).

PC091

Maternal Viral Infection in the Late Gestation Shortens Time to Puberty without Affecting Body Weight in Rat Offspring

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AIM: Viral infections during pregnancy result in neurological disorders in rat offspring. As reproduction is also controlled by neuroendocrine mechanisms, we postulated that viral infections might also perturb reproductive functions including timing of puberty in rat offspring. For that purpose, we injected a viral mimetic to pregnant rats and assessed the time to puberty in the offspring.
METHODS: Pregnant Sprague-Dawley rats were injected (i.p.) with saline or poly i:c, a viral mimetic, at the late pregnancy (day 17) and female and male offspring born were taken into the experiment. Finally, a total of four groups were formed: male poly i:c (n=10), male control (n=4) female poly i:c (n=5) and female control (n=4). Their body weight was followed from weaning to puberty. Vaginal opening and preputial separation was used to assess timing of puberty in female and male offspring. Data was analyzed using ANOVA wit-

hin MINITAB statistical software. P<0.05 was accepted as statistically different.
RESULTS: Body weight at weaning and puberty were indifferent between the groups (P>0.05). Both male and female offspring had similar body weight increases from weaning to puberty. Puberty was earlier in the poly i:c injected groups than the control groups (45.1±1.3 vs. 51.5±0.8 days; P=0.004).
CONCLUSIONS: As a preliminary study, it has been shown for the first time that viral infections in the late gestation might hasten puberty in the next generation. This finding might add new dimensions to the unresolved issue of precocious puberty observed in humans.
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PC092

Effect of the Incubation Time and High Dose Lead Application on Steroidogenic Luteal Cell Numbers

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AIM:According to recent data, heavy metals have detrimental effects on human and animal reproduction. Present study was designated to investigate effect of the incubation time and high dose lead application on the number of bovine luteal cells showing steroidogenic activity
METHODS:Luteal cells were isolated from midluteal bovine corpora lutea. Luteal tissue was decomposed into the cells in oxygenated culture media containing collagenase, bovine serum albumin, DNase, and antibiotic/antimycotic solution. Luteal cells were incubated without treatment to induce the adhesion of cells to the bottom of the plate for 24 h. Afterwards, cells were exposed to lead acetate trihydrate (500, 1000 or 2000 μM) for 12, 24, or 48 h. At the end of the incubation, cells were assessed with regard to the activity of 3β-HSD, and counted, via sampling technique according to “the equal opportunity rule” on the bottom of the plate under an inverted microscope.
RESULTS:All three doses of lead induced a significant reduction (P<0.05), depending on dose and time, in the number of luteal cells showing steroidogenic activity. Treatment of the cells with 500, 1000 or 2000 μM lead resulted in 23-46%, 33-58%, and 40-72% decrease in cell numbers respectively, at 12, 24, or 48 h of incubation.
CONCLUSIONS:Consequently, it was observed that even the lowest dose of the lead caused negative effects on the luteal cell count at 12 h incubation. Moreover, reduction in cell numbers was in parallel with the applied dose and time.

PC093

Effects of Regular Exercise on Endogenic Reproductive Hormones in Men

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AIM: The effects of regular exercise on hormones have been subject of many research and the idea that hormonal changes answered physical activity by metabolic and endocrine adaptation has gained weight. Also it has been reported that there is a relation between physical activity and FSH and LH of pituitary gonadotropins, estrogen and testosteron of reproductive hormones and prolaktin which is also pituitary. However, it is observed that these works had focused on females and works on males has not been enough. The purpose of the study is to examine in the blood the effects of regular exercise on the levels of FSH, LH, estradiol, total testosteron, TSH and prolactin hormones.
METHODS: In this work, approximately 10 ml of venousblood was taken from 40 males between 18-25 years old (20 control, 20 exercise) in the laboratory of Kayseri Medical Palace Hospital in the morning at 09:00 and was centrifuged at +4C, in 4000 rev/min for 5 min. Results were compared with each other as ng/mL. Obtained findings wereanalysed by independent t test and values which are at P<0.05 level were accepted as significantly different. All procedures were approved by The Clinical Ethics Committee of Ondokuz Mayıs University.
RESULTS: According to resulsts of analysis, averages of all parameters, except for TSH, were determined as high level in the sedantery group. Also, in the sedantery group, the levels of estradiol, LH and testosteron were determined as statistically significant. The body mass index of participants were significantly different.
CONCLUSIONS: According to these findings, we suggest that regular exercise programmes can affect some male reproductive hormones and would reduce body mass index. However, it is thought that to specify this affect, measurements should be made by testing the protocols of acute/chronic trainings and different energy systems (aerobic-anaerobic). Because, the present findings contradict with the hypothesis that regular exercise increases reproductive hormones.

PC094

Gestational Viral Mimetic Administration in Rats does not Alter Leptin and Corticosterone Levels in Male Offspring

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AIM: Resveratrol (RSV) is knownwithitsanticancer,anti-inflammatory, antioxidativeeffects.Theaim of presentstudywastoinvestigethemorphologic,biochemicalandfunctionaleffects of RSV on diabeticnephropathy (DN) in streptozotocin (STZ)-diabeticrat model.
METHODS: EthicalComitteefortheUseandCare of Laboratory Animals of Gazi Universityapprovedtheproceduresused in thisstudy. 30 adultmale Wistar albino ratssweighing 250-300g wereused in experiments.Theratsweredividedinto 4 groups as follows:1.Control, 2.Resveratrol, 3.Diabetes, 4.Diabetes+Resveratrol.STZ (65 mg/kg 0.1M incitratebuffer) were administered to diabetes groups, citratebuffer were administered to control groups intraperitoneally as a singledose.Twoweeksafter STZ administration,abasalbloodglucoselevelabove 250 mg/dl were considered diabetic. Application of RSV (10/mg/kg/daydose (dissolved in 0.1M ethanol) orvehicle wasstarted 2 weeksafterdiabetesformationandcontinuedthrough 8 weeksbyusing oral gavage.Attheend of experiments, rats were anaesthetized with Rompun+ketamine (50+60-100mg/kg), and sacrificed by cardiac puncture. During the study:Fasting blood glucose levels, renal functions were analyzed and renal vascular responsesand immunohistochemically, morphological research performed

by TEM, proinflammatory cytokines TGF-β, iNOS, eNOS, fibronectin levels were measured. However, kidney tissue oxidant (Malondialdehyde/MDA) andantioxidants (glutathione/GSH) parameters were studied, total nitricoxide (NOx) levels were also determined. Results in SPSS, Kruskal-Wallis and Mann-Whitney tests were compared. p<0.05 was considered significant.
RESULTS: and CONCLUSIONS: Fasting blood glucose, fluidintake, urine volume, ALP, ALT, BUN and creatinine levels in blood were determined to increase in diabetic groups and diminution in sodium-level (p<0.05). But, application of RSV doesnt have any effect on that parameters. Indiabetic and RSV applied groups; Angiotensin II (AngII) and Phenilephrine (Phe) on perfussion pressure weren't significant when compared with the control. However, both Ang II and Phe effects were significantly decreased in Diabetes+Resveratrol (p<0.05). In the same group, vasodilator responses of acetylcholine (ACh) were found to significantly decrease (p<0.05). By RSV treatment, diabetes induced increased kidney MDA levels were decreased (p<0.01) and GSH levels were increased (p<0.01) but NOx levels weren't affected. Examination of TEM: application of RSV, diabetes-related deteriorating renal tissue was significantly preserved. Increment of TGFβ,fibronectinandiNOSimmunreactivityarepartially-decreased, however, decreasede NOS level is increased with treatment of RSV.
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PC095

Comparison of Bioactivity of Dioxins in Breast Milk with Body Mass Index in Lactating Mothers

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AIM: Organochlorinated chemicals are persistent pollutants that pose a threat to the environment and human health. The aim of this study was to investigate bioactivity of dioxins and dioxin-like chemicals and a possible relationship with Body Mass Index (BMI) of breastfeeding mothers and fat content of donated milk.
METHODS: Milk samples were collected from 200 healthy lactating mothers who live in İstanbul. Sample collection procedure was approved by the local ethics committee. Each mother was asked to fill a questionnaire form including personal information, medical records and nutritional behavior. Mothers donated about 10 ml breast milk. 5 ml of milk samples was shaken for 10 min with 5 ml of isopropanol and 10 ml of n-Hexane. The upper phase was transferred to a glass tube and evaporated in a nitrogen-evaporator at 45 oC. Remained fat was weighted and suspended with n-Hexane including 3% diethyl ether. The solution was cleaned-up with a silica column. Dioxin bioactivity in the extract was analyzed by reporter gene assay (DR-CALUX). The hepatoma cells which have luciferase gene on Aryl Hydrocarbon promoter region were exposed to the extract for 24 hours. Dioxin bioactivity was determined by luminometric method.
RESULTS: Mean BMI values of the mothers studied was 26.8 (SD=4.9), and average of the fat percentage of the milk samples was 4.7 (SD=1.8). Dioxin activity was represented as "Toxic Equivalency" (TEQ) and calculated as 1.7 (SD=3.6) As a result of analysis a significant correlation was seen between DR-CALUX results and BMI and fat content (p<0.001).
CONCLUSIONS: High level of dioxins was observed in the samples with high fat content milk samples. This positive correlation is taken to reflect bioaccumulation of dioxins (that are lipophilic) in fat tissue. These findings obtained from a high number of breastfeeding mothers provide important information about VKI and nursing-health.
This study was supported by TUBITAK (Project # 113S115).

PC096

The Role of Central Arginine Vasopressin in Colonic Motor Maladaptation Induced by Chronic Heterotypic Stress

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AIM: Stress is known to play a role in etiopathogenesis and symptomatic exacerbation of irritable bowel syndrome (IBS). Arginine vasopressin (AVP) is mainly produced in paraventricular nucleus (PVN) and supraoptic nucleus (SON) of hypothalamus. Besides its well-defined physiological effects such as regulation of body water content and peripheral vascular resistance, along with corticotropin-releasing factor (CRF), AVP mediates stress response as a neurotransmitter and a neuromodulator in brain. Acute stress is known to activate hypothalamic AVP-producing neurons and AVP receptor-expressing cells in dorsal motor nucleus of N.vagus (DMV). In rodents, chronic heterotypic stress (CHeS) causes long-lasting increases in hypothalamic CRF production and colonic motility, however the role of AVP in relevant mechanism is not well-known. Using rat CHeS model, the aim of the present study is to clarify (1) the alterations in hypothalamic AVP production and (2) the role of central endogenous AVP in colonic motor maladaptation.
METHODS: The non-adaptive stress model CHeS was utilized in adult male rats by loading a combination of different stress models for 7 consecutive days. Microdialysates were obtained every 30 min from parvocellular region of PVN during pre-RS, RS and post-RS periods on 1st and 7th days of CHeS. AVP levels were measured using EIA method. In order to elucidate role of central endogenous AVP in CHeS-induced colonic motor maladaptation, selective AVP receptor antagonist SR-49059 was daily administered intracerebroventricularly (icv) throughout CHeS. CT was measured by determination of the geometric center using spectrophotometry. One-way (CT) or two-way (microdialysis) ANOVA with repeated measures followed by an appropriate post-hoc analysis were used to determine the significance among the groups.
RESULTS: CHeS significantly (p<0.05) increased AVP in RS and post-RS periods. At the end of CHeS, acute stress-induced accelerated colon transit was not adapted and still measured high. However, this maladaptation was abolished (p<0.05) by chronic icv administration of SR-49059 and colon transit was restored to control levels.
CONCLUSIONS: AVP plays a role in CHeS-induced colonic hypermotility and central AVP receptor antagonism seems to be a candidate for treatment of IBS.

PC097

Effects of Melatonin on High-Fat Diet-Induced Inflammation and Delayed Intestinal Transit: Involvement of Gut Microbiota

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AIM: Antibiotics-induced dysbiosis affects metabolism by means of fat accumulation. We aimed to elucidate the effects of melatonin on gut microbiota and gastrointestinal changes induced by short-term ingestion of high fat diet (HFD) and antibiotics.
METHODS: Six-week-old male Sprague Dawley rats (n=64) were randomly divided in to 8 groups; pair-fed with chow or HFD(45% fat), and were given either antibiotics (neomycin+ampicillin+metronidazole;1 g/L each) or melatonin (4 mg/kg/day) or melatonin+antibiotics(MA) in drinking water. Fecal output was used as an index for colonic motility and intestinal transit was assessed using charcoal propagation. Liver, epididymal and perirenal fat weight, plasma triglyceride, alanine aminotransferase, glucose levels and inflammatory parameters(MPO, MDA,NO, GSH) in liver and ileum were measured. Histologically ileal villus heights and fecal bacterial colonies were counted. Statistical analysis was made by ANOVA and Student's t tests.
RESULTS: HFD increased perirenal fat weight($p<0.05$), but melatonin prevented fat accumulation. In MA-treated HFD group, increases in perirenal fat and plasma glucose were abolished, while triglyceride levels were further elevated($p<0.05$). Reduced colonic and intestinal transits in HFD were further delayed with melatonin, while addition of antibiotics abolished this delay($p<0.001$). Villus heights were decreased significantly in HFD-rats with MA treatment($p<0.01$). Hepatic and ileal NO and chemiluminescence levels that were elevated by HFD were lower in melatonin-and MA-treated rats. HFD increased ileal and hepatic GSH content without changing MPO and MDA levels, while MA combination depleted GSH($p<0.001$). Total fecal bacterial count was reduced by antibiotics, but total bacteria was increased by melatonin and HFD.
CONCLUSIONS: The inflammation and fat accumulation observed following two-week HFD were reduced with melatonin, and the delayed gut transit associated with fat ingestion was further decelerated. Reversal of GSH and motility responses by antibiotics-induced dysbiosis suggest that melatonin-modulated gut microbiota are involved in altered GSH metabolism and gastrointestinal motility due to acute exposition to pro-oxidant lipids.

PC098

The Effects of Salusin Alpha and Salusin Beta on Cold Restricted Stress-induced Gastric Injury

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AIM: Salusin-α (sal-α) and salusin-β (sal-β) are recently discovered bioactive endogenous peptides with both haemodynamic and mitogenic activity. Sal-α and sal-β immunoreactivity have been detected in the stomach and intestine. Our study is designed to examine the oxidative stress, cytokines and histological effects of administration of sal-α and sal-β on cold-restricted stress (CRS)-induced gastric ulcers.
METHODS: A total of 32 Sprague-Dawley, male rats were divided into four groups (n=8/group) randomly. Group1: Control; Group2: CRS (Rats were placedindividually in the restriction chamber and were subjected to the cold restricted stress at 4°C for 4 hours); Group3: CRS+5nmol/kg Sal-α; Group4: CRS+5nmol/kg Sal-β. Animals were euthanized 4h after CRS administered and their stomachs and blood tissues were immediately collected. We determined malondialdehyde (MDA), myeloperoxidase (MPO), superoxide dismutase (SOD), salusin-α and salusin-β levels from stomach tissue and tumor necrosis factor-α (TNF-α) level from serum. Multiple comparison tests of Kruskal-Wallis and Dunn wereused for the analysis of the data. All the results were presented as mean±SD.
RESULTS: When compared to the control group; while sal-α level ($P<0.,001$) significantly increases in the group to which CRS has been applied, Sal-β has shown a slight increase. MDA, MPO ve TNF-α levels increased and SOD activity decreased in the CRS group, while MDA ($P<0.05$), MPO ($P<0.001$) ve TNF-α ($P<0.05$) significantly decreased, SOD activity increased with administration of sal-α ve sal-β. The mucosal injury and caspase-3 expression increasing with the application of CRS in the histological examinations decreased with the application of salusins.
CONCLUSIONS: The suppression of Sal-α and Sal-β on caspase-3 expression by means of their effects on oxidative injury and TNF-α levels shows that these two hormones could be an anti-ulcerative agent.
This study was supported by Atatürk University BAP (2014/145).

PC099

Investigation of the Effects of Olive Leaf Extract on Liver Enzymes in Streptozotocin-induced Diabetic Rats

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AIM: The aim of this study was to investigate effects of olive leaf extract (OLE) which is effective in glucose metabolism on liver enzymes in rats with induced diabet with streptozotocin (STZ).
METHODS: Thirty two male Wistar albino rats were randomly divided into four groups (for each n=8); Group 1 (control); Group 2 (STZ induced diabet); Group 3 (STZ+OLE); Group IV (OLE+STZ). Two diabetic groups (STZ+OLE, OLE+STZ) fed for 6 weeks with 0.5g/kg OLE by oral gavage. Blood glucose levels measured before surgery. Hexokinase (HK), pyruvate kinase (PK), glucose-6-phosphatase (G6P), fructose-1,6-bisphosphatase, glucose-6-phosphate dehydrogenase (G6PD) enzymes which are effective in glucose metabolism measured by Eastbiopharm ELISA kits. One-way Anova test (posthoc Bonferroni and Student's t-test) and Kruskal-Wallis test (posthoc Dun's test) were used for statistical analysis. $p<0.05$ values was considered statistically significant.
RESULTS: There was a significant decrease in only Group 4 between pre and post experiment outcomes in blood glucose values ($p<0.05$). HK levels increased when comparing treatment groups according to the diabetic group in intra-group measurement. Statistically significant increase was found in PK levels in Group 3. It was calculated that G6PD levels significantly rising between treatment groups. There was no significant differences in inter group rates in G6P and FBP1.
CONCLUSIONS: The present findings show that streptozotozin-induced experimental diabetes have caused several alterations in glucose metabolism enzymes. We suggest that administration of OLE may have beneficial effects on diabetic status and returning of enzyme levels to the control group values.

PC100

The Protective Effect of Taurine on Doxorubicin-induced Hepatotoxicity

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AIM: Doxorubicin (DOX) is a chemotherapeutic agent, widely used against different tumors. Its clinical use has been limited due to its toxic effects on several organs particularly the liver. Taurine, a sulphur-containing intracellular free β aminoacid is found in various mammalian tissues. It mediates physiological functions including calcium transport, osmoregulation and membrane stabilization. Its antioxidant effect by scavenging free radicals diminishes liver injury. This study was planned to examine the possible protective effect of taurine against DOX-induced hepatotoxicity.
METHODS: Sprague-Dawley male rats were used. Control group (n=7) received i.p. saline for 14 days, Taurine group (n=8) was administered i.p. taurine (150 mg/kg body weight/day) for 14 days, Doxorubicin group (n=8) received a total dose of 25 mg/kg body weight divided into 3 days (days 12, 13 and 14, i.p.).Taurine+Doxorubicin group (n=8) received the same doses of taurine and DOX with the same protocol. On the 15th day, having the rats anesthetized, blood samples were collected to determine the ALT, AST and ALP levels, and liver tissues were excised to evaluate the oxidative stress parameters and histopathological findings. Data were analyzed by Kruskal-Wallis followed by Dunn test. (This study was supported by scope of "Teaching Staff Training Program")
RESULTS: DOX administration increased tissue malondialdehyde (MDA) ($P<0.05$) and protein carbonyl ($P<0.05$), serum ALT ($P<0.01$), AST ($P<0,01$) levels and decreased ALP ($P<0.05$) level, but not affected catalase activity. Taurine pre-treatment ameliorated the DOX-induced tissue degeneration, congestion, cell infiltration, nuclear membrane pore enlargements. ALT, ALP, MDA, but not AST and protein carbonyl levels approached to control by taurine pre-treatment.
CONCLUSION: Taurine pre-treatment protects the liver tissue against DOX-induced injury by reducing lipid peroxidation and stabilizing the membranes.

PC101

The Effects of Menthol-nicotine Usage on Gastric Mucosal Damage and the Investigation of Possible Mechanisms

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AIM: Since the limited area for smoking tobacco products, the use of orally taken nicotine products increases. Some flavors such as menthol are added into those products to cover the bitter taste of nicotine. Previously, it has been shown that menthol has gastroprotective effects via its anti-apoptotic, anti-oxidant, anti-inflammatory properties. In this study we aimed to investigate the effects of menthol-nicotine combination on experimental gastric ulcer damage in stomach, intestine, liver and kidney.
METHODS: Sprague-Dawley, 63-male rats were used in the study. Voluntary two-bottle choice drinking was performed during 14 days. The bottles for water and drug solutions were separately placed on cages and swiched with the other daily. The dose of drug solutions were prepared as menthol 1g/L, nicotine 60mg/L. Subgroups were planned as vehicle, menthol, nicotine, menthol+nicotine-combination for main groups of ulcer-created and no ulcer-created. Gastric damage was created via orogastric administration of 1ml absolute-ethanol. Mucosal damage was scored macroscopically. Malondialdehyde(MDA), glutathione(GSH), mye-

loperoxidase (MPO), and superoxide dismutase(SOD) levels were measured in stomach, intestine, liver and kidney tissues.
RESULTS: Mucosal ulcer scores were found on average 4.5±5 for all groups. No statistical diffference wasfound in MDA values between groups. MPO levels were higher in stomach, intestine, liver and kidney in ulcer-created groups, however, GSH levels were lower. Menthol-nicotine combination decreased MPO levels in all tissues but liver in ulcer-created group. This combination has no affect on GSH levels. SOD levels were found in all tissues of ulcer-created group following menthol+nicotine use.
CONCLUSIONS: The voluntary choice drinking of menthol+nicotine combination did not affect gastric damage, but altered the GSH, MPO, SOD levels.

PC102

The Effects of 2.45 GHz Electromagnetic Radiation on the Rat Liver Tissue: Role of Melatonin

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AIM: The biological effects and the human health considerations of electromagnetic radiation (EMR) have been the subject of scientific investigations for most of this century. The present study was carried out to evaluate the effects of 2.45 GHz EMR exposure in liver of rat and possible ameliorative effects of melatonin.
METHODS: Thirty two male Wistar Albino rats were divided into four equal groups: Cage-Control Group; [dimethyl sulfoxide (DMSO) 10 mg/kg/day, i.p., without stress and EMR], Shame-Control Group; [rats stayed in restrainer without exposure to EMR and DMSO (10 mg/kg/day, i.p.)], rats exposed to 2.45 GHz EMR (EMR Group) (60 minutes/day/30 days), 2.45 MHz EMR exposed (60 minutes/day/30 days)+melatonin (10 mg/kg/day, i.p.) treated group (EMR+Melatonin Group). At the end of the study period, liver tissues were taken for oxidant-antioxidant examinations. Data was evaluated with Mann Whitney U ve ANOVA Test.
RESULTS: In the EMR group, MDA level were observed significantly increased when compared with Sham Group (p=0.019). Also, there was statistically significant difference between EMR Group and EMR+Melatonin Group. MDA level decreased in the EMR+Melatonin Group (p=0.006). Moreover, there was statistically significant difference between Sham Group and EMR Group in the CAT, SOD, GSH-Px enzyme activities. The enzyme activities were reduced in the EMR Group (respectively; p=0.005, p=0.028, p=0.009). In addition to, there was statistically significant difference between EMR Group and EMR+Melatonin Group. The same enzyme activities increased in the EMR+Melatonin Group (respectively; p=0.006, p=0.002, p=0.001).
CONCLUSIONS: Our results showed that 2.45 GHz EMR made changes on the rat liver tissue's oxidative-antioxidative parameters and administration of melatonin significantly ameliorated these changes.ported by Süleyman Demirel University Scientific Research Project Coordinator (2531-M-10)..

PC103

The Role of Lidocaine on Transient Receptor Potential Melastatin (TRPM) 6,7 Channels in Hepatic Ischemia/Reperfusion Rat Model

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AIM: Lidocaine is a common local anesthetic that blocks sodium channels, inhibits platelet aggregation and suppresses mitochondrial functions of neutrophils. Therefore, we aimed to investigate the effects of lidocaine on TRPM6,7 gene expressions levels in hepatic ischemia-reperfusion rat model by thinking of lidocaine will be effective in recovery after reperfusion injury.
METHODS: 40 male Wistar albino rats were randomly divided into 5 groups; group I: Control (n=8); group II: Sham (n=8); group III: Lidocaine (Lid; 2 mg/kg, n=8); group IV: 45 min Ischemia+60 min Reperfusion (IR, n=8); group V: Lid+IR (Lid; 2 mg/kg,45 min ischemia+60 min reperfusion, n=8). Single dose lidocaine (2 mg/kg) was intraperitoneally given to the rats of the treatment group (Lid+IR) before10 min of reperfusion period. At the end of reperfusion, rats were sacrificed and liver tissues, blood samples were collected for molecular, histopathological and biochemical analyses. The data was analyzed by Kruskal-Wallis test. Statistical significance was considered to be $p<0.05$.
RESULTS: Polymorphonuclear leukocytes (PNL), congestion, apoptosis, cellular swelling and the total oxidant status (TOS) increased significantly in IR group as compared to other groups. But total antioxidant status (TAS) decreased in I/R group as compared to other groups ($p<0.05$). While TAS increased in Lid+IRgroup as comparison with IR group; PNL, congestion, apoptosis, cellular swelling and TOS decreased significantly in Lid+IR group as comparison with IR group ($p<0.05$). Additionally TRPM6,7 genes expression levels were significantly higher in IR group when compared to Lid+IR group ($p=0.01$; $p=0.02$, respectively).
CONCLUSIONS: Based on these results, it was suggested that lidocaine may give beneficial results by effecting the apoptotic process and reducing TRPM6,7 genes expression levels as a sodium channel blocker for treatment of hepatic ischemia-reperfusion injury.

PC104

The Effect of Caffeic Acid Phenethyl Ester (CAPE) on TRPM 2, 8 Channels in Hepatic Ischemia-Reperfusion Model

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AIM: Ischemia-reperfusion (I/R) injury causes life-threatening problems in many organs and tissues especially in liver. It is the most type of cell injury in clinical medicine. Intracellular Ca+2 concen-

tration increases in I/R injury. It causes some physiopathologic problems which mechanism is not fully understood. Transient Receptor Potential Melastatin (TRPM) 2, 8 are important channels which have high permeability of Ca+2. Thus, we aimed to investigate the effects of CAPE on TRPM channels in experimental hepatic ischemia and reperfusion rat model.
METHODS: 32 male Wistar albino rats were divided into 4 groups. GroupI: sham; groupII: I/R (60 min ischemia+60 min reperfusion); groupIII: CAPE (10 µmol/kg of CAPE was given intraperitoneally for 7 days); groupIV: CAPE+I/R (after treatment of intraperitoneally 10 µmol/kg of CAPE for 7 days, I/R injury was administered). Then histopathological examinations and gene expression levels of TRPM 2, 8 were evaluated for determining the severity of I/R injury.
RESULTS: In physiopathologic examination, it was observed that polymorphonuclear leukocytes (PNL), congestion, apoptosis and cellular swelling increased significantly in I/R group as compared to sham and CAPE groups ($p<0.05$). It was observed that PNL, congestion, apoptosis and cellular swelling decreased significantly in CAPE +İ/R group as compared to I/R group. It was found that TRPM8 gene expression decreased significantly in CAPE+İ/R group as compared to I/R group ($P<0.001$). TRPM2 gene expression level decreased significantly only in CAPE group as compared to other other groups ($p<0.05$).
CONCLUCIONS: In conclusion, we showed that CAPE effects Ca+2entery into cell by reducing TRPM 8 gene expression level. Thus, we think that CAPE pretreatment attenuates the I/R injury.

PC105

Investigation of the Effect of Verapamil on Hepatic Ischemia Reperfusion Injury

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AIM: Intracellular Ca+2 concentration increases in I/R injury. TRPM is important channels which have high permeability of Ca+2 and Mg+2. Verapamil, a calcium channel blocker, is an effective cytoprotective agent. The study aimed to investigate the effects of the verapamil on hepatic ischemia/reperfusion(I/R) injury in rats.
METHODS: A total of 44 male Wistar albino rats were classified 5 groups as group I: control (C,n=7); groupII: sham (n=10); groupIII: verapamil (5mg/kg, n=7); groupIV: ischemia/reperfusion (I/R,n=10); groupV: ischemia/reperfusion with verapamil (Ver+I/R,n=10). Animals of groups IV and V were subjected to 45 min hepatic ischemia followed by 60 min reperfusion. 5 mg/kg/day verapamil was intraperitoneally administered to treatment group(Ver+I/R) before 10 min of reperfusion period. At the end of reperfusion, rats were sacrificed. Liver tissues and blood samples were collected for molecular, histopathological and biochemical analyses. Total oxidant status(TOS), total antioxidant status(TAS), polymorphonuclear leukocytes(PNL), congestion, apoptosis and cellular swelling were evaluated. Kruskal-Wallis test was used for statistical analysis. Statistical significance was considered to be $p<0.05$.
RESULTS: In the analyses, PNL, congestion, apoptosis, cellular swelling and TOS levels were significantly higher in I/R group than the other groups but the TAS level was lower in I/R group than the other groups($p<0.05$). PNL, congestion, apoptosis, cellular swelling parameters and TOS levels were significantly decreased in the treatment group when compared to I/R group but also TAS levels were significantly higher in the treatment group(Ver+I/R) than the I/R group($p<0.05$). The expression level of TRPM2,6,7,8 gene were significantly higher in I/R, verapamil, Ver+IR groups compared to sham group ($p<0.0024$,$p<0.0001$, $p<0.0002$, $p<0.0060$, respectively).
CONCLUSIONS: This is the first study reporting the effects of verapamil on the expression level of TRPM2,6,7,8 and hepatic I/R injury. Our results need to be confirmed with clinical studies in terms of introduction of use of verapamil in treatment of hepatic ischemia-reperfusion injury.

PC106

The Effect of Antifibrotic Drug Halofuginone on Caustic Oesophageal Injury in Rats

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AIM: Halofuginone, a specific inhibitor of collagen type 1 synthesis, is beneficial in ameliorating oxidative damage in different rat models. The aim of this study is to evaluate the putative anti-inflammatory effects of halofuginone in caustic oesophageal injury in rats.
METHODS: Caustic oesophageal injury (COI) was produced in male Wistar albino rats under anesthesia by applying NaOH (37.5%) onto distal oesophagus (n=40), while only saline was instilled in control group (n=8). Until the rats were decapitated on 3rd day (early group) or 28th day (late group) of COI induction, rats were treated intraperitoneally with saline or halofuginone (100 µg/kg/day) on each day (early group) or on alternate days (late group). Nitric oxide (NO), peroxynitrite, nuclear factor (NF)-kB, caspase-3 and luminol- and lucigenin-enhanced chemiluminescence (CL) levels were measured in the oesophageal tissues. Extra tissue samples were evaluated histopathologically. Statistical analysis was performed by ANOVA and Student's t-tests.
RESULTS: NFkB and caspase-3 levels were not different among groups. Microscopic damage scores were elevated in both early and late COI groups ($p<0.001$), while halofuginone treatment reduced the microscopic damage scores in both groups. NO, peroxynitrite and CL levels, which were elevated in the saline-treated early COI group ($p<0.05$-0.001), were suppressed by halofuginone treatment ($p<0.05$). COI-induced elevations in NO and peroxynitrite levels were reduced in late period of saline-treated group, while these levels were increased by halofuginone ($p<0.001$). COI -induced high

CL levels were not changed in late groups treated with either saline or halofuginone.
CONCLUSIONS: In the early period, halofuginone alleviated caustic oesophagus injury by reducing release of oxygen/nitrogen-derived free radicals. Despite that halofuginone was efficient in alleviating COI in the chronic phase, its oxidant scavenging effect was replaced by enhanced production of nitrogen radicals, suggesting the contribution of other anti-inflammatory mechanisms.

PC107

Comparison of Inflammatory Signal Responses of Monocytes and Hepatocytes in Mono and Co-culture Models

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AIM: Bacterial infection may have a detrimental effect on the course of acute and chronic liver diseases. Leukocytes are a vital part of the innate immune response to microbial infections and tissue trauma in many organs including the liver. Bacterial products especially endotoxin or lipopolysaccharide (LPS) can trigger inflammatory responses and cause further damage in liver. An excessive inflammatory response can lead to a dramatic aggravation of the existing injury.
METHODS: To elucidate the importance of the hepatocyte/immune cell interaction in liver inflammation and the effect of of bacterial infection on liver inflammation, we investigated the human hepatocellular cell line HepG2 in coculture with monocytic cells (THP-1) for survival and apoptotic activity. Inflammation level was measured by TNF-α expression/secretion. NFkb, IkB and mitogen activated kinase related pathways (p38, JNK/c-Jun, ERK1/2, akt) were evaluated. The cells were grown in monolayer single cultures or cocultures in transwell inserts and stimulated by LPS (1 µg/ml) for 24 h.RESULTS: Our results showed that THP-1 cells were more sensitive to inflammatory damage ($p<0.01$). LPS stimulation caused increased LDH secretion and caspase-3 activity ($p<0.01$), the effect was more prominent in coculture conditions. Coculture of THP-Hep G2 cells induced significant NFkb activation mainly in Hep G2 cells and TNF-α expression in both cell types ($p<0.01$). Total IkB levels were unchanged but phophoIkB levels were significantly decreased in LPS stimulated cocultured compared to monocultured HepG2 cells. Both total/Phospho Akt levels decreased and JNK/c-Jun levels increased in cocultured cells ($p<0.05$).
CONCLUSIONS: We found that NFkappaB related pathways and at a lesser extend ERK are important for the LPS-stimulated cytokine production in hepatocytes, whereas MAPK pathways involving p38 and JNK contribute to the exacerbation of the inflammation in monocytes. The data indicate that monocyte/hepatocyte coculture studies will supply new insights into the mechanisms of inflammation-mediated liver damage.

PC108

The Role of Solute Carrier Oatp1a4 in Brain Injury Pharmacotherapy

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AIM: Selective permeability characteristic of blood brain barrier (BBB) prevents pharmacological therapies following central nervous system injury. This restrictive role takes place by either blocking the entrance of pharmaceutical reagents and their accumulation or by active and passive transport systems found on the BBB that carry their substrates inside and outside of the brain. In this study, we aimed to investigate the role of one of these systems, the role of solute carrier Oatp1a4 following middle cerebral artery occlusion.
METHODS: In the first part of the study animals were divided into 6 groups (SF/DMSO, SF/Rosuvastatin 2 mg, SF/Rosuvastatin 20mg, Glutatyon/DMSO, Glutatyon/Rosuvastatin 2mg, Glutatyon/ Rosuvstatin 20mg) and evaluated in terms or neuronal survival, number of apoptotic cell death and activational status of intracellular signaling pathways after 30 min of middle cerebra artery occlusion following 72 hr reperfuison. The activity of Oatp1a4 was evaluated through effects of one of rosuvastatin substrates which have been previously shown to improve neuronal plasticity after cerebral ischemia. In the second part, time-dependent expressional profile of Oatp1a4 was investigated. Animals were divided into three groups with 30 min middle cerebral artery occlusion and varying reperfuison time points (12,24, 72hr). Upon sacrifice, the brain microvessels are isolated and protein level of Oatp1a4 was investigated.
RESULTS: Administration of 2mg/kg and 20mg/kg rosuvastatin has improved the neuronal survival and decreased the number of apoptotic cells whereas the inhibition of Oatp1a4 by glutathione has significantly reversed the favorable effects of 2mg/kg rosuvastatin and slightly reduced the effect of 20mg/kg rosuvastatin in a dose dependent manner.
CONCLUSIONS: Inhibition of Oatp1a4 solute carrier following cerebral artery occlusion has reversed the favorable effects of its own susbtrate. Thus, it can be concluded that they can be targeted in brain pharmacotherapies.

PC109

c-Abl Tyrosine Kinasemayhave Regulatory Effect on Estrogen Recetor-β and mTOR in GT1-7 Cells

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AIM: c-Abl is a member of non-receptor tyrosine kinase family and activated by DNA double-strand breaks and proteins involved in the repair of these lesions. It is shown that c-Abl has direct phosphorylation effect on estrogen receptor-β (ER-β). Estradiol is involved in regulation of gonadotropin-releasing hormone (GnRH) release through GnRH neurons expressing ER-β. The mammalian target of ra-

pamycin (mTOR), modulates GnRH production and regulates puberty onset and fertility. The relationship between mTOR and c-Abl was explained that c-Abl has inhibitory effect on mTOR in case of DNA damage. We hypothesized that c-Abl may have regulatory effect on ER-β and mTOR so we aimed to show whether c-Abl has an effect on ERβ and mTOR in GnRH neurons.
METHODS: GT1-7 cells were cultured in medium containing DMEM, 10% fetal bovine serum and 0.1% antibiotics. GT1-7 cells were treated with 10 µM ds-siRNA to silence c-Abl expression combining with siGLO green transfection indicator in serum-free medium. Cyclophilin-B was used as a control. After 24-hour-incubation, siRNA-transfected cells were examined under fluorescence microscope. Protein quantification was done after trypsinization. c-Abl, ER-β and mTOR was evaluated by using Western Blot.
RESULTS: Western Blot results presented that there is a decrease in ER-β level and increase in mTOR expression in c-Abl-siRNA-transfected GT1-7 cells.
CONCLUSIONS: GT1-7 cells provide a useful model system for studying the regulation of hypothalamo-pituitary axis. This study is the first examining the effect of c-Abl on ER-β and mTOR in GT1-7 cells.

PC110

Clopidogrel Exerts Neuroprotective Effect in Experimental Traumatic Brain Injury

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AIM: To observe the possible neuroprotective effect of clopidogrel in the context of traumatic brain injury.
MATERIAL-METHODS: In this study, four groups of mice were used. Traumatic brain injury was performed by used cryogenic trauma model for all groups. For each group different concentrations of clopidogrel were applied intraperitoneally. After sacrification, brain swelling and infarct volumes were calculated and evaluated. In addition, oxidative stress index (OSI) was determined.
RESULTS: Measured infarct volumes indicate that there is no statistically significant difference between experimental groups. However, we observe statistically significant decreases in group 3 (10 mg/kg clopidogrel) and group 4 (30 mg/ kg clopidogrel) with respect to control group. OSI value in group 2 (3 mg/kg clopidogrel) has been found to be decreased significantly.
CONCLUSIONS: Our study may provide important evidence for the neuroprotective effect of a well-known antiplatelet agent in an experimental brain trauma model. This suggests that in case of clinical acute traumatic haemorrhage and related hematoma volume expansion after brain injury, the increased bleeding tendency of clopidogrel may be outweighed by its neuroprotective effects that could be mediated via its antioxidant activity.

PC111

Evaluation of Retina and Retinal Nerve Fiber Layer Thicknesses with Vitamin B12 Deficiency

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AIM: To evaluate the retina and peripapillary retinal nerve fiber layer (RNFL) thicknesses of patients with vitamin B12 deficiency using optical coherence tomography (OCT) and compare them with healthy subjects. included in this study. Retinal thickness measurements taken at the central retina (fovea) and at 2 points that were 1500 µm nasal and temporal to the fovea using OCT. Independent samples t-test was used for the statistical analysis of the data.
RESULTS: Serum vitamin B12 levels of the healthy subjects and patients with vitamin B12 deficiency was 406.74±26.12 and 160.71±20.06 pg/ml, respectively.The mean central retinal thickness of healthy subjects and patients with vitamin B12 deficiency were 216.06±14.64 and 213.50±13.39 µm, respectively and this difference did not reach to statistical significance (p=0.448). The mean global peripapillary RNFL thickness of healty subjects and patients with vitamin B12 deficiency were 103.00±10.24 and 100.15±6.42 µm, respectively and this difference did not reach to statistical significance (p=0.217).
CONCLUSIONS: Patients with vitamin B12 deficiency had thinner central retina and peripapillary RNFL. As a preliminary report, our sample size might not to be sufficient to determine the statistical significance for RNFL and retinal thickness.

PC112

Plasticity-Promoting Effect of Melatonin After Experimental Cerebral Ischemia

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AIM: Stroke remains the leading cause of serious motor disabilities in adults. Stroke recovery is associated with reorganization of neu-

ronal circuits both at the cortical and subcortical level. In the ischaemic boundary zone, a cascade of events including neurogenesis, angiogenesis and inhibition of astrogliosis contribute to the remodelling of brain tissue. Previous studies have examined ipsilesional and contralesional recovery processes independent of each other. There are no studies evaluating how both processes are coordinated by melatonin.
METHODS: To elucidate melatonin's effects in the post-acute ischaemic brain, we examined how melatonin influences functional neurological recovery, perilesional tissue remodelling (angiogenesis, neurogenesis) and axonal sprouting in both hemisphers, when administered intraperitoneally (4 mg/kg/day) starting 3 days after 30 min. of middle cerebral artery occlusion. The behavioral and brain tissue examinations were performed on two groups of adult male C57BL/6 mice including four subgroups of animals (n=6-10 animals/group) that underwent30 min of left-sided middle cerebral artery occlusion (MCAO) only, and MCAO plus melatonin that are sacrified in four different (3, 14, 30, and 55 days) post-ischemic time points. Plasticity-promoting effect of melatonin was examined by behavioral tests, immunofluorescence staining, RT-PCR and Western blot analysis.
RESULTS: In the post-acute ischemic brain, melatonin increased grip strength of the paretic forelimb, improved motor coordination and exploration behavior. Neurological recovery by melatonin was associated with structural remodeling of ischemic brain tissue, reflected by increased angiogenesis and decreased reactive astrogliosis that resulted in reduced scar formation. Melatonin changed expression of pro/anti-plasticity genes (Gap43, Basp1, cntf, etc.) and genes responsible for angiogenesis (EPO, Hif1a etc.) as well as proteins related to inhibition of axonal sprouting, suggesting an improvement in neurogenesis and angiogenesis in both hemispheres in a different manner.
CONCLUSIONS: For the first time, these data establishe how melatonin coordinates plasticity in both hemispheres after brain ischemia.
This study was supported by TUBITAK (111S418).

PC113

The Investigation of the Protective Effect of Glucagon-like peptide (GLP-1) Analogue Exenatide on Glucose and Fructose-induced Neurotoxicity

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AIM: Diabetes mellitus is one of the most common metabolic disorders characterized by hyperglycemia due to insufficiency of insulin and/ or insulin resistance. Clinical studies have revealed a higher risk of neurodegenerative disorders such as Alzheimer'sdisease or Parkinson's disease in diabetic patients. Recently, glucagon-like peptide (GLP-1) is an attractive potential treatment modality for various neurodegenerative diseases. In our study, we aimed to investigate the toxic effects of both high glucose and fructose on neuronal cells. Also, we aimed to assess whether exenatide, a GLP-1 analogue, has neuroprotective effects against glucose and fructose-induced toxicity.
METHODS: SHSY5Y neuroblastoma cells were used to evaluate the toxic effects of glucose and fructose. Neurotoxicity was induced by incubating SHSY5Y cells with different doses (0-100 mM) of glucose and fructose for 24 hours. Following determination of the significant toxic doses of glucose and fructose, various doses of exenatide (0-100 nM) were added in the cultures to assess its protective effect. XTT (2,3-bis[2-methoxy-4-nitro-5-sulfophenyl]-2H-tetrazolium-5-carboxanilide) assay was used to measure cell viability in the cultures. The data were analyzed using independent t-test. P values <0.05 were accepted as statistically significant.
RESULTS: Both glucose and fructose treatments reduced cell viability dose-dependently in neuronal cells. The cell viability was significantly decreased in 50 mM glucose (71.6 ± 9.04%, $p<0.0001$) and in 50 mM fructose (66.42 ± 4.88%, $p<0.0001$) compared to controls. However, addition of exenadite in growth medium significantly prevented cell death in 50 mM glucose and fructose-treated cultures in a dose-dependent manner. The most prominent effect was observed in 100 nM exenatide-treated cultures ($p<0.05$).
CONCLUSIONS: Our results suggest that high doses of glucose and fructose lead to neurotoxicity and GLP-1 may have neuroprotective effects against neuronal damage.
This study was supported by TUBITAK (project no: 115S136).

PC114

Effects of Riboflavin on Traumatic Brain Injury Induced in Rats

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AIM: Presenting with high mortality and morbidity, traumatic brain injury (TBI) results from a head trauma due to a sudden strike. Riboflavin, also known as vitamin B2, is a water-soluble essential vitamin found in various nutrients. This study was aimed to investigate the possible protective effects of riboflavin on trauma-induced oxidative brain damage.
METHODS: Anesthetized male Sprague Dawley rats (n = 36) were divided into 3 groups: control group with scalp incision and vehicle (carboxymethyl cellulose; 1 ml/kg, intraperitoneally, i.p.) injection; traumatic brain injury (TBI) group with weight-drop following scalp incision and vehicle treatment; and TBI+Riboflavin (30 mg/kg/day; i.p.) group. Treatments were continued for 3 days and at 72nd h of trauma rats were decapitated. In brain tissues, levels of malondialdehyde (MDA), superoxide dismutase (SOD), glutathione (GSH), neuron-specific enolase (NSE), human soluble protein-100β (S100β), caspase-3 activity, caspase-3 protein expression were measured and reactive oxygen metabolites (ROM) were determined using chemiluminescence (CL). Data were analyzed by ANOVA and Student's t-test.
RESULTS: In TBI group, antioxidant GSH and SOD levels were decreased as compared to control ($p<0.001$), but were increased in ri-

boflavin-treated TBI group (p<0.001). MDA levels, caspase-3 activity and cleaved (activated) caspase-3 protein expression, luminol and lucigenin CL levels were increased in TBI group (p<0.001), while these elevations were reversed in riboflavin-treated TBI group (p<0.01). Compared to control group, elevated NSE and S100β protein levels in brain tissue and serum due to brain damage were reduced by riboflavin-treatment (p<0.01).
CONCLUSIONS: Riboflavin ameliorated trauma-induced oxidative brain damage by stimulating antioxidant mechanisms and by suppressing ROM production and apoptosis.

PC115

Effects of Black Cumin Seeds and Certain Species of Fungi Extracts on the Number and Degranulation of Mast Cells in Dura Mater in Rats

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AIM: It has been postulated that mast cell degranulation in dura mater plays key role in migraine pathophysiology by causing neurogenic inflammation and activating meningeal nociceptors. It was reported that certain species of fungi caused allergy and headache, but black-cumin seeds have antinociceptive and antihistaminic effects. In the present study, it was aimed to investigate effects of black cumin seeds and certain species of fungi extracts on number and degranulation states of mast cells in dura mater.
METHODS: Rats were divided into eight groups(n=5,male-Wistar,200-250g).Control and C-48/80 groups were fed with tap-water for three days,but at the end of third day C-48/80 group was injected with compound-48/80(2 mg/kg,i.p.),Nigella+C-48/80 group was fed with tap-water with extract ofNigella sativa(black cumin) seeds(4 mg/ml) for three days and at the end of third day,they were injected with compound-48/80. Condensata, Salmonicolor, Piperatus and Terreum groups were fed with tap-water including their own extracts (4 ml/kg), respectively. Because only Tricholoma terreum caused effects on mast cells, Nigella+Terreum group was fed with tap-water with their combination for three days. Mast cells were counted and evaluated their granulation/degranulation states. Data were analyzed with one-way ANOVA test using SPSS 17.0.
RESULTS: Compound-48/80 and Tricholoma terreum caused degranulation of dural mast cells, respectively (p<0.01 and p<0.05). Tricholoma terreum increased total number of mast cells(p<0.05). Nigella sativa inhibited mast cell degranulation induced by both compound-48/80 and Tricholoma terreum(p<0.05), respectively, and decreased increased mast cell numbers caused by Tricholoma terreum (p<0.05). Probably,Tricholoma terreum caused these effects on mast cells via an antigen which is absent in other fungi.
CONCLUSIONS: Inhibition of dural mast cell degranulation by black cumin seeds showed that black cumin may probably reveal analgesic, antihistaminic and anti-inflammatory effects by stabilizing mast cells. Black cumin seeds may prevent neurogenic inflammation may be responsible for migraine pathophysiology by stabilizing dural mast cells. However, this needs to be further investigated.

PC116

Investigation of Plasma PTX-3, IL-6 and CRP Levels in Rat Traumatic Brain Injury

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AIM: The prevalence and high cost of traumatic brain injury (TBI) increases with each passing day. Therefore, the severity of disease and the early diagnosis is very important in order to define the disease. The purpose of this study is to research the levels of PTX-3, IL-6 and CRP on the rats with TBI.
METHODS: During our research period, 8 months old (200-250 g) twenty eight Wistar albino male rats were used for testing. Before the implementation of traumatic brain injury, cardiac blood samples were taken from the each rat. TBI was implemented to all animals under deep anesthesia with weight-drop method. After TBI, the rats were grouped into 4 groups; in order to take cardiac blood samples in 1st, 3th, 5th and 7th hours. After that, the levels of PTX-3, IL-6 and CRP in plasma of the blood samples taken from each rat were measured by ELISA method. The results were evaluated with SPSS 17.0 software program by using Mann-Whitney U, Kruskal-Wallis, Wilcoxon and pearson correlation tests.
RESULTS: No significant difference was seen in PTX-3, IL-6 and CRP levels among these four groups as a finding of these experiments. It was observed that CRP levels in 7th hour group was statistically significantly different according to before and after the damage. In addition, the positive correlation was found between the CRP and PTX-3 levels after the damage.
CONCLUSIONS: The CRP level in blood sample, which is taken at 7th hour, increased, on the other hand the PTX-3 and IL-6 levels did not have a significant differance according to different hours of THI. The present studyshowed that CRP is a more sensitive biomarker than PTX-3 ve IL-6 in determination of early brain injury.

PC117

The Effects of Sirtuin 1 and Oxidative Stress on Oligodendrocyte Death in Cuprizone-induced Model of Demyelination

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AIM: Cuprizone (CPZ)-induced demyelination in rodents has been widely used as a model for multiple sclerosis (MS). The copper chelator cuprizone induces selective oligodendrocyte death, followed by myelin disruption, astrogliosis and microglia- and macrophage activation. Sirtuins are NAD-dependent deacetylases that counter aging and have a wide spectrum of metabolic and stress-tolerance functions. Of the seven mammalian sirtuins, the SIR2 ortholog SIRT1 deacetylates numerous regulatory proteins, such as PGC-1α, p53, FOXO, HSF and HIF-2α to trigger resistance to metabolic, oxidative, heat and hypoxic stres. SIRT1 has been directly implicated in neuronal protection against ischemia. SIRT1 has also been linked to neurodegenerative diseases, such as Huntington's disease and Alzheimer's disease, and MS. The present study aims to determine the

relationship between the tissue oxidative stress and SIRT-1 level in rat model of MS.
METHODS: In the current study, the rat model of chronic demyelination was constructed by continuous ingestion of 0.6% cuprizone for 2 weeks. Animals were divided into two groups each including 10 rats: CPZ group receiving CPZ for 14 days at 21st day of postnatal period; sham control group fed with standard pellet. Expressions of nitrothyrosine, NOGO A, and SIRT-1 as well as the tissue contents of malondialdehyde (MDA) and superoxide dismutase (SOD) were measured via immunohistochemical and spectrophotometrical techniques, respectively.
RESULTS: Tissue levels of lipid peroxidation and reduced glutathione in both groups were statistically indifferent ($p>0.01$) while SOD activity in CPZ group was three times more than that in control ($p<0.01$). Demyelination plates at 1st and 2nd degree of severity were observed in CPZ group, whereas normal myelin structures were evident in control. Intense increase in Nogo-A expression (particularly around plates) was evident in CPZ group compared to control. No expression of 3-Nitrotyrozine was detected in any group, supporting biochemical findings. However, level of Sirt-1 was significantly reduced in CPZ group when compared with control.
CONCLUSIONS: MS may not induce oxidative stress in central nervous system of rats but trigger a significant decrease in SIRT-1 with elevated SOD level.
The present study was funded by a project of Bülent Ecevit University (BAP 2012-20-00-25).

PC118

Effects of Neurotrophic Factors CDNF and MANF on Brain Plasticity and Repair After Brain Ischemia

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AIM: Neurotrophic factors play essential roles in development of neurons and the maintenance of neuronal synaptic function. Decrease or absence of neurotrophic factor levels play important roles in pathobiology of several neurodegenerative disorders. In this study, effects of MANF (Mesencephalic Astrocyte-Derived Neurotrophic Factor) and CDNF (Cerebral Dopamine Neurotrophic Factor) neurotrophic factors which differ from the other known neurodegenerative factors on cellular survival, apoptotic cell death, neurogenesis, gliogenesis, atrophy in striatum and corpus callosum and signal transduction pathways were investigated.
METHODS: 8-12 weeks old male C57/Bl6 mice were anesthetized with 1% isoflurane (30% O2, remainder N2O) and submitted to 30 minutes of middle cerebral artery occlusion, and reperfused for Day 3, 14, 28 and 55. Miniosmotic pumps that were randomly filled with vehicle (0.01 M PBS) or MANF or CDNF (for both 1 mg/kg/day diluted in 0.01 M PBS) were placed into the left lateral ventricle (n = 10 animals/group). These miniosmotic pumps were left in place during reperfusion. Apoptotic cell death, neurogenesis, gliogenesis, and atrophy were identifed by immunofluorescence staining on frozen brain slice and protein expressions were measured with Western blot.
RESULTS: In this study, MANF and CDNF treatments were shown to decrease DNA fragmentation, trigger neurogenesis and gliogenesis, alleviate glial scar formation and atrophy in striatum and corpus callosum in long term compared to the control group. Increased eNOS and decreased iNOS and time dependent changes in the activation of p38 and p21 were observed.
CONCLUSIONS: The obtained results demonstrated that MANF and CDNF treatments exerted their effects on programmed cell death, neurogenesis and gliogenesis after brain ischemia through increased eNOS and decreased iNOS, and through p38 and p21 proteins. To this end, these results will contribute to new targets and/or treatments that can direct brain ischemia treatments.
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PC119

The Effect of Glutathione Isopropyl Ester on 6-Hydroxydopamine-induced Model of Parkinson's Disease

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AIM: Parkinson's disease is characterized by selective degeneration of dopaminergic neurons in substantia nigra (SN) and progressive motor disabilities. The earliest known indicator of nigral degeneration is decrement of glutathione (GSH) which is one of the most important antioxidant in cell. It has been suggested that attempts that will be result in the increment of GSH synthesis or the inhibition of catabolism may slowdown the progression of the disease. The purpose of this study is to determine the possible effect and mechanism of YM737 (N-(N-T-I:glutamyl-L-cysteinyl) glycine l-isopropyl ester sulfate monohydrate), the GSH analogue which is known to cross the blood brain barrier (BBB), on experimental Parkinson model.
METHODS: Three month old male Wistar rats were randomly divided into four groups: control (Control), YM737-treated (YM737), 6-hydroxydopamine (6-OHDA)-injected (6-OHDA), 6-OHDA-injected and YM737-treated (6-OHDA+YM737). Rats received a unilateral stereotaxic injection of 6-OHDA (3x4µg/µl) into the right medial forebrain bundle (MFB). YM737 was administered intraperitoneally, at a single dose of 300mg/kg when experimental PD was created. Three days after the 6-OHDA injection, the rats were tested for motor activity (locomotor activity, catatonia and apomorphine-induced rotation tests). The dopaminergic cell death in SN were determined by immunohistochemical and stereologic estimation of tyrosine hydroxylase (TH)-immunopositive cells. Nigral GSH and 4-Hyroxynonenal (4-HNE) levels were determined spectrophotometrically. Differences in data were analyzed by ANOVA followed by Tukey's Post Hoc Test or Kruskal Wallis followed up Mann Whitney

U test. Significance levels were set at $p < 0.05$. Values are given as the mean ± standart error.
RESULTS: The deficits in motor activity due to 6-OHDA lesioning were significant however were not restored by YM737 treatment. Lesioning was followed by a decreased dopaminergic neuron number in SN (8125±721; 3469±377) which was not prevented with YM737 treatment. 6-hydroxydopamine injection significantly decreased nigral GSH levels (56±9; 13±1) and increased 4-HNE levels (16±0.9; 44±9) however YM737 treatment had no effect on these parameters.
CONCLUSIONS: The results demonstrated no beneficial effect of YM737 treatment in 6-OHDA lesioned rats by means of behavioural, histological and biochemical parameters.

PC120

The Protective Effect of Central Exogenous Neuropeptide-S on Parkinson's Disease

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AIM: Parkinson's disease (PD) is a neurodegenerative disorder characterized by the loss of dopaminergic neurons from the substantia nigra (SN). Its major clinical symptoms are tremor, rijidity, bradykinesia and postural instability. Neuropeptide-S (NPS), a novel brain peptide, selectively binds to its receptor NPSR expressed in several brain regions mediating locomotor activity, autonomic network and behavior. NPSR was shown to be expressed in SN, while NPS has been reported to protect neurons against apoptosis by decreasing lipid peroxidation in certain brain regions. The aim of the present study is to investigate the effect of chronic central exogenous NPS on reduced nigral dopaminergic cell population and disturbed motor functions in mouse experimental PD model.
METHODS: In this study, 3-month old male C57BL/6 mice were randomly divided into 3 groups as: Control, MPTP-induced PD and chronic central exogenous NPS-treated PD. MPTP was intraperitoneally injected at dose of 4x20mg/kg at 12-hr intervals. Intracerebroventricular NPS administration started on day of MPTP treatment and was performed for 7 days at dose of 0.1 nmol. In all groups, motor activity tests were performed before and on 7th day of the PD model. At the end of the 7-day period, brains were collected and tyrosine hydroxylase (TH) immunoreactive cells in SN and ventral tegmental area (VTA) were analyzed by immunohistochemistry.
RESULTS: Compared to control, MPTP decreased total locomotor activity and time exhibited on the rotating mill at 20, 30 and 40 rpm which were significantly ($p<0.05$) improved following chronic central NPS treatment. Furthermore, the reduced number of TH-positive cells in SN and VTA were remarkably increased by exogenous NPS.
CONCLUSIONS: The present findings suggest that central exogenous NPS might restore MPTP-induced impaired locomotion and TH-positive cell loss through nigral NPSR. Central NPSR agonism may contribute to the novel approaches for the clinical treatment of PD.

PC121

Neurotransmitters Levels in Experimentally Produced Alzheimer Model in Rats

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AIM: Alzheimer's disease (AD) is a progressive neurological disorder with memory dysfunction. There are studies that show that the changes in neurotransmitter systems, including noradrenaline, dopamine and serotonin, accompany the cholinergic inefficiencies in Alzheimer. It has been argued that the irregular noradrenergic innervations may be responsible for the reduced melatonin levels in the AD and in the melatonin rhythm loss. This study was designed to determine the possible relation between the AD, melatonin and neurotransmitters (serotonin, noradrenaline and dopamine) have an important role in axonal transfer and regulating the controlled balance of the excitator/inhibitor signals.
METHODS: 30 male rats weighing 220-280 gr were used in the study. The rats were divided into 3 groups (n=10): sham, intracerebroventricular streptozotocin and melatonin+streptozotocin. The intracerebroventricular streptozotocin injections were applied to the rats on the 1st and 3rd days as 3 mg/kg. Melatonin applications (as i.p.10 mg/kg/day) were started one hour before the first dose of STZ administration, and were continued for 14 days. The rats were sacrificed and blood samples were collected. The serum serotonin, noradrenaline and dopamine levels were determined with the ELISA method.
RESULTS: While no statistically significant differences were observed between the groups in terms of serum dopamine and serotonin levels, noradrenaline levels of all experiment groups were found to be lower than that of sham group ($p<0.05$).
CONCLUSIONS: The present findings suggest that deficiencies in the noradrenergic neurotransmitter system may play an important role in the development of neurodegenerative diseases such as AD.
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PC122

Effect of Different Exercise Methods on Anxiety-Like Behavior and Cerabral Plasticity in An Experimental Model of Alzheimer's Disease

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AIM: To investigate the probable improving effects of aerobic, resistance and combined exercise methods on anxiety-like behavior

and cerebral plasticity in an experimental Alzheimer's disease (AD) model.
METHODS: An AD model has been demonstrated with a long-term D-galactose injection combined with ovariectomy (D-GAL+OVX). Female Wistar rats (250-340) g were divided into two main groups as sham operated and D-GAL+OVX. D-GAL (100 mg/kg) or saline was administered by intraperitoneally to ovariectomized (OVX) and sham-operated rats (n=8) respectively for 6 weeks. Aerobic (AE; swimming) (1 hour/day), resistance (RE; climbing with weight on vertical ladder/8-12 sets) and combined exercises (CE; aerobic+resistance/ alternately) were performed for 3 times a week for 6 weeks. Some of the rats were sedentary. Anxiety via holeboard test, Nerve Growth Factor (NGF), Brain Derived Neurotrophic Factor (BDNF), Insulin Like Growth Factor-I (IGF-I) and Amyloid Beta (Aβ) immunoreactive neurons were evaluated via immunocytochemical technique in hippocampus and cortex.
RESULTS: Freezing time was increased in OVX+D-GAL sedentary group ($p<0.01$) compared with sham sedentary group, and decreased back with AE ($p<0.05$). Increased Aβ immunocytochemical scores in hippocampus in OVX+D-GAL sedanter group ($p<0.001$-0.05) were decreased via RE and CE ($p<0.01$). Hippocampal NGF immunocytochemical scores were increased in sham AE, RE group compared to sham sedentary ($p<0.05$). Decreased cortex NGF immunocytochemical score of OVX+D-GAL sedentary group ($p<0.01$) was increased by CE ($p<0.05$). BDNF immunocytochemical scores of sham operated AE ($p<0.01$) and CE ($p<0.05$) groups were elevated compared to sham sedentary group.
CONCLUSIONS: RE, CE via decreasing hippocampal Aβ score, CE via improving neuroplasticity and AE via decreasing anxiety-like behaviour may have protective effects in development stage of Alzheimer's disease.

PC123

Investigation of Oxidant/Antioxidant Balance in Alzheimer Patients

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AIM: Alzheimer's disease (AD) is an incurable neurodegenerative illness with progressive deterioration in cognitive functions accompanied with feelings and behavior change. Many mechanisms for neurodegeneration including oxidant stress has been presented. Harmful effects of oxidative stress is well-known and the body is protected by endogenous and exogenous antioxidants. There is tightly regulated balance between oxidants and antioxidants in the body. In our study, we aimed to investigate Total Oxidant Level (TOL), Total Antioxidant Level (TAL), and Oxidative Stress Index (OSI) in serum of Alzheimer patients and compared those parameters with healthy groups.
METHODS: The study was performed on AD (32) and healthy volunteers (31). Cognitive function of individuals in the study was evaluated with the Mini-Mental State Examination. The average age and gender of the patient and control groups has been noted to be close to each other. 8 ml of blood was taken from individuals and the serum TOL and TAL levels were evaluated by using of a commercial kits. The OSI value was calculated through TOL and TAL levels.
RESULTS: The TOL value in AD group was statistically found less than that of control groups ($p<0.05$). There was no significant difference in TAL and OSI values between the groups.
CONCLUSIONS: Our results showed that there was a statistically significant decrement in oxidative stress levels in AD group. This can be explained with some systemic diseases of individual's in healthy control group in addition to advance age of them.

PC124

The Effects of Ethyl Pyruvate on Cognitive Function, Oxidative Stress, and Na-K ATPase Levels in Vascular Dementia Model

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AIM: Vascular dementia, the second most common type of dementia, is mainly caused by alteration of blood supply to the brain. Chronic cerebral hypoperfusion (CCH) has been implicated to cause neurodegeneration and cognitive impairment through multiple mechanisms, including induction of oxidative stress, amyloid-β accumulation, tau hyperphosphorylation, neuronal loss, and neuroinflammation. Ethyl pyruvate (EP) has been shown to confer protective effects in various disease models. For example, EP administration improved survival in mice with established lethal sepsis and systemic inflammation and diminished ischemia-induced myocardial injury and infarct volumes in postischemic brain. The present study was, therefore, designed to evaluate the effects of EP treatment on the oxidative stres status by measuring the levels of malondialdehyde (MDA) and reduced glutathione (GSH), Na-K ATase levels and cognitive function in chronic cerebral hypoperfusion-induced neurodegeneration in two vessels occluded rats.
METHODS: Wistar Albino male rats were randomly divided into three groups each including 10 animals (sham control, CCH, and CCH with EP treatment). CCH was induced by bilateral carotid artery occlusion in rats. EP was given to rats daily (i.p., 10 mg/kg) for 15 days. 15 days later, contents of Na-K ATPase,MDA, and GSH were measured by methods of ELISA and spectrophotometry, respectively. For evaluation of cognitive function, Morris water maze was applied. Hippocampal memory was evaluated by escape latency, which is the time it takes to find hidden platform.
RESULTS: MDA content in CCH group was more than those in other groups after 15 days later ($p<0.05$). Treatment with EP significantly reduced MDA content compared to that of CCH group($p<0.05$). Levels of Na-K ATPase and GSH in all groups were indifferent from each other. Escape latecy time in treatment group was significantly less than that in CCH group.
CONCLUSIONS: These results may suggest that EP treatment improve cognitive function by reducing oxidative stress in chronic cerebral hypoperfusion.

PC125

Evaluation of Spatial Learning Performance in Selenium Supplemented Rats

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AIM: In our previous work we have shown that hypothyroidism develops hippocampal function deterioration and this deterioration improves with selenium supplementation. In this study, selenium(Se) deficiency and Se supplementation in rats learning and memory functions was evaluated.
METHODS: Male Wistar rats were divided into 4 groups; 1. Control, 2. Se supplementation (10 ppm, Se+10), 3. Se supplementation (20 ppm, Se+20), 4. Se deficiency (0.7 ppm, Se(-)).The rats was fed diets containing different dietary selenium. Learning and memory performance of rats evaluated in the Morris water maze and behaviour of animals during trial was recorded with NOLDUS monitoring system.
RESULTS: It was found a significant difference between the values of the hippocampal selenium amoung groups. Se supplementation (given in particular 20 ppm) and Se deficiency has adversely affected the learning functions. In Se(-) group, distance moved to find the platform on 2. and 3. days, escape latency on 2., 3. and 4. days significantly increased compared to the control group. The mean distance to platform of Se(-) group on 2., 3. and 4. days significantly increased compared to the control group. Se+20 group remained the least time in the target quadrant and this value is significantly different from the other groups.
CONCLUSIONS: Selenium deficiency impaired hippocampal functionsignificantly, in selenium supplemented group, in contrast to increase in hippocampal function, it was decreased. We believe that excess or deficiency of selenium adversely affects synaptic plasticity formation by affecting antioxidant stress. Selenium supplementation in pathological conditions, it has a significantly curative effect in neuronal cells but it could adversely affect cell functions in physiological conditions.

PC126

The Effect oF MK-801 and Dexmedetomidine on Spatial Learning and Memory

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AIM: The negative effects of N-methyl-D-aspartate receptor (NMDAR) antagonist, MK-801, on learning and memory are well known. It has recently been argued that alpha-2 adrenergic receptor agonist, dexmedetomidine affects learning and memory. In this study was evaluated the effects of the NMDAR system in combination with the alpha-2 adrenergic receptor system on spatial learning and memory.
METHODS: In this study, the spatial learning and memory skills of mice were tested using the Morris water maze. The mice were eight to ten week old adult male Balb/c mice. Before the Morris water maze testing, MK-801 (0.25 mg/kg), dexmedetomidine (10 mcg/kg) and MK-801+ dexmedetomidine (0.25 mg/kg+10 mcg/kg) were given to the experimental group intraperitoneal twice a day for a week. The control group received 0.9% NaCl (0.1 ml/10g body weight) in the same method. The data was analyzed by using Statistical Package for the Social Sciences (SPSS) program and the repeated measurements were analyzed by ANOVA.
RESULTS: In the Morris water maze test, MK-801 caused a significant increase in time taken to reach the platform, compared to the control group, on the second, third, fourth and fifth days (respectively $p<0.05$, $p<0.05$, $p<0.001$, $p<0.001$), while causing a decrease in time to stay on the target quadrant. Groups that were treated with dexmedetomidine and MK-801+dexmedetomidine had no significant difference in the time taken to reach the platform and the time spent on the target quadrant. MK-801+dexmedetomidine caused a significant decrease in time taken to reach the platform, compared to the MK-801 group, while causing a increase in time to stay on the target quadrant ($p<0,05$).
CONCLUSIONS: According to the findings, the negative effects of MK-801 on spatial learning and memory may be recovered with Dexmedetomidine application. NMDAR system and alpha-2 adrenergic receptor system may play a role on spatial learning and memory performance.

PC127

Effects of Coenzyme Q10 Supplementation on Doxorubicin Treatment-induced Cognitive Dysfunction in Rats

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AIM: Doxorubicin is an anthracycline derivative antibiotic which is commonly used in various cancer therapies. Adverse effects of anticancer agents are a major problem. It has been specified that the deterioration of cognitive functions can be observed particularly in patients with breast cancer after the chemotherapy. It is believed that the doxorubicin derived toxicity can be due to the oxidative stress. CoenzymeQ10 is a fat soluble vitamin, located on the inner phospholipid layer of the cell membrane. It is known as a strong antioxidant. In this study, we aimed to examine whether coenzymeQ10 supplementation had protective role doxorubicin induced cognitive dysfunction in rats and its relation with oxidative stress markers.
METHODS: The ethical approval was obtained from the Local Ethics Committee of Selçuk University. A total of 32 female Wistar albino rats were divided into four groups: Control (n=6), CoenzymeQ10 (n=6), Doxorubicin (n=10) and Doxorubicin-CoenzymeQ10 (n=10). From the first day of the study, CoenzymeQ10 treated groups were given 200 mg/kg CoenzymeQ10 via oral gavage for 21 days. On the 7th and 14th day of study, single dose of 4 mg/kg doxorubicin (totally 8mg/kg) were injected intraperitoneally. From the 21th day of study, open field and elevated plus maze tests were applied. At the end of the study brain samples were collected under anesthesia and oxidative stress markers were analyzed.RESULTS: In the doxorubicin group locomotor activity was decreased, anxiety level was increased compared to the control group ($p<0.05$). There was no significant difference among the Doxorubicin-CoenzymeQ10, control and CoenzymeQ10 groups ($p>0.05$). MDA and PC levels tended to increase and SOD activity tended to decrease in the doxorubicin group ($p>0.05$). CoenzymeQ10 supplementation led these values to be similar to the control group ($p>0.05$).CONCLUSIONS: CoenzymeQ10 supplementation may improve doxorubicin-induced cognitive dysfunction independent from the oxidant system in rats.

PC128

Investigation of Anxiolytic Effects of Meprobamate for Pharmaceuticals Determination of a New Derivative of Mepronarilmate Composes

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AIM: Compounds containing carbamate group are known to have anxiolytic effects. The aim of this study was to investigate the anxiolytic effects of newly synthesized 11 different meprobamate derivatives.

METHODS: Male wistar albino rats (4-6 months old) was used in this study. 11 diferent meprobamate derivatives were synthesized in AİBU department of chemistry for this study. These derivatives were named as 500, 501,502,503,504,505,506, 507,508,509,513. Single dose was selected for all the derivatives as 50 mg/kg. Animals were divided into three main groups The first group was called experimental group that was applied separately on 11 new derivatives of meprobamate. Second Group was called positive control group and received diazepam (1mg/kg). Third Group which received DMSO was called negative control group. 30 min before each tes,t the derivatives were applied intraperitoneally (50 mg/kg). After 30 minutes, the anxiolytic effect of the derivatives was determined by open field and elevated plus maze tests.

RESULTS: Firstly, in the open field test 505,501,508 and diazepam administrated rats took more total distance than control grouos rats ($p<0.05$). 505, 508,506,507,500 and diazepam andministrated rats spend more time at the side than control groups ($p<0.05$). 505,513,506,509,502 and diazepam admistrated rats took more total distance than control groups ($p<0.,05$). 506,503, 505,501,509, 508,513 and diazepam administrated rats spent less time at closed arm than control groups ($p<0.05$). 504 and 507 administrated rats spent more time at closed arm than control groups ($p<0,05$). 506,503,501 adminestrated rats spend more time at open arm than diazepam adminestrated groups and control groups($p<0,05$).

CONCLUSIONS: In this study, 505,501,509,508,513 and 501 substances can be said effective in open field also it reduced anxiety which is similar to diazepam ($p<0.05$). 506,503,505, 501,509,508, 513 substances can be said effective in elevated plus maze. These substance may be effective in closed arm and they reduces anxiety. These newly synthesised agents were planned to be used in further phase studies more comprehensivly for medical use in the treatment of anxiety disorders.

PC129

The Effects of Leptin Administration to Amygdala Region on Anxiety, Depression and Learning Behaviors: Change in Seretonine and Glutamate Levels

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AIM: Leptin is a hormone secreted by adipose tissue and involved in modulation of food intake. In addition to these functions, it plays a role in various physiological events such as anxiety, depression and learning. The aim of this study was the investigation of effects of leptin administration to amygdala on anxiety, depression and learning behaviors. In addition, changing of serotonin and glutamate neurotransmitter levels interaction between behavior.

METHODS: Present study used Wistar albino rats. Animals were separated 3 groups such as low dose (0.1µg/kg) and high dose (1µg/kg) leptin and saline (control) intraamigdalar administration group. In this study, we planned two procedures. Firstly, a special cannula was implanted into amygdala region of rats and leptin and saline were injected in this region by infusion pump. After leptin injections, behavioral tests were performed. In the second study, the extracellular fluid was collected by microdialysis from the amygdale region.The levels of serotonin and glutamate were measured by HPLC.

RESULTS: The first experiment demonstrated that in the open field, low dose leptin administrated rats spent more time at the center ($F(2,57)= 3.97$ $p=0.02$), showed more zone transition than control ones ($F(2,57)= 3.22$ $p=0.04$). In the elevated plus maze, high and low doses leptin administrated rats spent more time in the open arms ($F(2,55)= 6.77$ $p=0.002$) and also high dose leptin injected rats showed more frequency of entering open arms ($F(2,55)= 9.97$ $p=0.001$). In Porsolt test, low dose leptin administrated rats showed high mobility in center than sham group ($F(2,55)= 4.30$ $p=0.02$). In the Morris water maze, low dose leptin administrated rats spent more time over the platform ($F(2,45)= 3.50$ $p=0.04$). The second experiment demonstrated that serotonin and glutamate levels increased in the first hour after the leptin injections ($p<0.05$).

CONCLUSIONS: Present study suggests that both high and low leptin administration to rat brain playsa role as anxiolytic and antidepression agents in rats.

PC130

The Effects of *Lycium barbarum L.* Polysaccharides on Learning Behaviors of Young Ovariectomized Female Rats

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AIM*: Lycium barbarum Linnaeus* is also known as goji berry, wolfberry or super fruit. The red-orange and sweet fruits of goji berry

have been used in herbal medicine and health food for the thousand years. L. barbarum fruits have polysaccharides which have many beneficial effects for human such as ocular neuroprotective, antioxidant, immunomodulator, hepatic pretection and antitumor effects. In the present study, the aim was to investigate the effects of the L. barbarum polysaccharides (LBP) on learning behavior in ovariectomized young female rats (two months age) using the Morris water maze test.
METHODS: Two weeks after ovariectomy applications, rats were divided into five groups: control (distile water 3 mL/kg, gavage, per day), low dose LBP (20 mg/kg, 3 mL/kg, gavage, per day), high dose LBP (200 mg/kg, 3 mL/kg, gavage, per day), estrogen (1 mg/kg, 3 mL/kg, gavage, per day) and donepezil (1 mg/kg, 3 mL/kg, gavage, per day) and two subgroup within the each group: sham (pseudo ovariectomized rat) and overiectomized groups. After all treatments were applied for thirty consecutive days, behavioral test was applied. Blood serum samples of all rats were collected and levels of antioxidant enzymes (SOD, CAT, GPX, MDA and E2) of the samples were detected by ELISA method. All animals weights were measured weekly.
RESULTS: The findings of the present experiment demonstrated that platform finding time and travelled distance of the LBP administred ovariectomized groups were less than estrogen and donepezil administred groups.
CONCLUSIONS: In conclusion, LBP enhances the learning performance and antioxidant enzyme activity of ovariectomized female rats.

PC131

Evaluation of Cognitive Decline in Rheumatoid Arthritis: Predictive Value of Joint Destruction and Disease Severity

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AIM: Cognitive process of deterioration in Rheumatoid Arthritis (RA) are previously investigated in a few studies and to the best of our knowledge there have been no study about the correlation between radiological progression and cognitive decline in patients diagnosed with RA. The aim of the present study is to indicate the correlation between joint destruction and cognitive functions in RA.
METHODS: This cross-sectional study included forty five patients and forty healthy controls. Predictors of radiological progression (≥0.5 the modified Sharp/van der Heijde scores- MTSs), disease activity scores (DAS-28 and DAS-44) were evaluated in patients with RA. Mini Mental State Examination (MMSEs) and Hospital Anxiety Depression Scale (HADS) were evaluated and the results were compared between patients and control groups to determinate cognitive functions.
RESULTS: There was no statistically significant difference among groups in terms of age, sex and educational parameters ($p>0.05$). There was a statistically significant difference between groups in terms of MMSE scores ($p<0.01$). There weren't significant differences in terms of anxiety levels between both groups. MMSEs was correlated with MTSs and DAS-44($p<0.05$). Depression score was also correlated with DAS-44($p<0.05$). No relationship was found between disease duration, RF levels, anti-CCP levels and the cognitive function tests.
CONCLUSIONS: Although the brain has highly selective permeability that separates the circulating blood, inflammatory disorders such as RA cause cognitive problems including inability to concentrate, fuzzy and sluggish thought process via released mediators. The data obtained indicate that exposure to inflammatory mediators during long standing RA may lead to deterioration on central nervous system as long as affecting joints. Cognitive deterioration was correlated with disease severity and joint destruction. Thus, the radiographic joint destruction can be a positive predictor of reflecting the extent of neuronal damage and cognitive deterioration during this chronic process in rheumatoid arthritis.

PC132

Investigation of Selenium Effect on Long-term Potentiation

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AIM: Selenium has been recognized as a vital trace element of our diet with numerous beneficial effects on health. Se is required for the expression of Se-dependent enzymes such as glutathione peroxidase, thioredoxin reductase, iodothyronine deiodinases which are essential for several known major metabolic pathways, including thyroid hormone metabolism and antioxidant defense systems. In this study, we investigated the effect of selenium deficiency and excess in learning and memory function in rats.
METHODS: The Wistar male rats were divided into 4 groups;1-Control,2-Se supplement group(10ppm Se), 3-Se supplement group(20ppm Se), 4-Se deficient group(0.07ppm Se).For the evalution of long-term potentiation, high frequency stimulus giving the perforant path and the field potentials of dentate gyrus was recorded.After HFS 55-60 min, excitatory postsynaptic (EPSP) and population spike (PS) records analysis were evaluated and commented on the significance of the ANOVA test. In the plasma of animals, and the hippocampus tissue SA levels were measured.
RESULTS: Significant differences were found between the groups of the hippocampus Se values. Induction and maintenance period of population spike (PS) -Long Term Potentiation size were found lower than the control group. Excitatory postsynaptic potential(EPSP) of Se + 10ppm group decreased compared with the control group.
CONCLUSIONS: Long-term potentiation was impaired in Se deficient group.This impairment are thought to be due to reduction of antioxidant and deiodinase enzymes activity in hippocampus.We also observed reduction of hippocampal functions in Se supplement group.This shows that excess of Se affects the healthy neuronnegatively.

PC133

Comparing the Short-term Effect of Drinking Caffeinated Coffee on Hand Skill Rate Performance Ability Due to its Hotness, Smelling and Caffeine Ingredient

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AIM: Comparingthe short term effect of drinking caffeinated coffee on hand skill rate performance due to its hotness, smelling and caffeine ingredients with non-invasive methods.
METHODS: 34 healthy; 19 female(56%) and 15 maleright-handed (44%)students were participated. Average of age was 18–22y. Hand preference was assessed by Oldfield Test. Hand skill rate was assessed by Annett's Peg Moving Task-10. Each participant repeated the task five times for each hand before and after drinking beverages. Four applications performed (a-I/a-IV) within 3-4 days interval (a-I: control (no beverage), a-II:caffeinated coffee. a-III:hot water;a-IV decaffeinated coffee). Hand skill was measured twice before and afterdrinking beverage.Data were analyzed by statistical software package SPSS and $p<0.05$ was considered to be significant. Side-effects were lost in a short-time.
RESULTS: Hand skill rateperformance was not associated with the gender difference. Base on this result statistical evaluation was performed without gender discrimination. When the hand skill rate-performance values were compared for each hand,it was found that hand skill rate for both right and left hands were decreased after drinking beverage (a-II-IV)($p <0.05$).
CONCLUSIONS: This study may suggest that hotness, smelling and caffeine ingredient of coffee have equal effects on central nervous system.

PC134

The Role of Finger Tapping Task in the Assessment of Central Fatigue

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AIM:Fatigue is a general symptom of neuromuscular diseases and is described as progressive decrease observed in voluntary muscle activity during exercise. For formation of fatigue, 2 distinct levels of implications are mentioned as peripheral and central fatigue (CF). In the studies aiming the assessment of CF several technological methods have been used. Some studies also include the simple test of finger-tapping task (FTT) as additional method. The aim of this study was to investigate whether FTT could be used in the assessment of CF alone or not.
METHODS:Right-handed, male, first and second year students who have no declared neuromuscular disorders from Başkent University Faculty of Medicine participated in the study. CF was induced by "short-lasting repetitive maximal-rate activity model" and the assessment was made on FTT of 20 s. Task performances were analysed by linear regression, statistically. Independent groups were compared by "Student's t-test" in the case of satisfying parametric test's assumptions otherwise by "Mann-Whitney U Test". $\alpha=0.05$ was set as level of significancy.
RESULTS:Mean tapping rate was lower in CF group (n=44) compared with control group (n=58) ($p<0.05$). Non-linear temporal changes occured during the task and the performance patterns were found to be different in certain periods of the task. The boundaries of these periods were defined objectively by the numerical method of "sum of square of the difference". There were two distinguished points in both groups indicating three different sub-divisions in the task. Initial sub-division lasted shorter, fluctuations and intertap intervals increased significantly in three sub-divisions of CF group ($p<0.05$, $p<0.001$ ve $p<0.001$, respectively).
CONCLUSIONS:The results of this preliminary study suggest that the variations in temporal behavior of FTT may be used as an objective measure in the assessment of CF.

PC135

Autistic Feature and 2D: 4D Finger Ratio Relations Children and Adolescents with Congenital Adrenal Hyperplasia

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AIM: Because congenital adrenal hiperplazi (CAH) and Autism spectrum disorders (ASD) is rarely seen, it is difficult to assess whether the increased incidence of ASD in girls with CAH. ASD behaviors and 2D: 4D finger ratio changes in patients with androgen overproduction have been reported. The aim of this study is determining the 2D:4D finger ratios and ASD features in girls with CAH and normal control group.
METHODS: The study group will consist of thirty female children and adolescents between the ages of 3 and 15 who are diagnosed with classic CAH who were followed at the Pediatric Endocrinology Department of x and y Universites Medical Faculty Hospital. For the control group, 30 healthy children and adolescents equalized with CAH patients in terms of age and gender will be taken. All patients and controls were examined for psychiatric disorders by clinicians.

Patients and control groups filled Autism Behavior Checlist and semistructured sociodemogrphic form that evaluated the gender, age, pregnancy and birth complications, history of mothers' cigarette and alcohol use. 2D:4D ratios were measured in both of control and CAH groups.
RESULTS: CAH group right and left hand 2D:4D ratios were statistically lower compared to controls and also lower 2D:4D ratios had association with high ABC scores. When compared with control group, ABC scores were significantly higher in CAH group. In KAH group there was a positive correlation between 2D:4D ratios and ABC scores.
CONCLUSIONS: The present findings suggest that high androjen may have an effect on low 2D:4D ratios and high ASD symptoms. Further research with a large sample is needed in this field.

PC136

Laboratory Animal Tracking in Behavioral Experiments: An Alternative Low Cost Solution

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AIM: Behavioral animal experiments are widely used methods in neurophysiological and neuropharmacological studies. Animal tracking and analysis in such experiments are performed by either manually or automatically. There are several commercial tools permitting accurate automatic analysis within short time. However, relatively higher initial cost of these tools may prevent promising low budgeted projects to be initiated. In order to introduce alternative shareware solution for such a problem we developed our own system and the results were discussed in accordance with the reliability and the validity aspects.
METHODS: The system includes the software program which analyses set of image frames, the arena where the animal moves and standard webcam. The software extracts the coordinates of animal's instantaneous location, calculates previously defined experimental measures, displays on the screen and saves permanently for further analysis. The system was tested for two different arenas namely, Morris Water Maze (MWM) and Open Field (OF). The results were compared with that of manual method. Cronbach's alpha test was used for the internal consistency of the data sets. Accuracy of the results was evaluated by paired samples t-test and Pearson correlation. Statistical level of significance was set to $p<0.01$.
RESULTS: Video files of 25s and 138s were recorded during MWM and OF tests, respectively. Instantaneous travelled distances (ITD) that the animal moved within the two successive picture's time were computed by both method and, were compared by paired samples t-test. Statistical analysis didn't reveal any significant difference between the methods ($r=0.954, p=0.792$ forMWM test and $r=0.996, p=0.024$ forOF test).
CONCLUSIONS: The results suggest that the system consists of reliable and valid software algorithm for locating the instantaneous coordinates of experimental animal and may be evaluated as an high resolution low cost tool for the behavioral experiments. Therefore, we believe that this study may contribute to initiate low budgeted projects.

PC137

The Effect of P2X7 Receptor Antagonist A-438079 on Penicillin-induced Epileptiform Activity

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AIM: P2X7 receptor has been recently discovered member of the P2X receptor family, which is one of the three subgroups of purinergic receptors. It is present in almost all cells in the brain. The aim of this study was to determine the role of P2X7 receptor on penicillin induced epileptiform activity.
METHODS: 16-18 weeks of age male Wistar rats (n=35) were anesthetized with 1,25 mg/kg urethane and fixed to the stereotactic frame. Bipolar electrode was placed with surgery in occipitofrontal direction and was connected to the Powerlab data acquisition unit. Then, two more holes were drilled for intacortical (i.c.) and intracerebroventricular (i.c.v.) injections. Epileptic seizure was created with the injection of Penicillin-G potassium (i.c.) and interictal spike activities were observed through the Chart-7 software. A-438079 (5, 10, 20, 40 µg; i.c.v.) was administered after 30 minutes from beginning the spike activity and the results were analysed.
RESULTS: A-438079, a selective antagonist of the P2X7 receptor, did not change the spike frequency at a dose of 5 µg when compared to the control group ($p> 0.05$). On the other hand, the means of the spike frequency were decreased at a dose of 10, 20, 40 µg in the 100th ($p<0.05$), 60th ($p<0.01$) and 60th ($p<0.01$) minutes after A-438079 injection, respectively. There was no significant difference in the amplitudes between groups.
CONCLUSIONS: Releasing of ATP from neurons and neuroglias, activates the P2X7 receptor and causes calcium influx into the cells. These lead to increase the spike wave discharges, the exacerbation of seizures and neuronal deaths. In the present study, the suppression of the P2X7 receptor decreased the penicillin-induced spike wave discharges. After this stage, the effects of P2X7 receptors in the brain will be studied from a biochemical point.
This study is supported by TUBITAK (Project number: 115S361)

PC138

The Effect of Low Dose Memantine on Epileptic Activity in WAG/Rij Rats

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AIM: Absence epilepsy is a non-convulsive type of epilepsy that is characterized with spike-and-wave discharges (SWDs) on electro-

encephalogram (EEG) and behavioral pause at the same time. A non-competitive NMDA receptor antagonist, memantine has been known anti-convulsant in various experimental epilepsy models. The aim of present study is to investigate the effect of low dose of memantine on the absence epilepsy in Wag/Rij rats, which is a genetically determined model for absence epilepsy.
METHODS: Six adult male Wag/Rij rats were used in this study. Tripolar electrodes were placed on the skull. Animals were allowed to recovery after electrode implantation for a week. After basal electrocorticogram (ECoG) activity recording at 10:00 a.m. for 3 hours, memantine, at a dose of 1mg/kg (i.p.), was administered then ECoG activity was recorded for another 3 hours.
RESULTS: Low dose of memantine significantly decreased the cluster number, cluster duration and SWDs numbers compared to basal ECoG recordings ($p<0.05$). However, low dose of memantine didn't affect the mean amplitude of SWDs ($p>0.05$).
CONCLUSIONS: Although memantine, at dose of 1 mg/kg, was ineffective in convulsive experimental epilepsy models, it was anti-convulsant in non-convulsive genetic epilepsy model of WAG/Rij rats in this study. The pathophysiology of absence epilepsy is not exactly known. The molecular mechanism of this effect is needed to be highlighted by other analysis methods.

PC139

The Effects of Very Low Frequency Electromagnetic Fields on Morphine Analgesia and Tolerance in Rats

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AIM: Morphine is one of the most important drugs used in clinical severe and chronic pain. However, prolonged use of morphine leads to the development of tolerance to its analgesic effect. Several studies have demonstrated that the electromagnetic fields produce analgesic activity. The aim of this study was to investigate the effects of very low frequency electromagnetic field on morphine analgesia and tolerance in rats.
METHODS: This study used 78 adult male Wistar albino rats (approximately 240±12 g). The application of 50 Hz magnetic field, each day the same times for 30 min for 15 days, and a total of four times every 15 min intervals. To constitute morphine tolerance, high dose of morphine (50 mg/kg) was administered for 3 days in rats and tolerance was evaluated on the 4th day. The analgesic effect measurement was performed by tail-flick and hot-plate test equipment. Prior to analgesia tests, the effective dose (5 mg/kg) of morphine was injected in rats. The data was converted to % analgesic effect (%MPE). In the statistical analyzes of the data, analysis of variance (two-way ANOVA) was used and the multiple comparison determined by Tukey tests.
RESULTS: The maximum analgesic effect of the 5 militesla (mT) magnetic field was determined on 7 days (tail-flick: 26,11±3,06 and hot-plate: 62.24±3.16). Administration of morphine (5 mg/kg) in rats exposed to a magnetic field the analgesic effect (tail-flick: 72.32±5.08 and hot-plate: 85.43±5.54) was significantly higher compared to the magnetic field group ($p<0.05$). Morphine tolerant animals exposed to a magnetic field, the analgesic effect was found significantly higher than morphine tolerance group rats ($p<0.05$).
CONCLUSIONS: Analgesia test data demonstrated that application of low frequency electromagnetic field to rats increases the morphine analgesia and reduces morphine tolerance.

PC140

Effects of *Leontice leontopetalum* and *Bongardia chrysogonum* Extracts on Pentylenetetrazole Kindling Epilepsy Modelin Rats

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AIM: We investigated possible antiepileptic effects of aqueous extracts of roots of *Leontice leontopetalum* used for treatment of epilepsy in folk medicine and roots of *Bongardia chrysogonum* which belongs to the same family.
METHODS: 28 Wistaralbino male rats were divided into four groups; Control group (saline, 0.5 ml), pentylenetetrazole group (PTZ, 35mg/kg, 18 injections; 19th injection 75mg/kg), Leontice group (200mg/kg extract p.o. + PTZ, 35mg/kg, i.p., 18 injections; 19th injection 75mg/kg, i.p.) and Bongardia group (200mg/kg extract p.o. + PTZ, 35mg/kg, i.p., 18 injections; 19th injection 75mg/kg, i.p.). Bcl-2 and Cyclin-B1 levels were assessed with Western-blot method in hippocampus and whole brain. Expression of GABAA receptor was analyzed immunohistochemically with specific antibodies.
RESULTS: Bcl-2 level was decreased whereas cyclin-B1 level was increased in whole brain and hippocampus in PTZ group compared to control significantly ($p<0.01$). An increase in Bcl-2 level and a decrease in cyclin-B1 level in whole brain and hippocampus were observed in plant administered groups compared to PTZ group ($p<0.01$). Number of GABAA positive stained cells was significantly lower in plant administered groups compared to PTZ group, both in whole brain and hippocampus ($p<0.01$).
CONCLUSIONS: Plant administration ameliorates alterations induced by PTZ administration. Therefore, we suggest that aqueous extract of plant may exert neuroprotective effect against PTZ induced cell death.
This study was supported by YYU Scientific Research Projects Unit.

PC141

The Effects of *Cichorium intybus* Extract on Cerebellar Apoptosis and Oxidative Stress in Pentylenetetrazole-induced Kindling Model in Rats

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AIM: Epilepsy is among the most common neurological disorders which affects about 1% of general population. Current therapies used for epilepsy are symptomatic and have anti-convulsive rather than anti-epileptic effect. Roots of Cichorium intybus plant have been used for the traditional treatment of epilepsy in Europe as well as in Eastern Anatolia region. Pentylenetetrazol (PTZ) kindling model is widely used in antiepileptic drug discovery and has great importance in understanding the pathophysiology of epilepsy. The aim of this study is to investigate aqueous root extract of Cichorium intybus plant on cerebellar apoptosis and oxidative stress.
METHODS: Total phenolic content of the C. intybus aqueous root extract was determined by using a Folin-Ciocalteau colorimetric method. Also the determination of six phenolic acids [(Chlorogenic acid (ChA), Syringic acid (SA), Ferulic acid (FA), o-Coumaric acid (o-COU), p-Coumaric acid (p-COU), tr-Cinnamic acids (trCIN)] were achieved by using a modified Reverse phase-High pressure liquid chromatography (RP-HPLC) method. The amounts of the relevant phenolic acids were calculated by using their calibration equations. Twenty seven male Wistaralbino rats were randomly divided into 3 groups of control, epileptic and plant extract-treated (200 mg/kg, orally) epileptic group. Following PTZ kindling; endothelial nitric oxide synthase (eNOS), inducible NOS (iNOS), neuronal NOS (nNOS), caspase-3 levels were investigated by immunohistochemically and apoptotic cells were determined by TUNEL technique in cerebellum. Total antioxidant status (TAS), total oxidant status (TOS) and oxidative stress index (OSI) levels were also examined biochemically. The statistical significance was established by one-way ANOVA followed by Tukey post-tests. A value of $p<0.05$ was considered statistically significant.
RESULTS: The extraction yield as a percentage of plant material was 14.5% (wt/wt), and total phenolic content was 83.86 ± 3.24 mg of gallic acid equivalents/g of extract. According to the HPLC analysis; FA was most abundant (45.64 µg/g), followed by ChA (42.47 µg/g), SA (21.93 µg/g), p-COU (12.12 µg/g), o-COU (10.56 µg/g), and tr-CIN (9.25 µg/g) in the extract. Although PTZ treatment increased ($p<0.001$) the eNOS and iNOS levels, it decreased ($p<0.001$) the nNOS levels in cerebellum. Cichorium intybus treatment did not change eNOS levels, but decreased ($p<0.001$) the iNOS and increased ($p<0.001$) the nNOS levels when compared to PTZ. Cichorium intybus decreased ($p<0.001$) the PTZ-induced increase in caspase-3 level. In the TUNEL assay, the apoptotic index results were parallel to caspase-3 levels in cerebellum. Although PTZ treatment increased the TOS ($p<0.01$) and OSI ($p<0.05$) levels, Cichorium intybus treatment decreased ($p<0.05$) these parameters.
CONCLUSIONS: It was concluded that Cichorium intybus plant treatment might ameliorate the PTZ-induced neurodegeneration in the cerebellum regarding to apoptosis and oxidative stress.

PC142

Anticonvulsant Effect of Ramelteon on the Seizures Induced by Pentylenetetrazole in Rats

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AIM: There are many difficulties involved with the treatment of epilepsy. Thus, there is a need for new approaches in order to control epileptic seizures. Melatonin is an endogenous hormone that is secreted from the pineal gland. Anticonvulsant effects of melatonin were shown in a variety of experimental models. Ramelteon is an agonist that acts solely on melatonin receptors. In this study, we aimed to investigate the effects of ramelteon as a melatonin agonist in PTZ-induced epilepsy in rats.
METHODS: The rats were divided into six groups. All animals were subjected to cortical electroencephalographic (EEG) recordings. The first group was the control. The second group was 60 mg/kg PTZ applied. The third group was DMSO+PTZ injected. The fourth group was given 150 mg/kg VPA+PTZ. The fifth group was given 30 mg/kg Ramelteon+PTZ. The sixth group was given Ramelteon+VPA+PTZ. EEG traces, Racine's convulsion stages and the time of onset of the first myoclonic jerk were compared between the groups.
RESULTS: There were significant differences between the PTZ and Ramelteon+VPA+PTZ groups in terms of the Racine's convulsion stages, the onset of the first myoclonic jerk and the rate of the spikes in the EEG traces ($p<0.001$).
CONCLUSIONS: The selective melatonin receptor agonist ramelteon showed anticonvulsant properties in the PTZ model. It is necessary to elaborate which of the melatonin receptors is used by ramelteon in order to suppress epileptic seizures.
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PC143

Investigation of Possible Therapeutic and Preventive Effect of Omentin onto Absance Epilepsy

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AIM: Epilepsy is one of the frequently observed central nervous system disorder. Ethosuximide (ESX) is a drug of choice for the

symptomatic treatment of absence seizures. Omentin is an adipocytokine that is abundantly expressed in visseral fat tissue. Omentin increases AMP-activated protein kinase (AMPK) phosphorylation, GABAB receptors are intimately associated with 5'AMP-dependent protein kinase (AMPK). GABAB receptors are heterodimeric G protein-coupled receptors composed of R1 and R2 subunits. GABAB receptors mediate slow prolonged inhibition in the brain by activating postsynaptic inwardly rectifying K+ channels (GIRKs) and inactivating presynaptic voltage-gated Ca++ channels.
METHODS: For this experiment male (250- 350 gr) WAG/ Rij (n=16) and Wistar albino (n=40) rats were used. After stereotaxic surgical procedures, all rats were returned ready for direct measurement of cortical EEG. Animals were seperated into seven groups. Group A1: Control, Group A2: Pentilantetrazol (PTZ), Group A3: ESX+ PTZ, Group A4: ESX + PTZ combined with Omentin, Group A5: Omentin+ PTZ, Group A6: PTZ+ Omentin as a result of the implementation of six groups (n=8) in Wistar albino rats. ESX (125mg/ kg/ 3 day), Omentin (8 µg/ kg/ 3 day) and PTZ (40 mg/ kg) were administered intraperitoneally.
RESULTS: DDD group treated with ESX, number, latens period and average duration of the reduction (p<0. 05). Omentin and ETX ctiveness of the DDD group (p<0..05). Group B1(WAG/Rij) (n=8)was accepted as the control group and Group B2 (WAG/Rij) was used for Omentin experiment (p> 0.05).
CONCLUSIONS: As a result, ESX led to a decrease in the effective absence seizure. Omentin administered with ESX treatment was strenghened.

PC144

The Effect of Maternal Deprivation on Penicillin-induced Epilepsy

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AIM: Epilepsy is a neurological disorder manifested by recurrent seizures originated from abnormal electrical activity of the brain. Many epilepsy models were created specifically to reproduce particular types of epilepsy. Penicillin-induced epileptiform activity is a widely used experimental model of focal epilepsy. Maternal deprivation can be defined as loss of the care of the mother to the infant which may have intense or long continued even irreversible effects on the baby's brain activity. The aim of this study is to investigate the effects of short-term maternal deprivation on penicillin induced epileptiform activity in rats.
METHODS: In this study, total of 20 male Wistar rat puppies, aging 2 months were used. First group (stress group) (n=10) the rat's puppies were separated from their mother. Second group (control group) (n=10) the rat's puppies were not separated from their mother. The left cerebral cortex was exposed by craniotomy under urethane anesthesia (1.25 g/kg). Silver ball electrodes placed over the cortex and connected to a data acquisition system for the recording of electrocorticography (ECoG). The epileptiform activity was induced by microinjection of penicillin G (500 IU/2.5 µl) into the left cortex.
RESULTS: The maternal deprivation did not cause any change in the mean frequency and amplitude of penicillin induced epileptiform activity (p>0.05). The mean frequency and amplitude of epileptiform activity were 39.52 ± 5.23, 38.36 ± 6.90 the number of spike/minute ± standard error of mean, 711.75 ± 88.28, 663.76 ± 75.10 spike amplitude microvolt (µV)/minute ± standard error of mean between 45th and 50th minutes after injection in the control and stress group, respectively.
CONCLUSIONS: The stress of separation from mother has no effect on the penicillin induced epileptic activity. This result needs to be supported by the biochemical analyses.

PC145

Quercetin Decreased Penicillin-induced Epileptiform Activity in Rats

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AIM: Epilepsy is a common chronic neurological disorder that characterized with synchronized abnormal electrical discharges. Quercetin is a flavonoid that widely present in tea, red wine, fruits and vegetables; and frequently ingested in daily diet. Studies show that quercetin has anticonvulsant effect. Also, some studies suggest that quercetin acts as proconvulsant. Moreover, these studies are performed with behavioral methods that base on observation in animal models of epilepsy. The aim of this study is to research the effect of quercetin on epileptiform activity in experimental penicillin model of epilepsy by using electrophysiological methods.
METHODS: In this study, 30 Wistar albino female rats (180-240 g) were used in five groups as following (n=6): Control group (penicillin G), vehicle group (penicillin+dimethyl sulfoxide(DMSO)), quercetin 5, 20 and 50 mg/kg groups (penicillin+quercetin 5, 20, and 50mg/kg,respectively).Animals under urethane (1.25g/kg, intraperitoneally(i.p.)) anesthesia were put into stereotaxic device. Two recording electrodes were placed into holes that drilled on skull and connected to the PowerLab data acquisition system for electrocorticogram (ECoG) recording. Another hole was used for injecting penicillin (500 IU, 2.5µl, intracortical) to induce epileptiform activity. Quercetin (and DMSO (0.4ml/kg)) was administered intraperitoneally 30 min after penicillin injection. Recording was continued 180 min after quercetin injection.
RESULTS: Compared to the control group, 5mg/kg quercetin significantly decreased frequency of epileptiform activity from 100th minute to the end of the recording (p<0.001), but it didn't alter amplitude. Quercetin administration at dose of 20 and 50 mg/kg didn't cause any significant change in both frequency and amplitude. Vehicle group was statistically the same as control group.
CONCLUSIONS: In previous studies conflicting results were reported about effect of quercetin on epilepsy. In the present study; it is demonstrated that 5mg/kg (i.p.) quercetin decreased penicillin-induced epileptiform activity. To reveal the mechanism(s) of this action of quercetin, further researches are needed.

PC146

Effects of Caffeic Acid Phenethyl Ester on Penicillin-induced Epileptiform Activity

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AIM: Imbalance of brain excitatory and inhibitory processes due to different types of structural or functional alterations may cause epileptiform activities. Caffeic Acid Phenethyl Ester (CAPE) is a bioactive component of honeybee hive propolis. It exhibits antioxidant, antiinflammatory and antiproliferative properties. There is limited study concerning the effect of CAPE on epilepsy. Therefore, we investigated the effect of CAPE in experimental epilepsy both electrophysiological and biochemical on penicillin-induced epilepsy.
METHODS: Experiments were carried out on adult male Wistar albino rats. Animals were divided into five groups; Control (sham), penicillin, penicillin+CAPE 5 mg/kg, penicillin+CAPE 10 mg/kg and penicillin+DMSO groups. Epileptiform activity was induced by intracortical (i.c.) administration of penicillin (500 IU, 2 µl) and after 30 min, CAPE doses were given intraperitoneally. 24 h later, animals are decapitated for the collection of blood samples and brain tissue. We measured levels of nitric oxide and malondialdehyde or superoxide dismutase (SOD) and general glutation peroxidase (GPx-1) activity in the homogenized brain tissue; and serum S100B protein, neuron-specific enolase, Neuropeptide Y (NPY) and calcineurin levels.
RESULTS: The doses of CAPE did not cause any change on the frequency or amplitude of penicillin-induced epileptiform activity. However, injection of 10 mg/kg CAPE up-regulated significantly serum protein S100B level in comparison with the penicillin group ($p<0.001$). It was significantly increased serum NPY level penisilin+DMSO group comparison with the sham group. Moreover, the activity of GPx-1 in penicillin and penicillin+CAPE 5 mg/kg were higher compared to the sham group ($p <0.05$).
CONCLUSIONS: It was not found a significant anticonvulsant effect of CAPE in the electrophysiological study on penicillin-induced epileptiform activity. However, it caused significant changes in the biochemical parameters of brain and blood. This result was shown for the first time by electrophysiological and biochemical data the effect of CAPE on epileptic activity.

PC147

The Effect of β-Carotene on Spike Wave Discharges in Genetic Absence Epileptic WAG/Rij Rats

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AIM: β-Carotene, which is the main source of Vit A, is abundant in plants and fruits. It is a potent free radical scavenger and antioxidant chemical. The aim of this study was to determine the effect of β-Carotene, which is used as a dietary supplement. were randomly divided into 5 groups (n = 30). One week after placing the electrodes for EEG recording, animals were connected to the Powerlab data acquisition unit for observing the spontaneous seizure activities. Three hours after the EEG recording, the solvent of the β-Carotene soybean oil was applied to the control group and β-Carotene was applied to the other groups at doses of 25, 50, 100 and 200 mg/kg intraperitoneally (i.p.). EEG recording was started again after 15 min. and three more hours of recording were obtained. Seizure activities that were obtained after the drug, were analyzed by comparison with the pre-drug seizure activities.
RESULTS: Before injection of the drugs, the total number of seizures were 95 ± 12 during the three hours in all groups. The means of the percentage of seizure parameters were not change at a dose of 25 mg/kg when compared to the control group ($p>0.05$). β-Carotene, at doses of 50 ($p<0.05$), 100 ($p<0.001$) and 200 mg/kg ($p<0.001$) increased total number of seizures, total duration of seizures and total number of spike activities in a dose dependent manner. On the other hand, generalized seizures were observed in two rats at a dose of 200 mg/kg.
CONCLUSIONS: Studies demonstrated that β-Carotene reduces the reactive oxygen species and inhibits nitric oxide synthesis. Similarly, nitric oxide synthase inhibitor L-Name increases in seizures when administered to Wag/Rij rats. In the next stage of this study, β-Carotene's role on nitric oxide pathway will be investigated.

PC148

The Effects of Nigella Sativa Extract and Chronic Exercise Application on Penicillin-induced Epilepsy Model in Mongolian Gerbils

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AIM: The aim of this study is to investigate the effects of black cumin (Nigella sativa) extract with treadmill exercise on experimental penicillin induced epilepsy model in gerbil electrophysiologically.
METHODS: In this study 2-4 months male Mongolian gerbils were used. Animals were divided into 4 groups as; control (penicillin), control (exercise), black cumin and black cumin+ exercise group. Treadmill exercise was performed in every five days in a week for 2 months in exercise groups. 50 mg/kg dose of Nigella sativa extract were applied in every 5 days in a week for 2 months in Nigella sativa groups. After 2 months exercise and gavage application, epileptiform activity was induced by intracortically penicillin (500 IU) application. 120 minutes electrocorticography (ECoG) recording was taken and analyzed for each animal by using powerlab system. The time to onset of first epileptiform activity's latency, spike-wave frequency and spike-wave amplitude of epileptiform activities' data were analyzed statistically using the Mann-Whitney U test.

RESULTS: According to latency values Nigella sativa+execise group was prolonged time to onset of first epileptic seizure when compare the other groups (p<0.05). Nigella sativa + exercise were reduced spike wave frequency from time to onset of seizure to 13th period (p<0.05). When he left to be 5 minutes long period of time records acording to amplitude values, mean amplitude values of exercise group were high until 6th period, but Nigella sativa+ exercise group was the lowest (p<0.05). There was no significant difference among the groups after the 6th period.
CONCLUSIONS: These findings showed that combine application of Nigella sativa and exercise retarded to latency of the time to onset of first epileptiform activity, and reduced spike wave frequency and amplitude of epileptiform activity. This suggests that exercise with consumption of Nigella sativa may be beneficial to patients with epilepsy.

PC149

Effects of Exendin-4 on Anxiety, Epileptic Seizures and Memory Retrieval in Rats

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AIM: Exendin-4 is a long acting glucagon-like peptide-1 (GLP-1) agonist, which exerts significant effects on glucose homeostasis. GLP-1and GLP-1 receptors are widely distributed in the central nervous system and it is suggested that GLP-1 may be involved in several brain functions. In this study, we aimed to investigate the effects of intracerebroventricularly (i.c.v.)-injected Exendin-4 on anxiety, epileptic seizures and memory retrieval in rats.
METHODS: Rats were equipped with permanent i.c.v. cannulas under isoflorane anesthesia. First group of rats (n=21) were pretreated with Exendin-4 (0.3-1 nmol/5 µl; i.c.v.) or saline (5 µl; i.c.v.) 30 minutes before Elevated Plus Maze (EPM) test and time spent in open and closed arms were recorded. After the EPM, epileptic seizures were induced by by pilocarpine (400mg/kg; i.p.) and latency to status epilepticus was recorded. Second group of rats (n=21) were subjected to 4-day acqusition trials with the hidden platform in the Morris Water Maze and were pretreated with Exendin-4 (0.3-1 nmol/5 µl; i.c.v.) or saline (5 µl; i.c.v.) 30 minutes before the probe trial. Time spent in the target quadrant, number of platform crossings and distance swum were measured.
RESULTS: Exendin-4 (0.3-1 nmol/5 µl; i.c.v.) injected 30 min before pilocarpine did not significantly affect the latency to status epilepticus. Similarly, none of the applied doses of Exendin-4 produced statistically significant differences in the time spent in the target quadrant, number of platform crossings and distance swum compared to saline- treated rats. In the EPM, Exendin-4 (1 nmol/ 5µl) significantly decreased the time spent in the closed arms (p<0,05) and increased the time spent in the open arms (p<0,01).
CONCLUSIONS: Centrally-injected Exendin-4 did not have any significant effects on epileptic seizures and memory, but exerted a significant dose-dependent anxiolytic effect.

PC150

Effect of *Epigallocatechin gallate* on Penicillin-induced Epileptiform Activity in Rats

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AIM: Purpose of this study is to investigate effects of epigallocatechin gallate (EGCG), which is one of major constituents of Green Tea, on epilepsy via experimental penicillin-induced epilepsy model in rats.
METHODS: In this study, 48 adult Wistar male rats were used. Rats were divided into 6 groups, as control (penicillin) group, only 100 mg/kg of EGCG, preseizure administration 50 and 100 mg/kg of EGCG groups and during seizure 50 and 100 mg/kg EGCG groups. Rats were anesthetized by urethane. After the left part of the bone on cortex was removed, electrodes were placed onto somatomotor area and electrocorticogram (ECoG) recording was performed. After 5 minute of basal activity recordings 50 and 100 mg/kg EGCG were applied to preseizure groups. Thirty minutes later, intracortically penicillin (500 IU) was injected. In the application during seizure groups, penicillin (500 IU) was injected after 5 min basal activity recordings. 30 min later, 50 and 100 mg/kg EGCG were applied. The time to onset of first spike-wave latency, spike-wave frequency and spike-wave amplitude of epileptiform activity were analyzed statistically.
RESULTS: In the group treated with only EGCG, it was not observed any epileptiform activity. There was not statistically difference between control and EGCG groups according to median values of the latency time to onset of first epileptic seizure (P>0.05). Median of epileptiform activity frequency and amplitude of epileptiform activity were not significantly different among preseizure and during seizure groups except time periods between 11th-30th min for the amplitudes of EGCG application during seizure group (p>0.05).
CONCLUSIONS: In this study, it has been shown that 50 and 100 mg/kg EGCG has not any significant effect on latency, spike-wave frequency and amplitude of epileptiform activity in penicillin induced epilepsy model by electrophysiological methods.This study was supported by Düzce University Research Fund (Project Number: DÜBAP-2013.04.01.184).

PC151

Agonist and Antagonist Effects of ATP-dependent Potassium Channel on Penicillin-induced Epilepsy in Rats

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AIM: The purpose of this study was to investigate acute effects of KATP channel agonist (pinacidil) and antagonist (glibenclamide) on experimental epilepsy models.
METHODS: In this study, 32 adult male Wistar rats were used. Rats were divided into 4 groups as control (saline), 1.0 mg/kg glibenclamide, 0.01 mg/kg pinacidil and solvent (dimethyl sulfoxide). All rats

were anesthetized with urethane. Following removal of left part of the cortex, the electrodes were placed onto somatomotor area and electrocorticogram (ECoG) recording was performed. Epileptiform activity was induced by intracortical (ic) administration of penicillin (500 IU, 2.5 µl). At the 30th minutes of penicillin application, all substances (glibenclamide, pinacidil, DMSO, saline) were injected intraperitoneally. Obtained electrocorticographic (ECoG) data from recordings were analyzed by software. Spike-wave frequency and spike-wave amplitude of epileptiform activity were statistically analyzed.
RESULTS: When 120 minute's ECoG recordings of the pinacidil group were examined, it was found that 0.01 mg/kg pinacidil's mean values of epileptiform activity spike-wave frequency was significantly lower than the control group ($p<0.05$). However, there was no significant effect on spike-wave amplitude of epileptiform activity. Similarly, glibenclamide (a blocker of KATP channel) had no significant effect on spike-wave frequency and spike-wave amplitude of epileptiform activity.
CONCLUSION: The present results showed that administration of pinacidil has an antiepileptic effect in penicillin induced epilepsy model in rats. Pinacidil may be a potential antiepileptogenic drug in the future.
This study was supported by Düzce University Research Fund (Project Number: DÜBAP-2012.04.HD.070).

PC152

Effect of (R)-(-) and (S)-(+) Carvone on the Penicillin-induced Epileptiform Activity in Rats

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AIM: Aim of this studywas to investigate acute effects of (R)-(-) and (S)-(+) carvone on experimental penicillin-induced epilepsy model electrocorticographically in rats.
METHODS: In this study 91 adult male Wistar rats were used. Rats were divided into 13 groups as; sham, solvent, control (penicillin), only (R)-(-) and only (S)-(+) carvone group, and the doses of 100 and 200 mg/kg of (R)-(-) and (S)-(+) carvone preseizure and during the seizure. All of the substances were administered intraperitoneally except penicillin. Rats were anesthetized with the dose of 1.25 g/kg urethane intraperitoneally. After the bone on the left cortex was removed, the electrodes were placed onto somatomotor area and electrocorticogram (ECoG) recordings were taken. After taking 5 min basal activity recordings in all groups, (R)-(-) and (S)-(+) carvone were injected to preseizure groups. 30 min later, penicillin (500 IU) was injected intracortically. In seizure groups, penicillin (500 IU) was injected before (R)-(-) and (S)-(+) carvone were administered. The time to onset of first spike wave latency, spike-wave frequency and spike-wave amplitude of epileptiform activitiesdata were analyzed statistically.
RESULTS: In the group treated with only substance were not identified any epileptiform activity in the sham and solvent groups. Preseizure 100 mg/kg (S)-(+) carvone group's median values of latency time to onset of first epileptic seizure were found to be significantly lower than the control, preseizure 100 and 200 mg/kg (R)-(-) carvone ($p=0,008$) groups. Median of spike-wave frequency and spike-wave amplitude of epileptiform activity which measured between 0-120 minutes were not determined significantly different among the groups, except some time periods ($p>0.05$).
CONCLUSIONS: In this study, it has been shown that (R)-(-) and (S)-(+) carvone did not affect on spike-wave frequency amplitude in penicillin induced epilepsy model.
This study was supported by Düzce University Research Fund (Project Number: DÜBAP-2013.04.01.167).

PC153

Role of Cannabinoid cb1 Receptor in Proconvulsant Effect of Apelin-13 on Penicillin-induced Epileptiform Activity

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AIM: Epilepsy is a neurological disorder that starts suddenly and is transient onset of a group of neurons, resulting abnormal electrical discharges. Cannabinoids are heterogeneous group of compounds which have many functions in the central nervous system. The aims of this study was to evaluate interaction between cannabinoids and apelin-13 in experimental models of epilepsy.
METHODS: 36 male albino Wistar rats (180-270 g.) were divided into 6 groups. Groups: 1- Control, 2-Apelin-13 (15 µg, i.c.v.) 3- ACEA (7.5 µg, i.c.v.) 4- Ineffective dose of AM-251 (0.125 µg, i.c.v.) 5- Effective dose of ACEA (7.5 µg, i.c.v.) + effective dose of apelin-13 (15 µg, i.c.v.), 6- Ineffective dose of AM-251 (0.125 µg, i.c.v.) + ineffective dose of apelin-13 (5 µg, i.c.v) + effective dose of ACEA (7.5 µg, i.c.v.). Rats were placed in the stereotaxic frame after anesthetized by 1.25 g/kg urethane (i.p.). Substances were applied 30 min after penicillin injection. Tukey test was used for statistical analysis. $p< 0.05$ was considered statistically significant.
RESULTS: The effective dose of apelin (15 µg) increased the mean frequency of epileptiform activity starting from 20 min after apelin injection. ACEA reduced epileptiform activity from 50 min after ACEA injection. The simultaneous application of both substances significantly reduced epileptiform activity in the 50 min after injection. Administrations of ineffective doses of Apelin-13 and AM-251 with effective dose ACEA also reduced epileptiform activity from in the 50 min.
CONCLUSIONS: The observation of anticonvulsant effect in the ACEA and apelin-13 groups suggests that this effect was blocked intracelluler Ca+2 entries by apelin-13. Since ineffective doses of AM-251 and apelin-13 did not cause a synergistic effect and ACEA showed its anticonvulsant effect in this study. Therefore, it might be assumed that they use separate pathways for their effects.

PC154

The Effect of Theophylline Ethylenediamine on Seizures in Older WAG/Rij Rat

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AIM: Genetically epileptic WAG/Rij rats develop spontaneous absence-like seizures after 3 months of age, but seizure activity increases with age. Although it is known that adenosine receptor antagonist ssupresses inhibitory system in the brain and shows anticonvulsant effect on seizures in the non-convulsive-type of epilepsy models, the effect of adenosine receptor antagonist, theophylline ethylenediamine, on seizures in aged WAG/Rij rats are not known. In this study, the effect of theophylline ethylenediamine on increased seizure activity in aged WAG/Rij rats was studied.

METHODS: 28 male WAG/Rij rats (250-300 g), aged 18 months were divided into 7 groups. Rats were placed in the stereotaxic frame after anesthetized by ketamine (30 mg/kg, i.p.) xylazin (5 mg/kg, i.p.) and tripolar electrodes were placed on skull. Following the recovery period, electrocorticography (ECoG) were recorded at 09:00 am for 2 hours every day. Subsequently, saline (Group I;1ml/i.p.) and teofiline ethylenediamine (Group II: 12.5 mg/kg/i.p; Group III: 25 mg/kg/i.p, Group IV: 50 mg/kg/i.p) were administered. After substance injection, ECoGs were recorded for another 2 hours. The total number, the total duration and the amplitude of the spike-wave discharges (SWDs) were calculated for 2 hours.

RESULTS: Administrated doses of theophylline ethylenediamine (12.5 mg/kg/i.p; 25 mg/kg /i.p;50 mg/kg/ i.p) significantly decreased the total number ($p<0,05$) and the mean duration ($p<0,05$) of SWDs in the ECoG recordings, whereas the amplitudes of SWDs were not affected.

CONCLUSIONS: The pathogenesis of nonconvulsive epilepsy is related to increased inhibitory function in the brain. Administration of theophylline ethylenediamine may suppress the inhibitory system and cause the anticonvulsant effects in older WAG/Rij rats.

PC155

The Effect of N170 Lateralization on Different Gender

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AIM: Our aim was to investigate the gender effect on N170 lateralization using supraliminal angry human face visual expressions.

METHODS: In this study, 30 volunteers, 18 women (19 ± 3.5 years) and 12 men (20 ± 3.5 years) participated. Human face visuals were designed graphically using Face Gen Modeler 3.5.3 Suite as four neutral face images. One of the neutral face image prepared as "probe" stimuli by adding facial fierce appearance. Face stimuli are randomly shown consistent with odd ball paradigm by 70% neutral, 30% probe. Supraliminal visuals were displayed 500 ms duration simultaneously event related potentials (ERP) were recorded. Supraliminal probe's N170 amplitudes were recorded and compared to temporal cortex lateralization whether be the same in different gender or not. As a result of the differences in amygdala activity of different gender, N170 amplitude were compared in the T5 and T6 electrodes.

RESULTS: N170 amplitude data were detected in T5, T6 electrodes and analyzed using Mat Lab software. Student's t-test and Mann-Whitney U was used to compare data groups of different gender. When N170 amplitudes of supraliminal probe compared women's to men, women's probes values statistically more negative than men. Similarly when N170 recordings of probe compared between T6 and T5 electrodes, there was no significant amplitude differences between the genders.

CONCLUSIONS: Consistent with the literature, we found N170 recordings was higher in female volunteers response to supraliminal angry human face expressions. Several reports in the literature have shown sex differences effect N170 lateralization over the occipital/temporal electrodes, hpwever, there was no definitive information of cognitive neuroscience. We suggest that further studies with N170 recordings should be done in order to understand effects of gender difference on amygdala function.

PC156

The Effect of CDP-choline on Learning and Memory Parameters in Sleep Deprivated Rats

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AIM: The aim of our study was to investigate the effects of various doses of cytidine diphosphocholine (CDP-choline) on learning and memory in rats with REM (Rapid Eye Movement) sleep deprivation.

METHODS: The study was approved by Local Ethics Committee on Animal Experiments at Uludağ University (No:2014-01/04). Male Wistar rats (n=36; 300-350 g) were randomized to following groups:deprivation (SD) and saline injection (SD+Saline), Group 2: Sleep deprivation (SD) and 100 µmol/kg CDP-choline injection (SD+C100), Group 3: Sleep deprivation (SD) and 300 µmol/kg CDP-choline injection (SD+C300), Group 4: Sleep deprivation (SD) and 600 µmol/kg CDP-choline injection (SD+C600), Group 5: Saline injected Control Cage (CC) group (CC+saline) Group 6: 300 µmol/kg CDP-choline injected CC group (CC+C300) Sleep deprivation was ensured by leaving rats on a 6.5 cm diameter platform for 4 days according to "Flower Pot" method. Treatments were administered intraperitoneally twice on the first 4 days and once on the 5th day. Morris water maze experiments were initiated 30 min after injections. Rats were tested with regard to finding the hidden platform

on the first 4 days with twice a day training (trial phase) and time they spend in the platform quadrant on the 5th day (probe phase). Rats were then decapitated and p-CREB and CaMKII proteins were analyzed in hippocampus homogenates using Western blotting. RESULTS: Escape latency was reduced significantly in all groups through the 4th day in the trial phase. Rats in SD+Saline group were observed to spend less time in the platform quadrant in probe phase. Hippocampal levels of CaMKII and pCREB proteins were reduced in SD+Saline group while they increased significantly in SD+C600 group. CONCLUSIONS: These data show that CDP-choline at 600 µmol/kg dose can reduce the abolishment in memory performance in rats with REM sleep deprivation.

PC157

The Role of Cannabinoid Receptors on Pain Behavior-induced by REM Sleep Deprivation

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AIM: Sleep and pain are interrelated phenomena. While patients with sleep loss experience increased pain perception and lower pain threshold, painful conditions impair sleep quality and reduce sleep efficiency. In this study, we aimed to investigate the role of cannabinoid system in sleep/pain relationship by using cannabinoid WIN55 and cannabinoid receptor antagonists AM251 and SR144528 in REM deprivation model.
METHODS: Sixty balb/c mice were subjected to 72 hours REM sleep deprivation by modified flower-pot technique and were evaluated in 6 groups. Pain assessments were performed by hotplate and tailflick methods at the 0 (baseline), 72 (after sleep deprivation) and 73. (after drug administration) hours. Group 1 (control group) received i.p. vehicle (78% saline+1% Ethanol+1% Tween 80+20% DMSO). Group 2 (Cannabinoid agonist group) received i.p. cannabinoid agonist (WIN 55,212,2). Group 3 (Cannabinoid CB1 receptor antagonist + agonist group) received i.p. cannabinoid CB1 receptor antagonist (AM251) followed by WIN55 after 20 min. Group 4 (Cannabinoid CB2 receptor antagonist + agonist group) received i.p. cannabinoid CB2 receptor antagonist (SR144528) followed by WIN 55,212,2 after 20 min. Group 5 (Cannabinoid CB1 receptor antagonist group) received i.p. cannabinoid CB1 receptor antagonist (AM251). Group 6 (Cannabinoid CB2 receptor antagonist group) received i.p. cannabinoid CB2 receptor antagonist (SR144528). RESULTS: Occurrence of pain response was delayed in mice subjected to 72 hours REM sleep deprivation (P values for Group 1,2,3,4,5 and 6 were 0.009;0.028;0.009;0.014;0.594;0.009, respectively). Animals were tired and fatigued. CB1 or CB2 antagonists alone or in combination with WIN55,212,2 led to no change in pain behavior under the conditions of REM sleep deprivation.
CONCLUSIONS: We suggest that there is no relationship between cannabinoid receptor activity and REM sleep deprivation-induced pain behavior.

PC158

Electrophysiological Evaluation of the Relation Between the Levels of Body Mass Index and Apnea Hypopnea Index

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AIM: The purpose of this study was to investigate electrophysiological properties of a possible relationship between 'body mass index' (BMI) and 'apnea-hypopnea index' (AHI) and to emphasize the importance of this relation for sleep health.
METHODS: For this goal, 120 subjects, between 20 and 65 years of age, were divided to four groups according to BMI and presence or absence of sleep disordered breathing: (1) BMI=18,5-24,9 kg/m2, healthy (n=30), (2) BMI=25-29,9 kg/m2, overweight, sleep disordered brething (n=30), (3) BMI=30-39,9 kg/m2, obese, sleep disordered breathing (n=30), (4) BMI ≥40 kg/m2, morbidly obese, sleep disordered breathing (n=30). The electrophysiological properties achieved were AHI, sleep efficiency (%) and duration (in minutes) of total sleep, and of stage 1, stage 2, stage 3 of non-REM and of REM periods. While the effect of BMI values on these electrophysiological values was analyzed with ANOVA, Duncan's, Pearson.
RESULTS: While there was a highly significant positive correlation between BMI levels and AHI levels (correlation coefficient 0.470**), there was moderately significant negative correlation between BMI and sleep efficiency (correlation coefficient -0.235*) or duration of REM period (correlation coefficient -0.281**). AHI levels belonging to group 1 and 2 were statistically significantly lower than those of group 3 and 4 (p=0.000). The level of sleep efficiency was lower in group 4 in comparison to the other groups (p=0.027). The duration of stage 2 was significantly higher in group 2 and group 3 (p=0.092). The duration of stage 3 and REM period were significantly shorter in group 4 comparing with group 1 (respectively p=0.009; p=0.000).
CONCLUSIONS: This study revealed the effect of different BMI levels on the sleep electrophysiology. We showed that the subjects who had higher BMI levels might have higher AHI levels, and that changes in sleep efficiency and quality because of higher AHI levels could disturb sleep health.

PC159

The Effect of Post-Learning REM Sleep Deprivation on Hipocampal BDNF and miR-182 Expression in Mice

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AIM: Consolidation is stabilization of memories and that requires new gene expression and protein synthesis. Researches found that post-training sleep is important for memory consolidation and a specific time period of sleep is needed after learning. Studies indicates that BDNF is necessary for hippocampal-dependent lear-

ning.The effects of BDNF on protein synthesis may be regulated by specific microRNAs such as miR-182. The aim of study is to determine specific time period of sleep using a spatial memory test (Morris water maze) and to investigate the effect of SD on BDNF mRNA and miR-182 expression in hippocampus.
METHODS: 50 male BALB/c mice aged 2 month (n=10) were sleep deprived (SD) in one of the two after the last training session the mice were deprived of sleep for 3 h (SD1),in the second group after the last training session and a waiting period of 3 h the mice were deprived of sleep for 3 h (SD2) and the last group was Non-sleep deprivation (NSD) group. Quantitative RT PCR was used to measure changes in mRNA and miRNA. Repeated-measures ANOVA was used to analyze the changes in Distance Moved (DM) and Escape Latancy (EL). Probe trial, PT were analyzed using oneway ANOVA. For analyses of RNAs,the significance was determined by using ANOVA and Kruskal–Wallis H test.
RESULTS: We found that DM and EL reduced across trials in NSD and SD1 (P>0.05),but these parameters was higher in SD2 (P<0.05). In SD2, PT was found lower than SD1 and NSD (P<0.05). There was significantly increased BDNF mRNA in SD2 and decreased miR-182 in SD1(P<0.05).
CONCLUSIONS: Our findings indicate a specific 3-h period, extending from 3 to 6 h after last training,during which SD impairs spatial function. Although BDNF mRNA was upregulated by SD in hippocampus, its target miR-182 level may act as a decisive role.

PC160

Can There be a Genetic/Epigenetic Association Between Nicotine Addiction and Cognitive Processes?

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AIM: We selectively breed high and low nicotine-preferring (HINP, LOWNP) rat lines, based on free-choice oral-nicotine intake. Studying the phenotypic characteristics of these rats can elucidate genetic and neurobehavioral aspects of nicotine addiction. Male rats prefer spatial while females prefer visual cues to locate a platform in the water maze (WM); nicotine modifies this sexually dimorphic pattern in females. Our aim was to investigate if HINP and LOWNP rats, without nicotine exposure, use different strategies in the WM.
METHODS: HNP and LOWNP 15th generation and control male and female Sprague-Dawley rats (n=10 in each group) learned to locate a platform in the WM, in the same place but hidden or visible, for 12 days. On the probe trial of day 13, the visible platform was moved to another location, providing a choice between the non-existent hidden- and the visible platforms. HVS tracker and software were used to monitor latency-to-reach-the-platform (LAT), path-length and swimming-speed.
RESULTS: LAT decreased through days during both visible ($F(8,448)=163,306$;$p<0.001$) and hidden ($F(2,112)=104,663$; $p<0.001$) platform conditions (ANOVA). Additionally, there was a significant group effect (HINP-LOWNP-Control) for visible platform condition ($F(1,56)=3,355$;$p=0.042$). During probe trial, there was a group x sex interaction in time-spent-in-the-“old quadrant” ($F(2,56)=4,255$;$p=0.019$) and female control rats immediately went to the visible platform in the new location without spending any time (8/10 rats spent 0 time) in the “old quadrant” (Fisher’s Exact;$p=0.032$).
CONCLUSION: HINP and LOWNP rats in the 15th generation, unlike controls, do not show sexual dimorphism in the strategy they prefer in the WM. This finding may be the result of an epigenetic modification or may suggest a genetic association between cognitive processes and nicotine addiction.

PC161

Autonomic Reactivity Changes During Hypno-Meditation Session: An Experimental Electrophysiological Study

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AIM: A hypnotherapy or hypno-meditation session starts with hypnotic induction, which is the process conducted by a therapist to establish the state required for hypnotic trance. It is difficult to asses the subject’s degree of relaxation during hypnotic induction. The aim of the present studywas to assess the subjects hypnotic state objectively by monitoring autonomic responses using electrodermal activity (EDA).
METHODS: This experimental study was performed in the Medico-Social Center of the Sakarya University, Turkey. Study protocol was approved by the Local Ethics Committe and participants provided informed consent. Twenty-three healthy participants were enrolled. Participants with using medications, or have a chronic psychiatric illness were excluded. During the session, a standart self-hypnosis recording was played to each subject and skin conductance values at 0., 1., 5. and 10. min obtained by a biofeedback device were recorded simultaneously to evaluate autonomic responses. Skin conductance values at the first, fifth and tenth minutes were compared to basal values by using Wilcoxon Signed Ranks test.
RESULTS: Median values of skin conductivity at the beginning, first, fifth and tenth minutes were 9.5 µS (min. 3.6 µS - max. 23.0 µS), 8.8 µS (min. 3.0 µS - max. 19.3 µS), 5.6 µS (min. 2.2 µS - max. 12.6 µS) and 4.7 µS (min. 2.2 µS - max. 10.2 µS), respectively. p values indicated significant differences for all 3 comparisons ($p<0.001$).
CONCLUSIONS: Our data indicated a significant decrease in terms of skin conductance values during hypnotic induction process consistent with the duration of sessions. There are several tests which were used to infer the depth of hypnotic trance (1, 2). Also there are tests for evaluating hypnotic susceptibility (3). Analyzing the possible correlation between skin conductance values and results of these tests may be the focus of future studies.

PC162

Effects of Diabetes on Brainstem Auditory Evoked Potentials

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AIM: One of the long-term complications of Diabetes Mellitus (DM) associated with high blood glucose levels is hearing loss. Blood glucose level over 300 mg/dl in rats is defined as diabetes. In our study, the changes in the brainstem auditory evoked potentials (BAEP) were investigated in rats with diabetes and also in rats with high glucose levels.
METHODS: In this study, three month old female rats weighing 135-210 g were used. While control group applied with saline intraperitonelly, the other rats were administered with single dose (60 mg/kg) of streptozotocin to create DM. The fasting blood glucose levels were measured three months after injection. High Blood Glucose group (HBG) was accepted between 100 and 300 mg/dL. Rats with blood glucose level over 300 mg/dL were adopted as diabetes group. Fasting blood glucose levels were measured again at the end of 4th month, and 60 and 70 dB SPL in 8 and 16 kHz frequencies BAEP records were taken under anesthesia in testing room without noise.
RESULTS: Increased in hearing threshold due to rising of blood glucose level was observed. In HBG and DM groups, prolonged BAEP latency was observed at 8 kHz, 60 dB and 16 kHz 70 dB compared to control group. No significant difference was observed for interpeak latencies between groups.
CONCLUSIONS: Our data showed that keeping control of blood glucose levels in diabetic patients is important for hearing.
This study was supported by Akdeniz University Scientific Research Projects Coordination Unit (Project number: 474).

PC163

Effects of Ingested Sulfite on Auditory Evoked Brainstem Response

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AIM: Sulfite compounds (sodium metabisulfite, potassium metabisulfite, sodium bisulfite, potassium sulfate, sodium sulfite, etc.) are widely used in food, beverage and pharmaceutical industries. In consequence of the expansion of frozen and fast food consumption, sulfit exposure has increased in recent years. Because of the differences in people's eating habits, each individual takes sulfit orally at varying concentrations. In our study, effects of different doses sulfite (100 mg/kg and 260 mg/kg) on the Brainstem Auditory Evoked Potentials (BAEP) have been investigated.
METHODS: In our study, 40 adult male Wistar rats were randomly divided into three groups. One of these is control (K) which were given distilled water via gavage for 35 days, the other two groups are sulfite 1 (S1) and sulfite 2 (S2) which were given sodiummetabisulfite (100 mg/kg/day) and (260 mg/kg/day) in the same way. At the 36th day, all rats were anaesthetized with ketamine (50 mg / kg)-xylazine (6 mg/kg) and BAEP was recorded in acoustically isolated room.
RESULTS: Depending on the dose administered, latencies of all waveforms in the sulfit groups were extended compared with the control group at 8 kHz and 16 kHz. Interpeak latencies were also evaluated, but there was no significant difference between groups. Moreover, increments were found on the threshold of hearing due to increase in sulfit doses.
CONCLUSIONS: It has been shown that increments on the dose of sodium metabisulfite cause to increase of the hearing threshold and prolonged latencies of all waves.
This study was supported by Akdeniz University Scientific Research Projects Coordination Unit.

PC164

Verdi A (432 Hz) versus Standard A (440 Hz) in Music-related Electrical Activity of Brain: An EEG Analysis of Sultaniyegâh Ağır Semâi Composed by Hammamizâde İsmail Dede Efendi

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AIM: A debate has been continuing on the pitch value of musical note A, while some music authorities advocate so-called Verdi A of 432 Hertz (Hz), some others say that the standard pitch of 440 Hz for A should be maintained. As music appreciation is a function of brain, brain electrical activity as an aspect of brain function was planned to be studied. In this study, we compared the effects of these two pitch values on electrical activity of brain.
METHODS: Ten healthy young adult volunteers (Male/Female, 5/5; mean age, 19.4±0.8 year) included to the study. Two versions (A=432 Hz vs A=440 Hz) of Sultaniyegâh Ağır Semâi by Dede Efendi were used for music session. The study was performed in double-blind, cross-over design. After a standard audiologic evalution, each participant was taken into a sound-proof room and basal 4-channel EEG (F7, Fp1, Fp2, F8) was recorded for 1 minute by using a portable EEG device followed by music exposure (432 Hz or 440 Hz). Post-music EEG was recorded for 1 minute. In the following day, the same participant was taken into laboratory again and this time EEG recordings were taken by using other version of music. Percent change of frequency bands alpha, beta, delta, gamma, and theta under the influence of Sultaniyegâh Ağır Semâi compared between 440 Hz versus 432 Hz by non-parametric Wilcoxon test.
RESULTS: We failed to find any significant difference between two versions of recorded music. Although this study was limited in number of participants, two different music scales (Verdi A versus Standard A) were compared for the first time by using EEG recording.
CONCLUSIONS: We suggest that only 8 Hz difference in musical scale may not lead to significant difference in electrical activity of human brain.

PC165

Investigation of Sleep Quality and Sleep Disorders in the Secondary Teaching Students

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AIM: This study was to investigate the quality of sleep and sleep disorders and the factors affecting the quality of sleep in secondary education students different Faculty of the Süleyman Demirel University (SDU).
METHODS: In this cross-sectional study, which has created different classes of faculty in the secondary education (n = 205). Thirty two socio-demographic closed and open-ended questions, Pittsburgh sleep quality index (PSQI) questionnaire was administered under observation in the students. The data were evaluated of descriptive statistics, chi-square, independent t test, Pearson correlation and ANOVA.
RESULTS: In the study, 205 students were 77(38%) male and 128(62%) female, mean age 20.7+2.52, Body mass index (BMI) was 22.27+ 4.33.. Students 33(9.8%)Engineering, 58(17.2%)Arts and Sciences, 49(14.5%)Economics and Administrative Sciences and 65(19.3%) the Health Sciences. The average sleep latency of students 27.64±23.92 min, average night sleep 7.71±1.59 h, the average sleep time 10.36+2.06 h, PSQI scores were found to be 9.60+4.41. Students have 20(5.9%) accompanied by a chronic disease and there are drugs in use because of illness, 61(18.1%) students were smokers. PSQI average were significantly in terms of gende ($p<0.001$) and is lower in the men. PSQI scores difference between no smokers and lack of 1 pack for day, and it was higher in the smokers. PSQI scores were found higher statistically significant take caffein daily ($p=0.002$). PSQI scores were found statistically significant between no napping and sometimes napping ($p=0.003$) and often ($p = 0.001$) and it was increasing respectively. There was a significant difference between the PSQI scores and are not satisfied with the school's life ($p=0.001$) and it was lower in the satisfied students.
CONCLUSIONS: Sleep disorders were identified in the secondary education students participated in our research. Sex, smoking, caffeine use, chronic diseases and satisfied with the school's life might affect the quality of sleep.

PC166

The Evaluation of Complete Blood Count in the Patients of Laryngeal Carcinoma

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AIM: Laryngeal carcinoma is one of the common head and neck malignancy, its incidence increases with increasing age. Laryngeal carsinoma is usually asymptomatic, which leads to late diagnosis and poor prognosis. In this study,complete blood count of the patient and control groups were evaluated to investigate the possible relationship with tumor stages.
METHODS: This study data were obtained retrospectively from 89 patients' presurgical complete blood count data who had an operation because of laryngeal tumor between 2013-2016 in Atatürk University Hospital 's Otorhinolaryngology Department. In this study, data from Atatürk University Faculty of Medicine, ENT clinic, which operated for a total of 89 people laryngeal mass between the years 2013-2016 were obtained from retrospective preoperative blood count results. The patient group included 57 laryngeal carcinoma patients. The control group included 20 polyp patients and 12 nodul patients. Patient group was divided into four groups according to T staging. The levels of neutrophil-lymphocyte ratio (NLR), white blood cell (WBC), red blood cell distribution width (RDW), platelet (PLT), mean platelet volume (MPV) were compared between groups.
RESULTS: In this study, the levels of NLR and RDW in patient groups were significantly higher than the control group ($p<0.001$). No significant difference was determined in the comparison of patient and healthy groups in terms of WBC, PLT, MPV levels ($p>0.0.05$). According to T staging, the levels of NLR in the patients of T3 and T4 groups were significantly higher than in the T1 patient group ($p<0.05$).
CONCLUSIONS: The levels of NLR and RDW in patient group were significantly higher than the control group. This suggests that the values of NLR and RDW may be cheap and easily accessible biomarkers in the diagnosis and staging of laryngeal carcinoma. However, further more detailed studies with larger groups are needed.

PC167

Liver Enzymes and Ca/P Status in Rats Receiving Repeated Low-grade Bacterial Challenges Early in Life and Fed Long-term High-fat Diet

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AIM: High energy diets and bacterial infections early in life might cause permanent reorganization of the metabolism including the liver enzymes. Therefore, the aim of the current study was to investigate the effects of repeated bacterial challenges during postnatal period on liver enzymes and calcium/phosphorus status in rats under long-term high-fat diets.
METHODS: Rat pups (female, n=32; male, n=32) were injected (i.p.) either 15 µg/kg *Escherichia coli* cell wall constituent (lipopolysaccharide, LPS) or saline in the postnatal days 7, 9, 11, 13, 15, 17 and 19. Following weaning (pnd 21), they were divided into two subgroups and were either offered standard chow or high fat diet until day 150. Blood samples were analyzed for AST, ALP, ALT, Ca and P. Data were analyzed by General Linearized Models (GLM) and an alpha level of $p<0.05$ was accepted as significant.
RESULTS: Serum ALT and ALP were higher in males and in high-fat diet groups ($p<0.01$) but serum AST levels did not differ ($p>0.05$). Serum P was higher in males ($p<0.05$), but serum Ca levels did not differ ($p>0.05$).
CONCLUSIONS: Results show that both the diet and the gender affect liver enzymes and this suggests that the liver might react to high-fat diet in a sexually dimorphic way. Male and female rats Ca/P levels may be held regardless of the amount of fat in the diet.
This study was supported by TÜBİTAK (Project # 111S440), Turkey.

PC168

Viral Mimetic Polyinosinic: Polycytidilic Acid Administration Affects Body Temperature in a Dose-Dependent Manner

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AIM: Viral infections are widespread throughout the World and their treatment is difficult. Experimental studies in laboratory animals are required to find out the effects viruses but studying with live viruses possesses great dangers as they might cause uncontrolled spread of infections. Use of viral mimetics, in that respect, exists as an obligatory alternative. For that purpose, synthetic double strand RNA, namely polyinosinic:polycytidilic acid (or poly i:c) is commonly used as a viral mimetic. In the literature, there are studies dealing with the effects of poly i:c at various physiological stages. However, the effects of varying doses of poly i:c on body temperature, which is the main consequences viral infections, is not investigated for the doses commonly used in the literature (i.e. 5 to 10 mg/kg). Therefore, our aim was to test the doses used in the literature on the body temperature of female rats.
METHODS: Our experimental study was conducted on 20 female Sprague-Dawley rats, aged 6 months and weighing 250-300 g. Rats were injected (i.p.) with 0, 1, 5 or 10 mg/kg poly i:c and their rectal temperatures were followed hourly for 6 h and at 24th and 48th h. Statistical analyses were carried out by using MINITAB statistical program. One-way ANOVA was used to compare the groups; paired t-test was used to compare repeated measurements. $P<0.05$ was accepted as statistically significant.
RESULTS: Body temperatures were higher than control levels at 5th and 6th hour post-injection only in 5 and 10 mg/kg groups.
CONCLUSIONS: In conclusion, only higher doses of poly i:c was able to increase body temperature compared to control group and this needs to be taken into account in designing new studies.

PC169

Can Galectin-3 Serum Levels be Used as a Biomarker for the Diagnosis of Psoriatic Arthritis?

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AIM: Galectins are a group of lectins that have many roles in various disease conditions including inflammation and autoimmune diseases. Galectin-3 was implicated as a mediator of inflammation and associated with arthritis and rheumatoid arthritis (RA) by activating synovial fibroblasts. It may be used as a novel biomarker in RA. Hepcidin is a key hormone controlling iron homeostasis and a mediator of inflammation-induced anemia, and its prohormone is called pro-hepcidin. Psoriatic arthritis (PsA) is a chronic inflammatory joint disease associated with psoriasis. To our knowledge, the serum galectin-3 levels were analysed for the first time in patients with PsA to determine their role as novel biomarker in these patients. Prohepcidin is analysed due to its role in inflammatory diseseas.
METHODS: Forty three patients diagnosed as PsA (14 males/29 females, mean age 48.1) according to CASPAR classification criteria and 42 age and sex-matched healthy volunteers were included in the study. The serum galectin-3 and pro-hepcidin levels were measured by commercially available ELISA kits. Their relationship with clinical and laboratory parameters, including CRP (C-reactive protein) and ESR (Erythrocyte sedimentation rate), were assessed.
RESULTS: The PsA patients had significantly raised mean serum galectin-3 level ($P = 0.006$) when compared to the healthy group. However, the correlation between serum galectin-3 levels and diseases activity indices was not statistically significant. The mean serum level of pro-hepcidin was similar between the PsA patients and healthy group ($P = 0.310$). There was a positive correlation among serum pro-hepcidin levels and pain ($P = 0.046$) and nail involvement ($P = 0. 013$).
CONCLUSIONS: The mean serum galectin-3 level was elevated in PsA patients compared to controls, indicating that galectin-3 may represent a novel diagnostic biomarker in PsA patients. Pro-hepcidin levels were similar but there was a positive correlation between pro-hepcidin levels and pain and nail involvement.

PC170

A Survey of Undergraduate Physiology/Oral Physiology Education in Dental Faculties

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AIM: The purpose of this study was to evaulate physiology/oral physiology education in Dental Faculties in Turkey (1).
METHODS: The survey included thirty-six questions and it was posted on “Google Forms” and shared via social networks (facebook etc.). Collected data were evaulated by Excel 2016 and SPSS v.22.
RESULTS: Five hundred fifteen students responded to the survey. Overall, median age of participants is 21.8±2.4 and 60.2 % of them are women. Most of the students are currently studying in governmental universities (92 %) and receive education in Turkish. They generally (71.8 %) tend to apply for National Dental Speciality Examination. Weekly 2.8±1.2 credit hours are given in the physiology courses, usually by lecturers of the physiology department (83.6 %). Only 32.2 % of participants have oral physiology courses and 87.7 % of them do not have a physiology laboratory in their faculties. Opposing to oral physiology, even 84.7 % have a physiology laboratory, while the courses generally are not integrated with practical studies (47.7 %). According to students, physiology (29.3 %) and oral physiology (26 %) courses are invaluable for dental education and are not beneficial (26 % physiology, 32.5 % oral physiology) for succeeding in National Dental Speciality Exam. Approximately, half of the participants (52.5 %) do not have an information about PhD degree in physiology and are mostly not interested in getting a PhD in Physiology (73.1 %).
CONCLUSIONS: Physiology instruction varies among different faculties. Based on the platform of the Turkish Society for Physiological Sciences, it is recommended to organize collaborative studies to establish a core physiology programme suitable for Dental Faculties.

PC171

Examination of Physiology Course Laboratory Curriculum by Q Method

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AIM: Q-sort technique is a method used to measure thoughts and behavior of individuals. In our study, we aimed to investigate thoughts of students about the physiology laboratory curriculum.
METHODS: The research was conducted on 153 medical school students that completed of the physiology laboratory practice a year ago. During physiology laboratory practice of students 41 questions generated from verbal expression was collected in 4 groups (A,B,C,D group). These questions were placed on prepared paper up to 10 to 1 score. Than, the same students were performed with face to face interview technique.
RESULTS: The item mean score of A group (10 question) was 4.59±1.02. The lowest average in A group was "laboratory course is unnecessary" and the highest average was " after laboratories required reports are unnecessary". The item mean score of B group (12 question) was 5.19±0.79. "I think the course is a complete waste of time" was the lowest average item and "much practice so well in the laboratory course" was the highest average item in B group. The item mean score of C group (8 question) was 6.98±1.41. The lowest average item in C group "When I read the lecture notes I can learn", the highest average item was "I can learn visually". The item mean score of D group (11 question) was 5.44±0.97. The lowest average item in D group "I think laboratory course does not contribute to medical education" and the highest average item was "To practice in the laboratory and evaluate the results is very important for clinical training" according to our results.
CONCLUSIONS: Q methodology can be an effective method in the development of physiology course laboratory curriculum.

PC172

Smoking and Alcohol Consumption of Medical Students

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AIM: It was aimed to determine smoking and alcohol consumption habits of medical students.
METHODS: This cross-sectional and descriptive study was applied to medical students of Mustafa Kemal University (MKU). Based on voluntariness, a questionnaire was applied to determine students' ideas about medical education and their objectives for the future. In questionnaire, quetions about whether student smokes or does not smoke; if he/she (smokes), how is his/her situation of starting to smoke in medical faculty; situation of alcohol consumption and situation of starting to alcohol consumption in medical faculty were asked to students. All of medical students were determined as a sample size (n= 956). Questionnaire was applied to 644 students who agreed to work. 600 student were assessed after incompleted questionnaires were selected. The analyses were performed using GraphPadPrism V.5. The data were analyzed by chi-square test for correlation between categorical variables. Statistical significance was considered to be $p<0.05$.
RESULTS: We found that smoking of medical students increased significantly from first period (20.61%) to 6th period (52.24 %, p = 0.0001). Additionally alcohol consumption increased significantly from first period (24.85 %) to 6th period (56.72 %, p=0.0001). Besides the percentage of students who started to smoke in medical faculty (57.70 %) was higher than the percentage of students who started to smoke before starting to medical faculty. However, the percentage of students who started to alcohol drinking in medical faculty (34.7 %) was fewer than the percentage of students who started to alcohol drinking before starting to medical faculty.
CONCLUSIONS: According to the results, we found that smoking and alcohol consumption increased significantly in students of medical faculty. We suggest that taking the necessary measures for decreasing the smoking and alcohol consumption affecting health of our students who will be future doctors would be more beneficial in terms of medical education.

PC173

An Investigation of the Correlation Between Age, Obesity and Chronic Disease in Afyon Province Number 5 Family Healthcare Center Patient Profile Women Aged 20-40 Years

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AIM: Obesity is defined as excessive amount of fat accumulation in the body. What makes obesity significant is that it causes or intensifies the effect of many diseases by itself or by conjunction of other chronic diseases. Particularly, type-two diabetes, coronary heart disease, hypertension, and obstructive sleep apnea are known diseases that are associated with obesity. This study's objective was to investigate the correlation between chronic diseases and obesity, especially among aged women.
METHODS: 87 female patients that were aged between 20 and 40 were selected among Afyon Providence #5 Health Center's already monitored patients. Patients' age, weight, height, body mass index (BMI), waist and hip circumferences, and their chronic disease history were taken into evaluation as well. The simple method of obesity diagnosis consist of calculation of (BMI). A value of 30kg/m2 or greater is considered obesity. The statistical analysis of this study has been executed by using SPSS 22.00 program. T-test and chi-square test was used with the data analysis of independent groups. In a group, the analysis of direction and intensity of the variables, as well as the relations of variables between each other was completed by using Pearson Correlation Analysis. The analysis of averages between the groups, to determine whether there was any

statistically significant difference exist among them, was acquired by using One-Way ANOVA. Statistical significance value was set as p<0,05.
RESULTS: Compatible with the literature, weight, BMI, hip and waist circumference increase significantly as age grows. Mean age of women differentiates significantly as per the number of chronic diseases (F: 5,371, p:0,006). The BMI values of women with two or more chronic diseases were significantly greater than that of women with one chronic disease (F:6,792, p:0,002).
CONCLUSIONS: People should be made aware of the reasons of obesity and its relation with other chronic diseases. In particular, family health centers should provide services for the prevention of obesity. Therefore, it is essential for these services to become public health policy.

PC174

Effect of Cigarette Smoking on Body Composition in Current Smokers

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AIM: Smoking is a major risk factor for devastating cardiovascular disease together with a higher risk of insulin resistance and hyperinsulinemia. There is controversy in the literature explaining the relationship between smoking and obesity indices, especially in terms of body composition. Some report that smoking cause decreased appetite and increase energy expenditure; whereas others propose that it may increase propensity to abdominal obesity. We aimed to investigate effects of cigarette consumption quantity on body composition among current smokers.
METHODS: After obtaining ethical approval currently cigarette smoking 47 male volunteers were enrolled into the study. Participants had no known diseases, sedentary, and having non-restricted mixed diet. They were grouped according to the pack-year of cigarettes (=number of packs of cigarettes smoked per day x the number of years of smoking) they smoke [<10 (Group 1, n:11, age: 26.0±4,9), 10-20 (Group 2, n:14, age: 33.66±8.1), 20-40 (Group 3, n:14, age: 45.14±9.6), and >40 (Group 4, n:8, age: 49.83±6.7)]. Compartmental body composition was determined using Body Impedance Analyzer (TANITA BC418). For statistical analysis Kruskal Wallis and Spearman Correlation tests were used.
RESULTS: Group 4 had significantly bigger waist circumference than Group 1 and Group 2 (both p<0.05; means: 81.91±3.06, 85.33±2.4, 88.19±3.78, 96.33±2.5,respectively). Also the waist-hip ratio in Group 4 was higher than Group 1 (0.94±0.01 and 0.85±0.014; p<0.05). Internal fat amount was higher in Group 4 than Groups 1 and 2 (both p<0.05) and in Group 3 than Group 1 (p<0.05) (means: 3.91±0.74, 5.2±0.78, 8.21±1.23, 9.83±0.95,respectively). Both Groups 1 and 2 had lower metabolic age than both Groups 3 and 4 (p<0.05 for all). Waist-hip ratio, fat mass, visceral fat amount, body mass index, and metabolic age were found positively related to the amount of cigarettes smoked (all p<0,05).
CONCLUSIONS: Smoking is known to decrease appetite and many smokers retrain from quitting as they do not want to gain weight. However our results show that chronic heavy smoking seems related to higher risk of obesity. Also the relation observed between heavy smoking and visceral fat amount indicates an especially higher risk for metabolic syndrome.